CHAPTER IV

RESULTS

Effects of Intravenous Sodium Metavanadate Infusion on General Circulations.

The results of changes in general circulations in dogs given intravenous sodium metavanadate infusion without pretreatment of various drugs (group I) and with pretreatment of intrarenal arterial infusion with prazosin (group II), atenolol (group III), acetylcholine (group V), verapamil (group VI), and intravenous injection with MK422 (group IV) are summerized in Table 1 and Figure 1.

Group I : Animals Pretreated With Isotonic Normal Saline Solution Before Sodium Metavanadate Infusion.

The intrarenal arterial infusion of saline caused no changes in any of the measurements made. The intravenous sodium metavanadate infusion produced a profound hypertension with significant increase in mean arterial blood pressure (MAP) from the control value of 109±4 to 141±4 mmHg ($P<0.05$), but heart rate (HR) significantly decreased from the control value of 146±2 to 129±2 beats/min ($P<0.05$). Packed cell volume (PCV) slightly increased throughout the experimental period without statistical significance. Stopping the sodium metavanadate infusion, the measurements made returned reversible to basal values immediately. Mean arterial blood pressure significantly remained lower than the experimental value of 141±4 to 121±4 mmHg ($P<0.001$). Heart rate was persistantly lower than the control value and unchanged from the sodium metavanadate infusion value without statistical significane. There was also no significant change in packed cell volume.

Group II : **Animals Pretreated With Prazosin (Pra) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of prazosin alone produced a significant fall in mean arterial blood pressure to 13.74±3.84 % of the control value ($P<0.05$). No significant change in heart rate and packed cell volume were observed. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of prazosin did not change in mean arterial blood pressure from the control value, while it significantly rose up from the given prazosin alone value 100±6 to 111±7 mmHg ($P<0.05$). Heart rate insignificantly fell either from the control value or from the given prazosin alone value. Packed cell volume significantly raised in from the control value of 32±1 to 37±1 % ($P<0.05$) without a significant from the given prazosin alone value. These indicated that prazosin effectively prevented the response elicited by sodium metavanadate. Stopping infusion of prazosin and sodium metavanadate caused no alteration in any of the measurements made.

Group III : **Animals Pretreated With Atenolol (AT) Before Sodium Metavanadate Infusion**

Intrarenal infusion of atenolol alone induced a small but significant depression in mean arterial blood pressure to 1.83±0.59 % of the control value ($P<0.05$) and heart rate to 15.57±1.71 % of the control value ($P<0.01$). No significant change in packed cell volume was observed. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of atenolol led to a significant raise in mean arterial blood pressure to 11.55±2.75 % of the control value ($P<0.05$) and from the given atenolol alone value of 108±3 to 122±3 mmHg ($P<0.05$), but heart rate significantly futher fell to 24.96±3.79 % of the control value ($P<0.01$) and from the given atenolol

alone value of 103±3 to 91±5 beats/min (P<0.05). Packed cell volume insignificantly slightly elevated throughout the experimental period. Stopping infusion of atenolol and sodium metavanadate resulted in a significant still depression in heart rate to 25.11±4.79 % of the control value (P<0.01) without a significant change from the experimental period value. Mean arterial blood pressure restored toward the basal value immediately with a significant reduced from the experimental period value of 122±3 to 109±2 mmHg (P<0.001). Packed cell volume remained unchanged.

Group IV : **Animals Pretreated With Enalapril Maleate (MK 422) Before Sodium Metavanadate Infusion.**

Single dose intravenous injection of MK422 alone caused a significant marked decrease in mean arterial blood pressure to 18.45±1.01% of the control value (P<0.001) and heart rate to 10.27±1.90 % of the control value (P<0.05). No significant change in packed cell volume was observed. When intravenous infusion of sodium metavanadate produced a significant elevation in mean arterial blood pressure to 9.52±2.94 % of the control value (P<0.05) and from the given MK422 alone value of 80±1 to 107±3 mmHg (P<0.001) and in packed cell volume either from the control value of 31±1 or the given MK422 alone value of 32±2 to 36±2 % (P<0.05). Heart rate significantly further depressed to 17.09±1.61 % of the control value (P<0.01) and from the given MK422 alone value of 139±4 to128±2 beats/min (P<0.05). Stopping infusion of sodium metavanadate induced a significant rise in packed cell volume from the control value of 31±1 with a significantly fall from the experimental period value of 36±2 to 35±2 % (P<0.05). Heart rate restored to the basal value immediately and significantly rose up from the experimental period value of 128±2 to145±3 beats/min (P<0.01). There was also no significant alteration in mean arterial blood pressure during the recovery period.

Group V : **Animals Pretreated With Acetylcholine (ACh) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of acetylcholine led to a significant depression in mean arterial blood pressure to 10.31±2.32 % of the control value ($P<0.05$) and heart rate to 4.60±0.78 % of the control value ($P<0.01$). There was no significant change in packed cell volume. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of acetylcholine resulted in a significant increase in mean arterial blood pressure to 14.56±2.68 % of the control value ($P<0.01$) and the given acetylcholine alone value of 96±3 to 123±3 mmHg ($P<0.01$) and in packed cell volume either from the control value of 34±1 or the given acetylcholine alone value of 35±1 to 39±1 % ($P<0.05$). Heart rate significantly futher decreased to 19.56±0.97 % of the control value ($P<0.001$) and the given acetylcholine alone value of 133±1 to 113±2 beats/min ($P<0.001$). Stopping infusion of acetylcholine and sodium metavanadate caused a significant raise in mean arterial blood pressure to 9.24±1.53 % of the control value ($P<0.01$) and in packed cell volume from the control value of 34±1 to 37±2 % ($P<0.05$), however, they were also no significant difference from the experimental period value. Heart rate significantly fell to 14.77±2.30 % of the control value ($P<0.01$) without a significant change from the experimental period value.

Group VI : **Animals Pretreated With Verapamil (Ver) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of verapamil alone produced a small but significant reduction in mean arterial blood pressure to 4.42±1.18 % of the control value ($P<0.05$) and heart rate to 5.74±1.66 % of the control value ($P<0.05$). There was no significant change in packed cell volume. When intravenous infusion of sodium metavanadate and

sustaining intrarenal infusion of verapamil did not change in mean arterial blood pressure neither from the control value nor from the given verapamil alone value. Heart rate, although it did not different from the control value, significantly increased from the given verapamil alone value of 136±4 to 141±3 beats/min ($P<0.05$). Packed cell volume slightly increased throughout the experimental period without statistical significance. These indicated that verapamil effectively prevented the response elicited by sodium metavanadate. Stopping infusion of verapamil and sodium metavanadate induced a significant decrease in mean arterial blood pressure to 11.25±3.68 % of the control value ($P<0.05$) without a significant change from the experimental period value. No significant change in heart rate and packed cell volume were observed.

In comparison, the intrarenal infusion of prazosin (group II), acetylcholine (group V) and verapamil (group VI) and intravenous injection of MK422 (group IV) led to a significant fall in mean arterial blood pressure as comparable to intrarenal infusion of saline (group I) at the same time interval ($P<0.05$) and without a significant reduction in intrarenal infusion of atenolol (group III) (Figure 1, upper panel). Heart rate was significantly lower than group I in group III ($P<0.001$), group IV ($P<0.01$), group V ($P<0.01$), and group VI ($P<0.01$), but it insignificantly raised in group II (Figure 1, lower panel). Packed cell volume caused unchanged in all groups.

The intravenous infusion of sodium metavanadate produced a marked hypertension which significantly marked elevated in mean arterial blood pressure and significantly depressed in heart rate, on the other hand, vanadate appeared to directly affect the increase of systemic vascular resistance and the decrease of cardiac output, these effects which were totally blocked by verapamil and patially by prazosin.

As comparable to the responses elicited by sodium metavanadate alone (group I) at the same time interval, mean arterial blood pressure was lower significantly when intravenous sodium metavanadate infusion in the presence of prazosin (group II) ($P<0.01$) and verapamil (group VI) ($P<0.01$). Mean arterial blood pressure significantly elevated from the control value of each group as group I, still it was significantly lower than group I in the animals response to sodium metavanadate in the presence of atenolol (group III) ($P<0.05$) and pretreatment of MK422 (group IV) ($P<0.05$) but insignificantly in animals response to sodium metavanadate in the presence of acetylcholine (group V) (Figure 1, upper panel). Heart rate was significantly higher than group I in group VI ($P<0.05$) without a significant in group II, however, it was significantly lower than group I in group III ($P<0.05$) and group V ($P<0.05$) without a significant in group IV (Figure 1, lower panel). No change in packed cell volume was observed during the experiment period of all groups.

Withdrawal of sodium metavanadate and various drugs restored mean arterial blood pressure and heart rate toward basal control value. Mean arterial blood pressure was significantly lower than group I in group II ($P<0.05$) and group VI ($P<0.05$) and heart rate was significantly lower than group I in group III ($P<0.05$). Packed cell volume did not different throughout the recovery period value in all groups.

Table 1. Changes in mean arterial blood pressure, heart rate, and packed cell volume in response to intravenous sodium metavanadate infusion in six groups.

Parameter	MAP (mmHg)		HR (beats/min)		PCV (%)	
Group I (n=5)						
Control	109 ± 4		146 ± 2		30 ± 1	
NSS(IR)	112 ± 4		147 ± 3		29 ± 1	
NSS(IR)+$NaVO_3$(IV)	141 ± 4	* $	129 ± 2	* $	33 ± 2	
Recovery	121 ± 4	$$$	134 ± 5		31 ± 3	
Group II (n=5)						
Control	116 ± 4		125 ± 5		32 ± 2	
Pra(IR)	100 ± 6	*	135 ± 8		30 ± 2	
Pra(IR)+$NaVO_3$(IV)	111 ± 7	$	111 ± 7		37 ± 1	*
Recovery	104 ± 9		136 ± 8		36 ± 2	
Group III (n=5)						
Control	110 ± 3		121 ± 2		35 ± 1	
AT(IR)	108 ± 3	*	103 ± 3	**	35 ± 1	
AT(IR)+$NaVO_3$(IV)	122 ± 3	* $	91 ± 5	** $	37 ± 1	
Recovery	109 ± 2	$$$	91 ± 6	**	36 ± 2	
Group IV (n=5)						
Control	98 ± 2		155 ± 2		31 ± 1	
MK422(v)	80 ± 1	***	139 ± 4	*	32 ± 2	
MK422(V)+$NaVO_3$(IV)	107 ± 3	* $$$	128 ± 2	** $	36 ± 2	* $$$
Recovery	99 ± 3		145 ± 3	$$	35 ± 2	* $
Group V (n=5)						
Control	107 ± 2		140 ± 2		34 ± 1	
ACh(IR)	96 ± 3	*	133 ± 1	**	35 ± 1	
ACh(IR)+$NaVO_3$(IV)	123 ± 3	** $$	113 ± 2	*** $$$	39 ± 1	*** $
Recovery	117 ± 2	**	119 ± 3	**	37 ± 2	*
Group VI (n=5)						
Control	106 ± 4		145 ± 2		37 ± 1	
Ver(IR)	101 ± 4	*	136 ± 4	*	38 ± 2	
Ver(IR)+$NaVO_3$(IV)	98 ± 5		141 ± 3	$	42 ± 4	
Recovery	93 ± 4	*	138 ± 5		40 ± 4	

Values are means±SEM. Abbreviations : $NaVO_3$, sodium metavanadate; Pra, prazosin; AT, atenolol; MK 422, enalapril maleate; ACh, acetylcholine; Ver, verapamil; IR, intrarenal arterial infusion; IV, intravenous infusion; v, intravenous injection; MAP, mean arterial blood pressure; HR, heart rate; PCV, packed cell volume.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$, different from previous values.

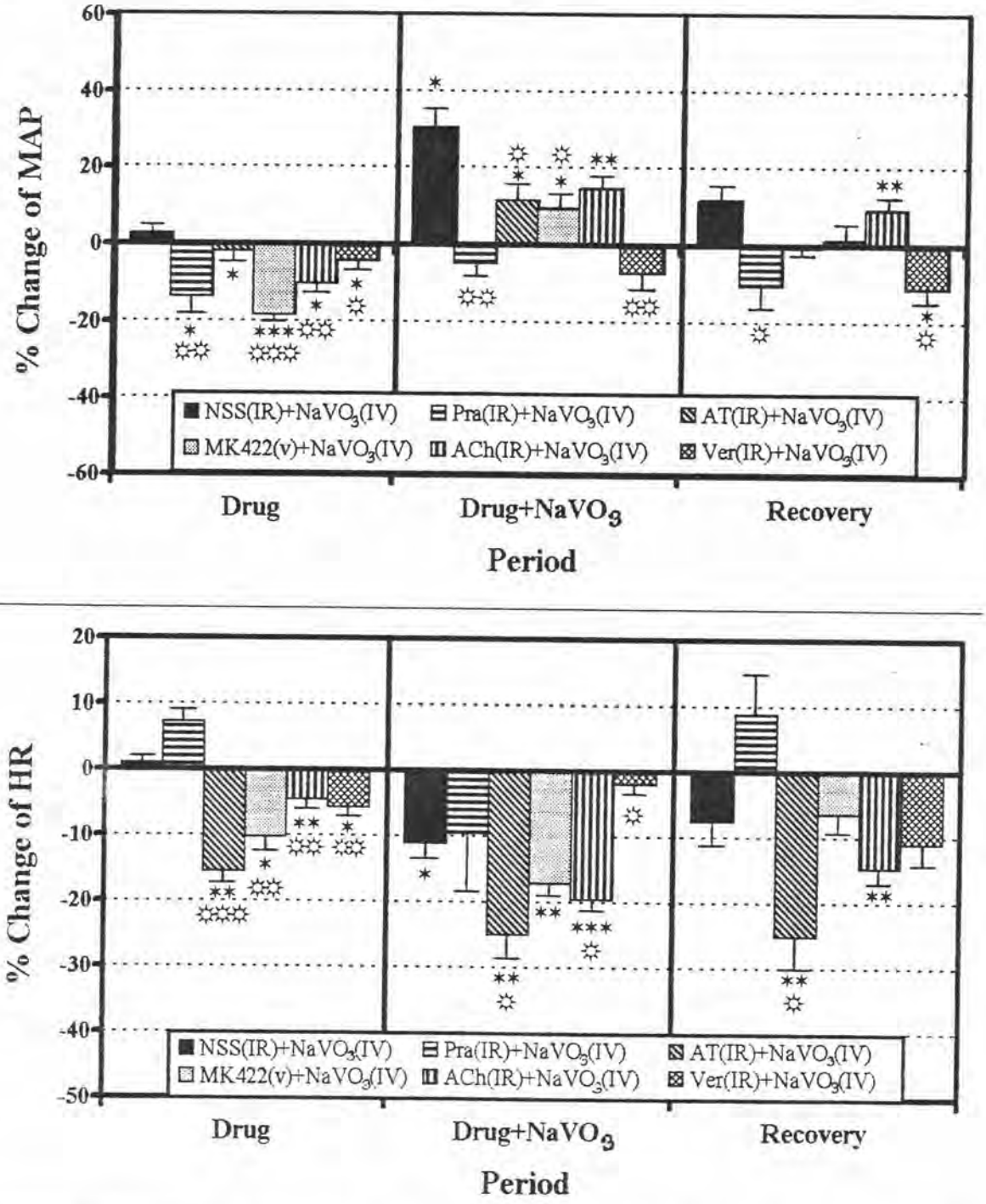


Figure 1 Percetage changes in mean arterial blood pressure (MAP) and heart rate (HR) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).

Significant difference values using paired t'test are indicated by * P<005, **P<0.01, ***P<0.001 compaired to the control value of each group.

Significant difference values using unpaired t'test are indicated by ☼ P<005, ☼☼P<0.01, ☼☼☼P<0.001 compaired to group I at the time interval.

Effects of Intravenous Sodium Metavanadate Infusion on Renal Hemodynamics.

The results of changes in renal hemodynamics in dogs given intravenous sodium metavanadate infusion without pretreatment of various drugs (group I) and pretreatment of intrarenal arterial infusion with prazosin (group II), atenolol (group III), acetylcholine (group V), verapamil (group VI), and intravenous injection with MK422 (group IV) are summerized in Table 2 and Figure 2-4 .

Group I : **Animals Pretreated With Isotonic Normal Saline Solution Before Sodium Metavanadate Infusion.**

After intrarenal arterial saline infusion caused no change in any of the measurements made. The intravenous sodium metavanadate infusion produced a marked predominant efferent arteriolar vasoconstriction than afferent arteriole with significant marked increase in renal vascular resistance (RVR) to 84.77±8.10 % of the control value ($P<0.001$) whereas filtration fraction (FF) insignificantly increased to 12.27±5.86 % of the control value. There was also a significant marked decrease in effective renal plasma flow (ERPF) to 32.85±2.13 % of the control value ($P<0.001$), effective renal blood flow (ERBF) to 29.22±2.55 % of the control value ($P<0.001$), and glomerular filtration rate (GFR) to 25.17±2.15 % of the control value ($P<0.001$), which resulted in a significant decrease in urine flow rate (V) to 44.02±2.48 % of the control value ($P<0.001$). Stopping the sodium metavanadate infusion, urine flow rate returned to basal control value and significantly elevated from the given sodium metavanadate infusion period value ($P<0.05$). Glomerular filtration rate significantly persistently decreased from the control value ($P<0.001$) without a significant increase from the experimental period value. Effective renal plasma flow and effective renal blood flow significantly fell from the control value ($P<0.01$) but they significantly raised from

the experimental period value ($P<0.01$). Renal vascular resistance significantly progressively elevated from the control value ($P<0.01$) with a significant depression from the experimental period value ($P<0.01$). Filtration fraction insignificantly depressed either from control value or the experimental period value.

Group II : **Animals Pretreated With Prazosin (Pra) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of prazosin alone initially induced a marked afferent and efferent arteriolar vasodilatatiion with significant marked reduced in renal vascular resistance (RVR) from the control value ($P<0.05$) whereas filtration fraction (FF) remained unchanged. There was also a significant marked increase in effective renal plasma flow (ERPF) from the control value ($P<0.05$) and glomerular filtration rate (GFR) from the control value ($P<0.01$) and insignificantly in effective renal blood flow, which resulted in a significant increase in urine flow rate (V) from the control value ($P<0.05$). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of prazosin led to renovasoconstriction with significant marked rose up in renal vascular resistance (RVR) to 94.44±25.76 % of the control value ($P<0.05$) and from the given prazosin alone value of 9.42±0.62 to 23.22±2.70 mmHg/ml/min/kg.bw. ($P<0.01$). There was also a significant marked fall in glomerular filtration rate to 57.52±8.14 % of the control value ($P<0.01$) and from the given prazosin alone value of 1.61±0.04 to 0.58±0.10 ml/min/kg.bw. ($P<0.001$), effective renal plasma flow to 51.07±6.29 % of the control value ($P<0.01$) and from the given prazosin alone value of 7.43±0.21 to 3.19±0.38 ml/min/kg.bw. ($P<0.001$), effective renal blood flow to 47.38±6.40 % of the control value ($P<0.01$) and from the given prazosin alone value of 10.69±0.25 to 5.04±0.58 ml/min/kg.bw. ($P<0.001$), filtration fraction to 16.20±5.12 % of the control value ($P<0.05$) and from the given prazosin alone value

21.7±0.5 to 17.7±1.2 % ($P<0.05$). These resulted in a significant mark decrease in urine flow rate (V) to 77.96±5.57 % of the control value ($P<0.001$) and from the given prazosin alone value of 26.59±1.74 to 3.44±0.80 μl/min/kg.bw. ($P<0.001$). It was indicated that prazosin did not block the renal hemodynamics effects of sodium metavanadate. Stopping infusion of prazosin and sodium metavanadate, urine flow rate returned to basal control value and significantly markedly increased from the experimental period value ($P<0.001$). Glomerular filtration rate, effective renal plasma flow, and effective renal blood flow significantly progressively decreased from the control value ($P<0.05$) but they significantly markely raised from the experimental period value ($P<0.01$), respectively. Filtration fraction significantly elevated either to from the control value ($P<0.05$) or from the experimental period value ($P<0.05$). Renal vascular resistance insignificantly persistantly rose up from the control value while it also significantly reduced from the experimental period value ($P<0.01$).

Group III : Animals Pretreated With Atenolol (AT) Before Sodium Metavanadate Infusion.

Intrarenal infusion of atenolol alone resulted in a marked afferent and efferent arteriolar vasodilatatiion by significant raise in urine flow rate from the control value ($P<0.01$) which was associated with significant increase in glomerular filtration rate, effective renal plasma flow, and effective renal blood flow from the control value ($P<0.05$), whereas renal vascular resistance little but significantly fell from the control value ($P<0.05$). No significant change in filtration fraction was observed. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of atenolol caused vasoconstriction with significant decrease in glomerular filtration rate to 36.11±6.42 % of the control value ($P<0.05$) and from the given atenolol alone value of 1.47±0.06 to 0.82±0.06 ml/min/kg.bw. ($P<0.01$), effective renal plasma flow to

41.37±2.73 % of the control value (P<0.001) and from the given atenolol alone value of 7.32±0.18 to 3.92±0.15 ml/min/kg.bw. (P<0.001), effective renal blood flow to 39.79±2.38 % of the control value (P<0.001) and from the given atenolol alone value of 11.21±0.28 to 6.19±0.27 ml/min/kg.bw. (P<0.001), whereas renal vascular resistance significantly marked increased either to 86.31±6.84 % of the control value (P<0.001) or from the given atenolol alone value of 9.62±0.27 to 19.92±1.12 mmHg/ml/min/kg.bw. (P<0.01), while filtration fraction remained unchanged throughout the experimental period value. These effects resulted in a significant depression in urine flow rate to 21.57±6.39 % of the control value (P<0.05) and from the given atenolol alone value of 53.62±3.03 to 29.55±3.29 µl/min/kg.bw. (P<0.001). It was indicated that atenolol did not block the renal hemodynamics effects of sodium metavanadate. Stopping infusion of atenolol and sodium metavanadate, urine flow rate and glomerular filtration rate returned to basal control value and significantly raised from the experimental period value (P<0.05). Effective renal plasma flow and effective renal blood flow significantly progressively depressed from the control value (P<0.01) but they significantly elevated from the experimental period value (P<0.01). Filtration fraction significantly rose up either from the control value (P<0.05) or from the experimental period value (P<0.01). Renal vascular resistance significantly persistantly increased from the control value (P<0.01) whlie it also decreased significantly from the experimental period value (P<0.01).

Group IV : Animals Pretreated With **Enalapril Maleate (MK 422) Before Sodium Metavanadate Infusion.**

Single dose intravenous injection of MK422 alone produced a marked afferent arteriolar renovasodilatatiion but not efferent arteriolar capillaries with significant elevation in glomerular filtration rate from the control value (P<0.01) and

filtration fraction from the control value ($P<0.05$) whereas renal vascular resistance small but significant reduced from the control value ($P<0.05$). Effective renal plasma flow and effective renal blood flow insignificantly little fell from the control value. There was also no significant rise in urine flow rate from the control value. When intravenous infusion of sodium metavanadate induced renovasoconstriction by a significant marked reduction in urine flow rate to 28.14±5.00 % of the control value ($P<0.05$) and from the given MK422 alone value of 43.23±3.81 to 25.12±1.36 μl/min/kg.bw. ($P<0.01$) which was associated with significant decrease in glomerular filtration rate to 35.88±6.69 % of the control value ($P<0.01$) and from the given MK422 alone value of 1.68±0.03 to 0.88±0.09 ml/min/kg.bw. ($P<0.01$), effective renal plasma flow to 53.07±2.22 % of the control value ($P<0.001$) and from the given MK422 alone value of 5.93±0.26 to 3.10±0.30 ml/min/kg.bw. ($P<0.001$), and effective renal blood flow to 49.13±3.06 % of the control value ($P<0.001$) and from the given MK422 alone value of 8.83±0.53 to 4.93±0.54 ml/min/kg.bw. ($P<0.001$). Renal vascular resistance significantly marked raised either to 119.25±14.07 % of the control value ($P<0.01$) or from the given MK422 alone value of 9.16±0.43 to 22.99±2.35 mmHg/ml/min/kg.bw. ($P<0.01$) and filtration fraction significantly elevated to 36.71±10.12 % of the control value ($P<0.05$) without significant from the given MK422 alone value. It was indicated that MK422 did not block the renal hemodynamics effects of sodium metavanadate. Stopping infusion of sodium metavanadate led to a significant rise in urine flow rate either from the control value ($P<0.01$) or from the experimental period value ($P<0.01$). Glomerular filtration rate returned to basal control value and significantly rose up from the experimental period value ($P<0.05$). Effective renal plasma flow and effective renal blood flow significantly progressively depressed from the control value ($P<0.01$) but they significantly increased from the experimental period value ($P<0.01$). Filtration fraction insignificantly slightly increased throughout the experimental period. Renal vascular resistance significantly

raised from the control value ($P<0.01$) while it significantly fell from the experimental period value ($P<0.05$).

Group V : **Animals Pretreated With Acetylcholine (ACh) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of acetylcholine alone resulted in a marked afferent arteriolar and efferent arteriolar vasodilatatiion by significant increase in urine flow rate from the control value ($P<0.01$) which was due to significant increase in glomerular filtration rate, effective renal plasma flow, and effective renal blood flow and filtration fraction from the control value ($P<0.05$). Renal vascular resistance significantly decreased from the control value ($P<0.01$). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of acetylcholine caused renovasoconstriction by a significant marked reduction in urine flow rate to 34.51±5.75 % of the control value ($P<0.01$) and from the given acetylcholine alone value of 45.74±1.84 to 21.87±2.15 µl/min/kg.bw. ($P<0.001$) which was associated with a significant decrease in glomerular filtration rate to 38.52±1.45 % of the control value ($P<0.001$) and from the given acetylcholine alone value of 1.64±0.05 to 0.80±0.02 ml/min/kg.bw. ($P<0.001$), effective renal plasma flow to 58.43±2.04 % of the control value ($P<0.001$) and from the given acetylcholine alone value of 6.70±0.07 to 2.51±0.16 ml/min/kg.bw. ($P<0.001$), and effective renal blood flow to 54.80±1.89 % of the control value ($P<0.001$) and from the given acetylcholine alone value of 10.31±0.15 to 4.13±0.27 ml/min/kg.bw. ($P<0.001$). Whereas renal vascular resistance and filtration fraction significantly marked raise in to 155.64±11.87 % of the control value ($P<0.001$) and 50.03±9.22 % of the control value ($P<0.01$), respectively, and from the given acetylcholine alone value of 9.31±0.29 to 30.34±2.34 mmHg/ml/min/kg.bw.($P<0.001$) and 24.4±0.5 to 32.3±2.1 % ($P<0.05$), respectively. These effects resulted in

significant decrease in urine flow rate to 34.51±5.75 % of the control value (P<001). It was indicated that acetylcholine did not block the renal hemodynamics effects of sodium metavanadate. Stopping infusion of acetylcholine and sodium metavanadate, urine flow rate significantly reduced from the control value (P<0.05) without a significant rose up from the experimental period value. Glomerular filtration rate restored to basal control value and significantly elevated from the experimental period value (P<0.01). Effective renal plasma flow and effective renal blood flow significantly progressively decreased from the control value (P<0.001) but they significantly increased from the experimental period value (P<0.001). Filtration fraction significantly persistantly raised from control value (P<0.01) without a significant from the experimental period value. Renal vascular resistance significantly elevated from the control value (P<0.01) while it also significantly depressed from the experimental period value (P<0.01).

Group VI : **Animals Pretreated With Verapamil (Ver) Before Sodium Metavanadate Infusion.**

Intrarenal infusion of verapamil alone induced a marked afferent arteriolar and efferent arteriolar vasodilatatiion by significant marked elevation in urine flow rate from the control value (P<0.05) which was associated with glomerular filtration rate, effective renal plasma flow, and effective renal blood flow from the control value (P<0.01). There was no significant changes in filtration fraction. Renal vascular resistance little but significantly reduced from the control value (P<0.05). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of verapamil led to a significant markedly rise in urine flow rate to 110.61±35.96 % of the control value (P<0.05) and from the given verapamil alone value of 80.59±6.17 to 96.48±9.37 µl/min/kg.bw. (P<0.05). Due to glomerular filtration rate and effective

renal blood flow were not fall significantly from the control value, although they significantly decreased from the given verapamil alone value of 1.55±0.09 to 1.08±0.10 ml/min/kg.bw. ($P<0.05$), and 12.30±0.32 to 7.68±0.66 ml/min/kg.bw. ($P<0.01$), respectively, while effective renal plasma flow progressively significantly depressed either to 29.83±8.36 % of the control value ($P<0.05$) or from the given verapamil alone value of 7.60±0.24 to 4.37±0.29 ml/min/kg.bw. ($P<0.01$). Filtration fraction and renal vascular resistance were not rose up significantly from the control value, although they significantly increased from the given verapamil alone value of 20.6±1.6 to 24.6±1.2 % ($P<0.05$), and 8.24±0.43 to 2.94±0.68 mmHg/ml/min/kg.bw. ($P<0.01$), respectively. It was indicated that verapamil effectively antagonized the renal hemodynamics elicited by sodium metavanadate. Stopping infusion of verapamil and sodium metavanadate, urine flow rate significantly raised from the control value ($P<0.01$) without a significant fall from the experimental period value. Glomerular filtration rate, effective renal plasma flow, and effective renal blood flow significantly reduced from the control value ($P<0.05$) without a significant from the experimental period value. There were also no significant changes in filtration fraction and renal vascular resistance.

Intrarenal infusion of prazosin (group II), atenolol (group III), acetylcholine (group V), and verapamil (group VI) resulted in a significant increase in urine flow rate as comparable to intrarenal infusion of saline (group I) at the same time interval ($P<0.05$) where intravenous injection of MK422 (group IV) slightly decreased without statistical significance (Figure 2, upper panel). Glomerular filtration rate was significantly higher than group I at the same time interval in group II ($P<0.01$), group III ($P<0.01$), group IV ($P<0.01$), group V ($P<0.001$), and group VI ($P<0.001$) (Figure 2, lower panel). Effective renal plasma flow as effective renal blood flow were significantly higher than group I at the same time interval in group II ($P<0.01$),

group III ($P<0.01$), group V ($P<0.01$), and group VI ($P<0.01$), whereas they were significantly lower than group I at the same time interval in group IV (Figure 3, upper and lower panel). Filtration fraction was significantly higher than group I at the same time interval in group IV ($P<0.05$) and group V ($P<0.001$), but the other groups remained unchanged from group I (Figure 4, upper panel). Renal vascular resistance was significantly lower than group I at the same time interval at the same time interval in all group II ($P<0.01$), group III ($P<0.01$), group IV ($P<0.01$), group V ($P<0.001$), and group VI ($P<0.001$) (Figure 4, lower panel).

The intravenous infusion of sodium metavanadate produced a significant marked fall in urine flow rate, glomerular filtration rate, effective renal plasma flow, and effective renal blood flow, still it induced a significant raise in filtration fraction and renal vascular resistance, these effects which were totally blocked by verapamil. When intravenous sodium metavanadate infusion and sustaining intrarenal infusion of prazosin (group II) led to a significant depression in urine flow rate as comparible to intravenous infusion of sodium metavanadate alone (group I) at the same time interval ($P<0.01$). Although urine flow rate significantly depressed in the same manner as group I, still it was significantly higher than group I in animals given sodium metavanadate and sustaining infusion with atenolol (group III) ($P<0.05$) and pretreatment of MK422 (group IV) ($P<0.05$) without significant in animals given sodium metavanadate and sustaining infusion with acetylcholine (group V), where they resulted in a marked significant elevation in animals given sodium metavanadate and sustaining infusion with verapamil (group VI) (Figure 2, upper panel). Glomerular filtration rate was significantly lower than group I at the same time interval in group II ($P<0.01$) and group V ($P<0.01$) without significant in group III-IV, whereas it insignificantly little increased in group VI (Figure 2, lower panel). Effective renal plasma flow was significantly lower than group I at the same time interval in group II

($P<0.05$), group IV ($P<0.001$), and group V ($P<0.001$) without a significant in group III and group VI (Figure 3, upper panel). Effective renal blood flow was significantly lower than group I at the same time interval in group II ($P<0.05$), group III ($P<0.05$), group IV ($P<0.01$), and group V ($P<0.001$), whereas it insignificantly small raise in group VI (Figure 3, lower panel). Filtration fraction was significantly lower than group I at the same time interval in group II ($P<0.05$) without significant in group III, but it was significantly higher than group I at the same time interval in group V ($P<0.05$) without significant in group IV and group VI (Figure 4, upper panel). Renal vascular resistance was significantly higher than group I the same time interval only in group V ($P<0.01$) without significant in group II-IV, whereas it was significantly lower than group I at the same time interval in group VI without significant in group IV and group VI (Figure 4, lower panel).

Withdrawal of sodium metavanadate and various drugs infusion caused a restoration to basal control value of the measurements made in all groups. Urine flow rate was significantly higher than group I at the same time interval in group III ($P<0.05$), group IV ($P<0.001$), and group VI ($P<0.01$) without significant in group II, whereas it insignificantly fell in group V. Glomerular filtration rate was significantly higher than group I in group IV ($P<0.05$) and group V ($P<0.001$) without significant in group III, whereas it insignificantly elevated in group II and group VI. Effective renal plasma flow was significantly lower than group I at the same time interval in group II ($P<0.05$), group III ($P<0.05$), and group V ($P<0.05$) without significant in group IV and VI, while effective renal blood flow was significantly lower than group I at the same time interval in group III ($P<0.05$), and group V ($P<0.05$) without a significant in group II, IV, and V. Filtration fraction was significantly higher than group I at the same time interval in group II ($P<0.05$), group III ($P<0.05$), and group V ($P<0.001$) without significant in group IV and group VI. No significant chage in renal vascular resistance was observed.

Table 2. Changes in renal hemodynamics in response to intravenous sodium metavanadate infusion in all groups.

Parameter	V (μl/min/kg.bw.)	GFR (ml/min/kg.bw.)	ERPF (ml/min/kg.bw.)	ERBF (ml/min/kg.bw.)	FF (%)	RVR (mmHg/ml/min/kg.bw.)
Group I (n=5)						
Control	28.94 ± 1.64	1.65 ± 0.06	7.36 ± 0.27	10.46 ± 0.38	22.4 ± 0.3	10.50 ± 0.63
NSS(IR)	28.98 ± 1.71	1.63 ± 0.06	7.13 ± 0.21	10.08 ± 0.36	22.9 ± 0.4	11.18 ± 0.72
NSS(IR)+$NaVO_3$(IV)	16.31 ± 1.45 ***$$$	1.23 ± 0.04 ***$$$	4.95 ± 0.28 ***$$$	7.44 ± 0.50 ***$$$	25.2 ± 1.5	19.35 ± 1.20 ***$$$
Recovery	24.87 ± 0.91 $	1.26 ± 0.05 ***	6.00 ± 0.23 **$$	8.71 ± 0.40 **$$	21.2 ± 1.2	13.99 ± 0.59 **$$
Group II (n=5)						
Control	15.88 ± 0.82	1.38 ± 0.04	6.57 ± 0.22	9.60 ± 0.24	21.1 ± 0.5	12.16 ± 0.62
Pra(IR)	26.59 ± 1.74 *	1.61 ± 0.04 **	7.43 ± 0.21 *	10.69 ± 0.25	21.7 ± 0.5	9.42 ± 0.62 *
Pra(IR)+$NaVO_3$(IV)	3.44 ± 0.80 ***$$$	0.58 ± 0.10 **$$$	3.19 ± 0.38 **$$$	5.04 ± 0.58 **$$$	17.7 ± 1.2 *$	23.22 ± 2.70 *$$
Recovery	16.64 ± 1.78 $$$	1.00 ± 0.07 *$$$	4.16 ± 0.37 **$$$	6.56 ± 0.57 **$$	24.4 ± 1.4 *$	16.66 ± 2.27 $$
Group III (n=5)						
Control	37.46 ± 2.02	1.30 ± 0.06	6.70 ± 0.09	10.27 ± 0.07	19.5 ± 0.8	10.67 ± 0.32
AT(IR)	53.62 ± 3.03 **	1.47 ± 0.06 *	7.32 ± 0.18 **	11.21 ± 0.28 *	20.1 ± 0.5	9.62 ± 0.27 *
AT(IR)+$NaVO_3$(IV)	29.55 ± 3.29 *$$$	0.82 ± 0.06 *$$	3.92 ± 0.15 ***$$$	6.19 ± 0.27 ***$$$	20.8 ± 1.0	19.92 ± 1.12 ***$$
Recovery	40.04 ± 2.48 $	1.37 ± 0.12 $$	4.66 ± 0.14 ***$$$	7.37 ± 0.37 **$$	29.4 ± 2.3 *$$	14.90 ± 0.63 **$$
Group IV (n=5)						
Control	35.27 ± 1.28	1.37 ± 0.05	6.57 ± 0.43	9.60 ± 0.70	21.4 ± 1.9	10.40 ± 0.59
MK422(v)	43.23 ± 3.81	1.68 ± 0.03 **	5.93 ± 0.26	8.83 ± 0.53	28.6 ± 1.4 *	9.16 ± 0.43 *
MK422(V)+$NaVO_3$(IV)	25.12 ± 1.36 *$$	0.88 ± 0.09 **$$	3.10 ± 0.30 ***$$$	4.93 ± 0.54 ***$$$	28.4 ± 2.0 *	22.99 ± 2.35 **$$
Recovery	60.96 ± 4.88 **$$	1.24 ± 0.06 $	4.76 ± 0.14 **$$	7.35 ± 0.37 *$$	26.2 ± 1.3	13.59 ± 0.48 **$
Group V (n=5)						
Control	33.20 ± 1.17	1.30 ± 0.02	6.02 ± 0.15	9.12 ± 0.31	21.6 ± 0.4	11.82 ± 0.56
ACh(IR)	45.74 ± 1.84 **	1.64 ± 0.05 **	6.70 ± 0.07 *	10.31 ± 0.15 *	24.4 ± 0.5 ***	9.31 ± 0.29 **
ACh(IR)+$NaVO_3$(IV)	21.87 ± 2.15 **$$$	0.80 ± 0.02 ***$$$	2.51 ± 0.16 ***$$$	4.13 ± 0.27 ***$$$	32.3 ± 2.1 **$	30.34 ± 2.34 ***$$$
Recovery	26.65 ± 2.00 *	1.47 ± 0.08 $$	4.10 ± 0.24 ***$$$	6.57 ± 0.47 ***$$$	36.4 ± 2.9 **	18.33 ± 1.58 **$$
Group VI (n=5)						
Control	48.72 ± 5.27	1.34 ± 0.08	6.42 ± 0.34	10.21 ± 0.60	21.2 ± 1.9	10.60 ± 0.96
Ver(IR)	80.59 ± 6.17 *	1.55 ± 0.09 **	7.60 ± 0.24 **	12.30 ± 0.32 **	20.6 ± 1.6	8.24 ± 0.43 *
Ver(IR)+$NaVO_3$(IV)	96.48 ± 9.37 *$	1.08 ± 0.10 $	4.37 ± 0.29 *$$	7.68 ± 0.66 $$	24.6 ± 1.2 $	12.94 ± 0.68 $$
Recovery	86.80 ± 5.60 **	1.00 ± 0.07 *	4.66 ± 0.29 **	7.89 ± 0.60 *	21.9 ± 2.0	12.29 ± 1.18

Values are means±SEM. Only one experimental kidney values were presented. Abbreviations : V, urine flow rate; GFR, glomerular filtration rate; ERPF, effective renal plasma flow; ERBF, effective renal blood flow; FF, filtration fraction; RVR, renal vascular resistance.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.

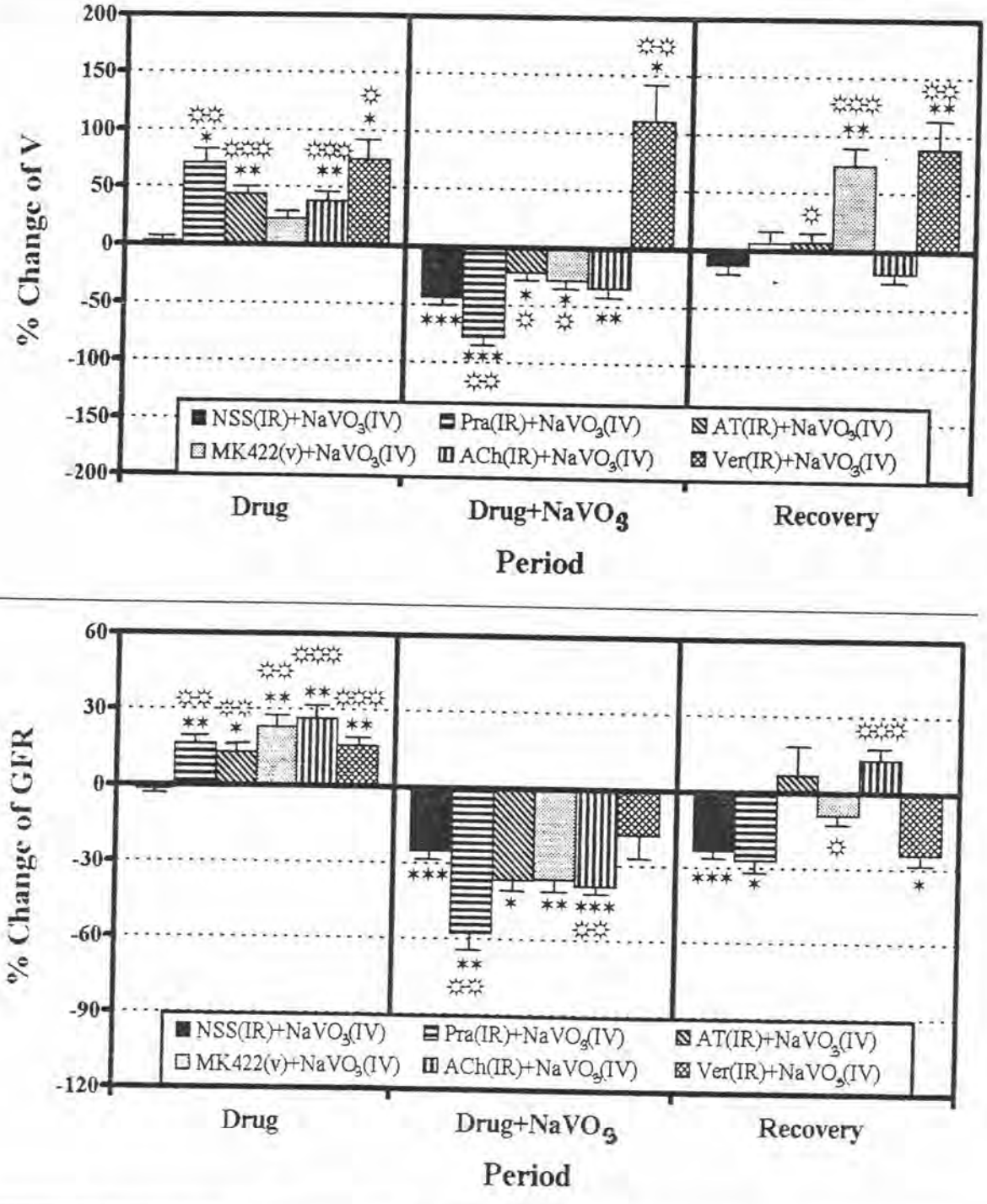
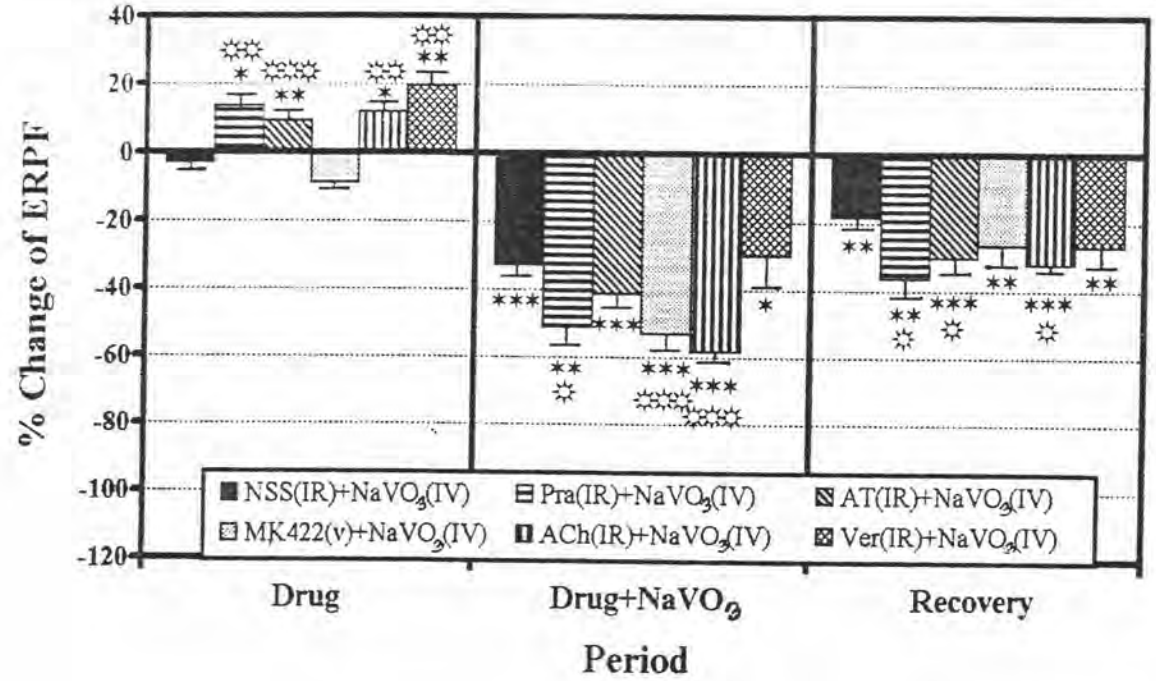


Figure 2 **Percentage changes in urine flow rate (V) and glomerular filtration rate (GFR) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).**
Significant difference values using paired t'test are indicated by * P<0.05, **P<0.01,*P<0.001 compaired to the control value of each group.**
Significant difference values using unpaired t'test are indicated by ☼P<0.05, ☼☼P<0.01,☼☼☼P<0.001 compaired to group I at the same time interval.



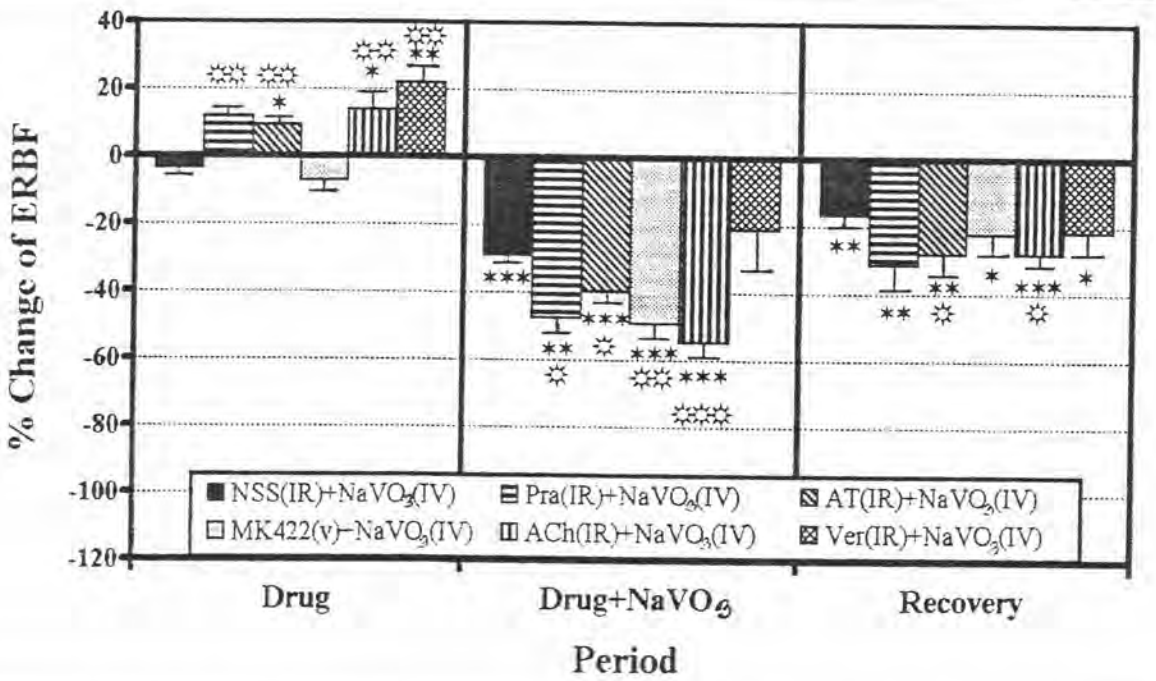


Figure 3 Percentage changes in effective renal plasma flow (ERPF) and effective renal blood flow (ERBF) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are ndicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

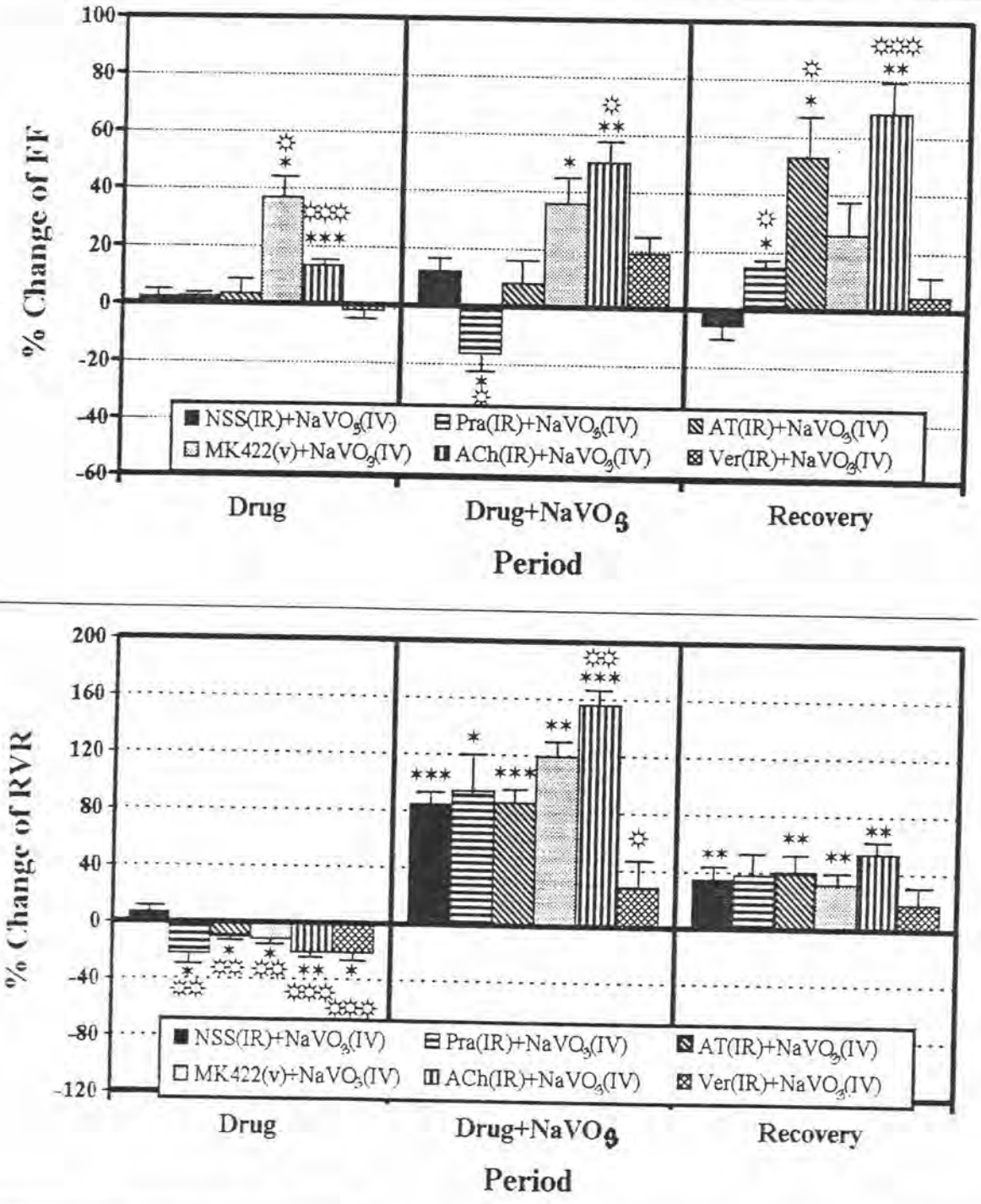


Figure 4 Percentage changes in filtration fraction (FF) and renal vascular resistance (RVR) in dogs intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).
Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.
Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

Effects of Intravenous Sodium Metavanadate Infusion on Urinary Electrolytes Excretion.

The results of changes in urinary electrolytes excretion in dogs given intravenous sodium metavanadate infusion without pretreatment of various drugs (group I) and pretreatment of intrarenal arterial infusion with prazosin (group II), atenolol (group III), acetylcholine (group V), verapamil (group VI), and intravenous injection with MK422 (group IV) are summerized in Table 3-7 and Figure 5-15 .

Group I : **Animals Pretreated With Isotonic Normal Saline Solution Before Sodium Metavanadate Infusion.**

After intrarenal arterial saline infusion caused no change in any of the measurements made. The intravenous sodium metavanadate infusion caused a significant raise in plasma sodium concentration (P_{Na}) to 4.68±1.40 % of the control value ($P<0.05$), whereas filtered load of sodium ($GFR \times P_{Na}$) significantly less fell to 21.72±2.11 % of the control value ($P<0.01$) than urinary excretion of sodium ($U_{Na}V$) to 37.77±2.87 % of the control value ($P<0.001$), therefore fractional excretion of sodium (FE_{Na}) significantly fell to 20.27±3.66 % of the control value ($P<0.05$), still absolute tubular reabsorption of sodium (T_{Na}) did not raise but significantly fell to 21.30±2.15 % of the control value ($P<0.01$) nearly percentage change of the reduction of filtered load which would due to the renal hemodynamic alterations and glomerulotubular balance (Table 3). Plasma potassium concentration (P_K) markedly significantly increased to 58.61±3.08 % of the control value ($P<0.001$). Filtered load of potassium ($GFR \times P_K$) significantly increased to 18.60±4.05 % of the control value ($P<0.05$), but urinary excretion of potassium (U_KV) markedly significantly decreased to 39.84±2.56 % of the control value ($P<0.001$), so absolute tubular reabsorption of

potassium (T_K) significantly increased to 31.41±5.36 % of the control value ($P<0.01$), whereas fractional excretion of potassium (FE_K) markedly significantly decreased to 48.88±3.27 % of the control value ($P<0.001$). On the other hand, potassium secretion reduction would result in a direct reduction in potassium excretion (Table 4). Plasma chloride concentration (P_{Cl}) significantly raise to 11.19±1.87 % of the control value ($P<0.01$). Filtered load of chloride ($GFR \times P_{Cl}$) significantly less fell to 16.87±2.34 % of the control value ($P<0.01$) than urinary excretion of chloride ($U_{Cl}V$) to 55.27±1.04 % of the control value ($P<0.001$), thus, fractional excretion of chloride (FE_{Cl}) significantly fell to 45.92±2.22 % of the control value ($P<0.001$), still absolute tubular reabsorption of chloride (T_{Cl}) did not rise but significantly fell to 15.71±2.44 % of the control value ($P<0.01$) nearly percentage change of the reduction of filtered load which would due to the renal hemodynamic alterations and glomerulotubular balance (Table 5). Blood bicarbonate concentration (B_{HCO_3}) markedly significantly fell to 25.55±2.18 % of the control value ($P<0.001$). Filtered load of bicarbonate ($GFR \times B_{HCO_3}$) equality as tubular reabsorption of bicarbonate (T_{HCO_3}) significantly fell to 44.31±2.14 % of the control value ($P<0.001$) and 44.44±2.14 % of the control value ($P<0.001$), respectively, whereas urinary excretion of bicarbonate ($U_{HCO_3}V$) unchanged from the control value, therefore fractional excretion of bicarbonate (FE_{HCO_3}) markedly significantly raise to 99.75±18.72 % of the control value ($P<0.01$) (Table 6). No significant alteration in plasma anion gap was observed, while urine anion gap markedly significantly raise to 106.99±18.41 % of the control value ($P<0.01$) (Table 7). Unidentical in filtered load, urinary excretion and tubular reabsorption of electrolytes was indicated that sodium metavanadate not only interfered to renal hemodynamics but also directly interfered to renal tubular function.

Stopping the sodium metavanadate infusion, plasma concentration of sodium remained significantly increased from the control value ($P<0.05$) without significant difference from the experimental period value. As for plasma concentration of potassium and chloride remained significantly increased to from the control value ($P<0.05$), but they significantly reduced form the experimental period value ($P<0.05$). Blood bicarbonate concentration returned to basal control value and significantly raised from the experimental period value ($P<0.05$). Filtered load of sodium and chloride remained significantly decreased from the control value ($P<0.001$) without significant change from the experimental period value. Filtered load of bicarbonate remained significantly decreased from the control value ($P<0.05$), but it significantly incresed from the experimental period value ($P<0.05$). Filtered load of potassium significantly fell from the experimental period value ($P<0.01$), while it unchanged from the control value. Tubular reabsorption of sodium and chloride remained significantly decreased from the control value ($P<0.001$), but they unchanged from the experimental period value. Tubular reabsorption of bicarbonate remained significantly decreased from the control value ($P<0.05$), but it significantly incresed from the experimental period value ($P<0.05$). Tubular reabsorption of potassium significantly fell from the experimental period value ($P<0.01$) while it unchanged from the control value. Urinary excretion of sodium, potassium, and chloride returned to basal control value and significantly raised ($P<0.05$). Urinary excretion of bicarbonate unchanged during the recovery period. Fractional excretion of sodium and potassium, although they insignificantly increased from the control value, significantly elevated from the experimental period value ($P<0.05$). No significant alteration in fractional excretion of chloride was observed. Fractional excretion of bicarbonate insignificantly raise from the control value, but it significntly fell from the experimental period value ($P<0.05$). Plasma anion gap remained unchanged, while urine anion gap remained significantly raise from the control value ($P<0.05$), but it significantly fell from the experimental period value

($P<0.05$). These indicted that the effects of sodium metavanadate may be temporary actions.

Group II : **Animals Pretreated With Prazosin (Pra) Before Sodium Metavanadate Infusion.**

After intrarenal infusion of prazosin alone, there was no different in plasma concentration of sodium, potassium, and chloride from the control value. Only blood bicarbonate concentration significantly fell from the control value ($P<0.01$). While it produced renovasodilation with a significant percentage elevation from control value nearly in filtered load of sodium ($P<0.01$), potassium ($P<0.001$), chloride ($P<0.05$), and bicarbonate ($P<0.05$) and tubular reabsorption of sodium ($P<0.01$), potassium ($P<0.001$), chloride ($P<0.05$), and bicarbonate ($P<0.05$), which would due to the renal hemodynamic alterations and glomerulotubular balance. Urinary excretion of sodium, potassium, chloride, and bicarbonate were not different from the control value. Fractional excretion of sodium, potassium, and chloride reduced but fractional excretion of bicarbonate rose up without statistically significantly from the control value. No significant change in plasma anion gap and urine anion gap were observed.

When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of prazosin, there was no significant different in plasma concentration of sodium, and potassium. Plasma chloride concentration significantly rose up to 13.34 ± 4.06 % of the control value ($P<0.05$) and from the given prazosin alone value ($P<0.05$). Blood bicarbonate concentration significantly fell to 16.85 ± 0.95 % of the control value ($P<0.001$) and from the given prazosin alone value ($P<0.001$). While it caused profound progressively renovasoconstriction by vanadate actions with a significant percentage depression from the control value and from the given prazosin

alone value nearly in filtered load of sodium ($P<0.01$), potassium ($P<0.01$), chloride ($P<0.01$), and bicarbonate ($P<0.01$) and tubular reabsorption of sodium ($P<0.01$), potassium ($P<0.05$), chloride ($P<0.01$), and bicarbonate ($P<0.01$), which would due to the renal hemodynamic alterations and glomerulotubular balance. Urinary excretion of sodium significantly fell to 47.74±3.66 % of the control value ($P<0.001$) and from the given prazosin alone value ($P<0.01$) less than the reduction of filtered laod, therefore fractional excretion of sodium, although it insignificantly raised from the control value, significantly raised from the given prazosin alone value of 2.3±0.1 to 3.4±0.3 % ($P<0.05$). As for urinary excretion of chloride significantly fell to 45.32±2.81 % of the control value ($P<0.001$) and from the given prazosin alone value ($P<0.001$) less than the reduction of filtered laod, thus, fractional excretion of chloride raised without statistically significance. Urinary excretion of potassium significantly fell to 53.19±9.86 % of the control value ($P<0.05$) and from the given prazosin alone value ($P<0.001$) higher than the reduction of filtered laod, so fractional excretion of potassium fell without statistically significance. Urinary excretion of bicarbonate significantly fell to 84.47±2.66 % of the control value ($P<0.001$) and from the given prazosin alone value ($P<0.01$) higher than the reduction of filtered laod, therefore fractional excretion of bicarbonate significantly fell to 54.32±5.01 % of the control value ($P<0.01$) and from the given prazosin alone value ($P<0.05$). No significant change in plasma anion gap and urine anion gap were observed.

Withdrawal of sodium metavanadate and prazosin, plasma concentration of sodium and chloride returned to basal control value and significantly fell from the experimental period value ($P<0.05$). Plasma concentration of potassium remained significantly increased from the control value ($P<0.01$) without significant from the experimental period. Blood bicarbonate concentration remained reduced without statistically significance during recovery period. Filtered load of sodium, chloride,

and bicarbonate, though they remained significantly decreased from the control value ($P<0.05$), significantly incresed from the experimental period value ($P<0.01$). Filtered load of potassium returned to basal control value and significantly rose up from the experimental period value ($P<0.001$). As for tubular reabsorption of sodium, chloride, and bicarbonate, though they remained significantly decreased from the control value ($P<0.05$), significantly incresed from the experimental period value ($P<0.01$). Tubular reabsorption of potassium significantly fell from the experimental period value ($P<0.001$), but it unchanged from the control value. Urinary excretion of sodium, although it significantly fell from control value ($P<0.01$), significantly rose up from the experimental period value ($P<0.05$). Urinary excretion of potassium significantly elevated from control value ($P<0.05$) and from the experimental period value ($P<0.001$). Urinary excretion of chloride returned to basal control value and insignificantly raised from the experimental period value. Urinary excretion of bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.01$). Fractional excretion of sodium returned to basal control value and significantly reduced from the experimental period value ($P<0.05$). Fractional excretion of potassium significantly increased from control value ($P<0.01$) and from the experimental period value ($P<0.01$). No significant change in fractional excretion of chloride was observed during the recovery period. Fractional excretion of bicarbonate, although it insignificantly raised from the control value, significantly raised from the experimental period value ($P<0.05$). There were also no significant change in plasma anion gap and urine anion gap during recovery period.

Group III : **Animals Pretreated With Atenolol (AT) Before Sodium Metavanadate Infusion**

After intrarenal infusion of atenolol alone, there was no different in plasma concentration of sodium, potassium, and chloride from the control value. Only blood bicarbonate concentration significantly fell from the control value ($P<0.05$). While it produced renovasodilation with a significant or nonsignificant percentage elevation from control value nearly in filtered load of sodium ($P<0.05$), potassium ($P<0.05$), chloride ($P<0.05$), bicarbonate (NS) and tubular reabsorption of sodium ($P<0.05$), potassium (NS), chloride ($P<0.05$), bicarbonate (NS), which would due to the renal hemodynamic alterations and glomerulotubular balance. Urinary excretion of sodium was not different from the control value. Urinary excretion of potassium, chloride, and bicarbonate significantly elevated from the control value ($P<0.05$). Fractional excretion of sodium, potassium, and chloride raised without statistically significantly, but fractional excretion of bicarbonate significantly rose up from the control value ($P<0.05$). Plasma anion gap remained unchanged, while urine anion gap significantly reduced from the control value ($P<0.01$).

When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of atenolol, there was no significant different in plasma sodium concentration. Plasma potassium concentration significantly rose up to 23.56 ± 1.73 % of the control value ($P<0.001$) and from the given atenolol alone value ($P<0.01$). As for plasma chloride concentration significantly increased to 7.09 ± 2.06 % of the control value ($P<0.05$) and from the given atenolol alone value ($P<0.05$). Blood bicarbonate concentration significantly fell to 17.50 ± 3.44 % of the control value ($P<0.05$) without significant from the given atenolol alone value. While it caused profound progressively renovasoconstriction by vanadate actions with a significant percentage depression

from the control value and from the given atenolol alone value nearly in filtered load of sodium ($P<0.05$), chloride ($P<0.05$), and bicarbonate ($P<0.01$) and tubular reabsorption of sodium ($P<0.05$), chloride ($P<0.05$), and bicarbonate ($P<0.01$), which would due to the renal hemodynamic alterations and glomerulotubular balance. In contrast, filtered load of potassium insignificantly decreased, while urinary excretion of potassium significantly fell to 45.89±4.57 % of the control value ($P<0.01$) and from the given atenolol alone value ($P<0.001$) more than the reduction of filtered laod, so absolute tubular reabsorption of potassium insignificantly decreased less than the reduction of filtered load, whereas fractional excretion of potassium markedly significantly decreased to 30.44±3.15 % of the control value ($P<0.001$) and from the given atenolol alone ($P<0.05$). On the other hand, potassium secretion reduction would result in a direct reduction in potassium excretion. Urinary excretion of sodium significantly fell to 49.04±3.26 % of the control value ($P<0.001$) and from the given atenolol alone value ($P<0.001$) more than the reduction of filtered laod, therefore fractional excretion of sodium significantly suppressed to 19.60±5.89 % the control value ($P<0.05$) and from the given atenolol alone value ($P<0.05$). As for urinary excretion of chloride significantly fell to 43.79±5.51 % of the control value ($P<0.01$) and from the given atenolol alone value ($P<0.01$) higher than the reduction of filtered laod, thus, fractional excretion of chloride reduced without statistically significance. No significant change in urinary excretion of bicarbonate was observed., therefore fractional excretion of bicarbonate significantly rose up to 77.15±14.64 % of the control value ($P<0.05$) without significant from the given atenolol alone value. Plasma anion gap remained unchanged, while urine anion gap significantly reduced to 40.18±5.09 % the control value ($P<0.01$) without significant from the given atenolol alone value.

Withdrawal of sodium metavanadate and atenolol, plasma concentration of sodium and chloride returned to basal control value and significantly fell from the experimental period value ($P<0.05$). Plasma concentration of potassium remained significantly increased from the control value ($P<0.01$) without significant from the experimental period. Blood bicarbonate concentration remained reduced without statistically significance during recovery period. Filtered load of sodium, chloride, and bicarbonate, though they remained significantly decreased from the control value ($P<0.05$), significantly incresed from the experimental period value ($P<0.01$). Filtered load of potassium returned to basal control value and significantly rose up from the experimental period value ($P<0.001$). As for tubular reabsorption of sodium, chloride, and bicarbonate, though they remained significantly decreased from the control value ($P<0.05$), significantly incresed from the experimental period value ($P<0.01$). Tubular reabsorption of potassium significantly fell from the experimental period value ($P<0.001$), but it unchanged from the control value. Urinary excretion of sodium, although it significantly fell from control value ($P<0.01$), significantly rose up from the experimental period value ($P<0.05$). Urinary excretion of potassium significantly elevated from control value ($P<0.05$) and from the experimental period value ($P<0.001$). Urinary excretion of chloride returned to basal control value and insignificantly raised from the experimental period value. Urinary excretion of bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.01$). Fractional excretion of sodium returned to basal control value and significantly reduced from the experimental period value ($P<0.05$). Fractional excretion of potassium significantly increased from control value ($P<0.01$) and from the experimental period value ($P<0.01$). No significant change in fractional excretion of chloride was observed during the recovery period. Fractional excretion of bicarbonate, although it insignificantly raised from the control value, significantly raised from the experimental period value ($P<0.05$). There were also no significant change in

plasma anion gap and urine anion gap during recovery period.

Group IV : **Animals Pretreated With Enalapril Maleate (MK 422) Before Sodium Metavanadate Infusion.**

Single dose intravenous injection of MK422 alone, there was no different in plasma potassium concentration from the control value. Plasma concentration of sodium and bicarbonate significantly fell from the control value ($P<0.05$). Only blood chloride concentration significantly rose up from the control value ($P<0.01$). While it produced renovasodilation with a significant or noninsignificant percentage elevation from control value nearly in filtered load of sodium ($P<0.05$), potassium ($P<0.05$), chloride ($P<0.01$), bicarbonate (NS) and tubular reabsorption of sodium ($P<0.05$), potassium ($P<0.05$), chloride ($P<0.01$), bicarbonate (NS), which would due to the renal hemodynamic alterations and glomerulotubular balance. Urinary excretion of sodium, chloride, and bicarbonate were not different from the control value. Urinary excretion of potassium significantly elevated from the control value ($P<0.01$). Fractional excretion of sodium, potassium, and bicarbonate unchanged without statistically significantly, but fractional excretion of chloride significantly reduced from the control value ($P<0.001$). Urine anion gap remained unchanged, while plasma anion gap significantly reduced from the control value ($P<0.05$).

When intravenous infusion of sodium metavanadate, there was no significant different in plasma bicarbonate concentration. Plasma concentration of sodium, potassium, and chloride significantly rose up to 4.24 ± 1.16 % of the control value ($P<0.05$), 19.47 ± 2.47 % of the control value ($P<0.01$), and 11.15 ± 1.99 % of the control value ($P<0.01$), respectively, and from the given MK422 alone value ($P<0.05$).

While it caused profound progressively renovasoconstriction by vanadate actions with a significant percentage depression from the control value and from the given MK422 alone value nearly in filtered load of sodium ($P<0.05$), chloride ($P<0.05$), and bicarbonate ($P<0.01$) and tubular reabsorption of sodium ($P<0.05$), chloride ($P<0.05$), and bicarbonate ($P<0.05$), which would due to the renal hemodynamic alterations and glomerulotubular balance. In contrast, filtered load of potassium significantly decreased to 23.48±7.66 % of the control value ($P<0.05$) and from the given MK422 alone ($P<0.05$), while no significant change in urinary excretion of potassium was observed, so absolute tubular reabsorption of potassium significantly decreased to 29.60±9.30 % of the control value ($P<0.05$) and from the given MK422 alone ($P<0.05$) more than the reduction of filtered load, whereas fractional excretion of potassium rose up without statistically significance. Urinary excretion of sodium significantly fell to 29.75±6.83 % of the control value ($P<0.05$) and from the given MK422 alone value ($P<0.05$) less than the reduction of filtered laod, therefore fractional excretion of sodium rose up without statistically significance. While urinary excretion of chloride significantly fell to 42.19±4.17 % of the control value ($P<0.01$) and from the given MK422 alone value ($P<0.01$) higher than the reduction of filtered laod, thus, fractional excretion of chloride reduced without statistically significance. Urinary excretion of bicarbonate significantly fell to 35.95±3.13 % of the control value ($P<0.01$) without significant from the given MK422 alone value less than the reduction of filtered laod, therefore fractional excretion of bicarbonate rose up without statistically significance. Urine anion gap insignificantly raised , while plasma anion gap significantly reduced to 35.03±9.03 % the control value ($P<0.05$) without significant from the given MK422 alone value.

Withdrawal of sodium metavanadate and MK422, plasma concentration of sodium, potassium, and chloride remained significantly increased from the control value ($P<0.05$) without significant from the experimental period. Blood bicarbonate

concentration remained unchanged during recovery period. Filtered load of sodium, chloride, and bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.05$). Filtered load of potassium significantly increased from the control value ($P<0.05$) and from the experimental period value ($P<0.01$). Tubular reabsorption of sodium, potassium, chloride, and bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.05$). Urinary excretion of sodium, potassium, and bicarbonate significantly rose up from control value ($P<0.05$) and from the experimental period value ($P<0.05$). Urinary excretion of chloride returned to basal control value and significantly elevated from the experimental period value ($P<0.05$). No significant increase in fractional excretion of sodium and chloride was observed during the recovery period. Fractional excretion of potassium significantly rose up from the control value ($P<0.05$) without significant from the experimental period value. Fractional excretion of bicarbonate significantly increased from control value ($P<0.01$) and from the experimental period value ($P<0.05$). No significant change in plasma anion gap and urine anion gap were observed.

Group V : Animals Pretreated With Acetylcholine (ACh) Before Sodium Metavanadate Infusion.

Intrarenal infusion of acetylcholine alone, there was no different in plasma concentration of sodium, potassium, and bicarbonate from the control value. Only blood chloride concentration significantly rose up from the control value ($P<0.01$). While it produced renovasodilation with a significant or noninsignificant percentage elevation from control value nearly in filtered load of sodium ($P<0.01$), potassium ($P<0.01$), chloride ($P<0.01$), and bicarbonate ($P<0.01$) and tubular reabsorption of sodium ($P<0.01$), potassium (NS), chloride ($P<0.01$), and bicarbonate (NS),

which would due to the renal hemodynamic alterations and glomerulotubular balance. Urinary excretion of sodium, potassium, chloride, and bicarbonate significantly elevated from the control value ($P<0.05$). Fractional excretion of sodium significantly rose up from the control value ($P<0.01$). Fractional excretion of potassium, and bicarbonate unchanged, while fractional excretion of chloride reduced from the control value without statistically significantly. Plasma anion gap remained unchanged, while urine anion gap significantly increased from the control value ($P<0.05$).

When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of acetylcholine, there was no significant different in plasma sodium concentration. Plasma concentration of potassium and chloride significantly rose up to 7.60 ± 2.37 % of the control value ($P<0.05$) and 9.80 ± 1.68 % of the control value ($P<0.01$) and from the given acetylcholine alone value ($P<0.05$). Blood bicarbonate concentration significantly fell to 11.41 ± 2.46 % of the control value ($P<0.05$) and from the given acetylcholine alone value ($P<0.001$). While it caused profound progressively renovasoconstriction by vanadate actions with a significant percentage depression from the control value and from the given acetylcholine alone value nearly in filtered load of sodium ($P<0.001$), chloride ($P<0.001$), and bicarbonate ($P<0.01$) and tubular reabsorption of sodium ($P<0.05$), chloride ($P<0.05$), and bicarbonate ($P<0.001$), which would due to the renal hemodynamic alterations and glomerulotubular balance. In contrast, filtered load of potassium significantly decreased to 33.87 ± 2.02 % of the control value ($P<0.001$) and from the given acetylcholine alone value ($P<0.001$), while urinary excretion of potassium remained unchanged, so absolute tubular reabsorption of potassium significantly fell to 13.03 ± 11.16 % of the control value ($P<0.001$) and from the given acetylcholine alone value ($P<0.001$) more than the reduction of filtered laod, whereas fractional excretion of potassium significantly rose up to 71.33 ± 18.43 % of the control value ($P<0.05$) and from the given acetylcholine alone ($P<0.05$).

Potassium secretion reduction would result in a direct reduction in potassium excretion. Urinary excretion of sodium significantly fell to 46.80±3.09 % of the control value ($P<0.001$) and from the given acetylcholine alone value ($P<0.001$) more than the reduction of filtered laod, therefore fractional excretion of sodium significantly fell from the given acetylcholine alone value ($P<0.05$) without significant from the control value. As for urinary excretion of chloride significantly fell to 51.80±3.51 % of the control value ($P<0.001$) and from the given acetylcholine alone value ($P<0.001$) more than the reduction of filtered laod, thus, fractional excretion of chloride reduced to 27.79±6.80 % of the control value ($P<0.05$) without significance from the given acetylcholine alone value. Urinary excretion of bicarbonate significantly fell to 34.64±4.44 % of the control value ($P<0.01$) and from the given acetylcholine alone value ($P<0.01$) less than the reduction of filtered laod, thus, no significant increase in fractional excretion of bicarbonate was observed. There were also no significant changed in plasma anion gap and urine anion gap during experimental period.

Withdrawal of sodium metavanadate and acetylcholine, plasma concentration of sodium and chloride returned to basal control value and insignificantly fell from the experimental period value. Plasma concentration of potassium remained significantly increased from the control value ($P<0.01$) without significant from the experimental period. Blood bicarbonate concentration remained reduced without statistically significance during recovery period. Filtered load of sodium and bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.01$). Filtered load of potassium and chloride significantly increased from the control value ($P<0.05$) and from the experimental period value ($P<0.01$). As for tubular reabsorption of sodium, and bicarbonate returned to basal control value and significantly rose up from the experimental period value ($P<0.01$). Tubular reabsorption of potassium and chloride significantly increased from the control value

($P<0.05$) and from the experimental period value ($P<0.01$). Urinary excretion of sodium and chloride, although it significantly fell from control value ($P<0.05$), significantly rose up from the experimental period value ($P<0.05$). No significant reduced in urinary excretion of potassium were observed. Urinary excretion of bicarbonate significantly remained fell from the control value ($P<0.01$) without significant from the experimental period value. Fractional excretion of sodium and chloride significantly reduced from the control value ($P<0.001$) without significant from the experimental period value. Fractional excretion of potassium returned to basal control value and significantly decreased from the experimental period value ($P<0.01$). No significant reduction in fractional excretion of bicarbonate was observed. There were also no significant change in plasma anion gap and urine anion gap during recovery period.

Group VI : Animals Pretreated With Verapamil (Ver) Before Sodium Metavanadate Infusion.

Intrarenal infusion of verapamil alone, there was no different in plasma potassium concentration from the control value. Plasma sodium concentration significantly depressed from the control value ($P<0.05$). Plasma concentration of chloride, and bicarbonate significantly rose up from the control value ($P<0.05$). While it produced renovasodilation with a significant percentage increase from the control value nearly in filtered load of sodium ($P<0.01$), chloride ($P<0.01$), and bicarbonate ($P<0.001$) and tubular reabsorption of sodium ($P<0.01$), chloride ($P<0.01$), and bicarbonate ($P<0.001$), which would due to the renal hemodynamic alterations and glomerulotubular balance. In contrast, filtered load of potassium significantly increased from the control value ($P<0.01$), while absolute tubular reabsorption of potassium remained unchanged, so urinary excretion of potassium significantly increased from the

control value ($P<0.01$) and fractional excretion of potassium significantly rose up from the control value ($P<0.05$). Urinary excretion of sodium significantly raised from the control value ($P<0.05$) more than the increase of filtered laod, therefore fractional excretion of sodium insignificantly raised from the control value. Urinary excretion of chloride significantly rose up from the control value ($P<0.05$) more than the increase of filtered laod, thus, fractional excretion of chloride rose up from the control value ($P<0.05$). Urinary excretion of bicarbonate insignificantly increased from the control value more than the increase of filtered laod, thus, no significant increase in fractional excretion of bicarbonate was observed. There were also no significant changed in plasma anion gap, but urine anion gap significantly suppressed from the control value ($P<0.05$).

When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of verapamil, there was no significant different in plasma concentration of sodium, and potassium. Plasma chloride concentration significantly rose up to 9.80 ± 1.68 % of the control value ($P<0.05$) without significant from the given verapamil alone value. Blood bicarbonate concentration significantly fell to 11.84 ± 2.01 % of the control value ($P<0.01$) and from the given verapamil alone value ($P<0.01$). Filtered load and tubular reabsorption of sodium insignificantly reduced to 16.30 ± 8.90 % of the control value, 18.82 ± 2.83 % of the control value, respectively, with significant from the given verapamil alone value ($P<0.05$), but urinary excretion of sodium significantly increased to 74.04 ± 20.34 % of the control value ($P<0.05$) and from the given verapamil alone value ($P<0.05$), therefore fractional excretion of sodium significantly elevated to 113.82 ± 20.83 % of the control value ($P<0.01$) and from the given verapamil alone value ($P<0.01$). Filtered load insignificantly reduced to 7.59 ± 8.55 % of the control value with significant from the given verapamil alone value ($P<0.05$), While tubular reabsorption of potassium insignificantly reduced to 24.17 ± 8.78 % of the control

value with significant from the given verapamil alone value ($P<0.05$) but urinary excretion of potassium significantly increased to 51.35±5.38 % of the control value ($P<0.01$) without significant from the given verapamil alone value, therefore fractional excretion of potassium significantly elevated to 69.45±12.65 % of the control value ($P<0.01$) and from the given verapamil alone value ($P<0.01$). As for filtered load and tubular reabsorption of chloride insignificantly reduced to 12.39±9.21 % of the control value, 14.67±9.01 % of the control value, respectively, with significant from the given verapamil alone value ($P<0.05$), but urinary excretion of chloride significantly increased to 67.54±25.61 % of the control value ($P<0.05$) without significant from the given verapamil alone value, therefore fractional excretion of chloride significantly elevated to 92.53±19.30 % of the control value ($P<0.01$) and from the given verapamil alone value ($P<0.05$). However, filtered load and tubular reabsorption of bicarbonate significantly reduced to 28.06±6.40 % of the control value ($P<0.05$), 28.52±6.30 % of the control value ($P<0.05$), respectively, with significant from the given verapamil alone value ($P<0.01$), but no significant increased in urinary excretion of bicarbonate was observed, therefore fractional excretion of bicarbonate significantly elevated to 127.10±52.31 % of the control value ($P<0.05$) and from the given verapamil alone value ($P<0.01$). There was also no significant change in plasma anion gap. Urine anion gap remained unchanged from the control value, but it significantly increased from the given verapamil alone value ($P<0.01$).

Withdrawal of sodium metavanadate and verapamil, plasma concentration of sodium significantly raised from the control value ($P<0.05$) and from the experimental period value ($P<0.01$). No significant increase in plasma concentration of potassium and chloride were observed. Blood bicarbonate concentration significantly remained reduced from control value ($P<0.05$) without significant from the experimental period value. Filtered load of sodium, chloride, and bicarbonate, though they remained

significantly decreased from the control value ($P<0.05$) without significant from the experimental period value. There was no significant in filtered load of potassium during the recovery period. As for tubular reabsorption of sodium, chloride, and bicarbonate, though they remained significantly decreased from the control value ($P<0.05$) without significant from the experimental period value. No significant different change in tubular reabsorption of potassium was observed. Urinary excretion of sodium, although it significantly raised from control value ($P<0.05$), insignificantly fell from the experimental period value. Urinary excretion of potassium and chloride returned to basal control value and significantly reduced from the experimental period value ($P<0.05$). Urinary excretion of bicarbonate remained increased without statistically significance. Fractional excretion of sodium and bicarbonate significantly remained raised from the control value ($P<0.05$) without significant from the experimental period value. No significant increase in fractional excretion of potassium was observed during the recovery period. Fractional excretion of chloride, although it significantly raised from the control value ($P<0.05$), significantly fell from the experimental period value ($P<0.01$). There were also no significant change in plasma anion gap and urine anion gap during recovery period.

Comparison, plasma sodium concentration (Figure 5, upper panel) and chloride in group (Figure 6, upper panel) in group II-VI increased in the same manner as after intravenous infusion of sodium metavanadate alone (Group I) which insignificantly differed respect to group I at the same time interval. Plasma potassium concentration (Figure 5, lower panel) in group II-VI increased in the same manner as group I but it were significantly less than group I at the same time interval ($P<0.001$). Blood bicarbonate concentration (Figure 6, lower panel) in group II-VI decreased in the same manner as group I which were significantly higher than group I at the same time interval in group II ($P<0.05$), group IV ($P<0.05$), group V ($P<0.01$), and group VI ($P<0.01$).

Filtered load of sodium (Figure 7, upper panel) and tubular reabsorption of sodium (Figure 11, upper panel) in group II-VI decreased in the same manner as group I which were significantly lower than group I at the same time interval in group II ($P<0.01$), group V ($P<0.001$). Filtered load of potassium (Figure 7, lower panel) and tubular reabsorption of potassium (Figure 11, lower panel) in group II-VI decreased in the opposite manner of group I which were significantly lower than group I at the same time interval in group II ($P<0.001$), group III ($P<0.01$), group IV ($P<0.01$), group V ($P<0.001$), and group VI ($P<0.05$). Filtered load of chloride (Figure 8, upper panel) and tubular reabsorption of chloride (Figure 12, upper panel) in group II-VI decreased in the same manner as group I which were significantly lower than group I at the same time interval in group II ($P<0.01$), group V ($P<0.05$). Filtered load of bicarbonate (Figure 8, lower panel) and tubular reabsorption of bicarbonate (Figure 12, lower panel) in group II-VI decreased in the same manner as group I which were significantly lower than group I at the same time interval in group II ($P<0.05$). Urinary excretion of sodium (Figure 9, upper panel) in group II-V decreased in the same manner as group I which were significantly lower than group I at the same time interval in group II ($P<0.05$), however, in group VI increased in the oppersite manner of group I which were significantly higher than group I at the same time interval ($P<0.01$). Urinary excretion of potassium (Figure 9, lower panel) in group II-III insignificantly decreased in the same manner as group I, however, in group IV-VI increased in the opposite manner of group I which were significantly higher than group I at the same time interval in group IV ($P<0.01$), group V ($P<0.01$), and group VI ($P<0.001$). Urinary excretion of chloride (Figure 10, upper panel) in group II-V decreased in the same manner as group I which were significantly lower than group I at the same time interval in group II ($P<0.05$), group IV ($P<0.05$), however, in group VI increased in the oppersite manner of group I which was significantly higher than group I at the same time interval ($P<0.01$). Urinary excretion of bicarbonate (Figure 8, lower panel) in group VI

insignificantly increased in the same manner as group I, however, in group II-VI decreased in the oppersite manner of group I which was significantly lower than group I at the same time interval in group II ($P<0.001$), group IV ($P<0.01$), and group V ($P<0.01$). Fractional excretion of sodium (Figure 13, upper panel) in group III ,V insignificantly decreased in the same manner as group I, however, in group II, IV, and VI increased in the oppersite manner of group I which were significantly higher than group I at the same time interval in group II ($P<0.01$) and group VI ($P<0.001$). Fractional excretion of potassium (Figure 13, lower panel) in group II-III decreased in the same manner as group I which were significantly higher than group I at the same time interval in group II ($P<0.01$), group III ($P<0.01$), however, in group IV-VI increased in the opposite manner of group I which were significantly higher than group I at the same time interval in group IV ($P<0.01$), group V ($P<0.001$), and group VI ($P<0.001$). Fractional excretion of chloride (Figure 14, upper panel) in group III-V decreased in the same manner as group I which were significantly lower than group I at the same time interval in group III ($P<0.01$), however, in group II, VI increased in the oppersite manner of group I which were significantly higher than group I at the same time interval in group II ($P<0.01$) and group VI ($P<0.001$). Fractional excretion of bicarbonate (Figure 14, lower panel) in group III-VI raised in the same manner as group I which were significantly lower than group I at the same time interval in group IV ($P<0.05$), and group V ($P<0.05$), but in group II decreased in the oppersite manner of group I which was significantly lower than group I at the same time interval in group II ($P<0.001$). Plasma anion gap (Figure 15, upper panel) in group III raised in the same manner as group I, however, in group II, IV-VI decreased in the oppersite manner of group without significant difference from grom I. Urine anion gap (Figure 15, lower panel) in group II-V raised in the same manner as group I which were significantly lower than group I at the same time interval in group III ($P<0.001$), but in group VI fell in the oppersite manner of group I at the same time interval ($P<0.01$).

Table 3. Changes in sodium excretion in response to intravenous sodium metavanadate infusion in all groups.

Parameter	P_{Na} (mEq/L)	$GFR \times P_{Na}$ (μEq/min/kg.bw.)	$U_{Na}V$ (μEq/min/kg.bw.)	T_{Na} (μEq/min/kg.bw.)	FE_{Na} (%)
Group I (n=5)					
Control	140.6 ± 0.5	231.70 ± 8.06	5.79 ± 0.15	225.91 ± 7.94	2.5 ± 0.1
NSS(IR)	141.0 ± 0.8	230.01 ± 7.48	5.73 ± 0.14	224.27 ± 7.41	2.5 ± 0.1
NSS(IR)+$NaVO_3$(IV)	147.2 ± 2.3 *$	181.23 ± 7.33 **$$	3.60 ± 0.19 ***$$$	177.63 ± 7.18 **$$	2.0 ± 0.1 *$
Recovery	145.8 ± 1.5 *	184.32 ± 8.46 ***	5.53 ± 0.25 $	178.79 ± 8.53 ***	3.0 ± 0.2 $
Group II (n=5)					
Control	141.8 ± 0.8	196.2 ± 5.02	5.08 ± 0.15	191.11 ± 5.08	2.6 ± 0.1
Pra(IR)	142.2 ± 0.8	228.29 ± 4.60 **	5.27 ± 0.26	223.03 ± 4.64 **	2.3 ± 0.1
Pra(IR)+$NaVO_3$(IV)	146.4 ± 2.8	84.43 ± 14.52 **$$$	2.66 ± 0.23 ***$$	81.77 ± 14.31 **$$$	3.4 ± 0.3 $
Recovery	140.8 ± 2.2 $	140.78 ± 10.85 *$$$	3.38 ± 0.20 **$	137.40 ± 10.65 *$$$	2.4 ± 0.1 $
Group III (n=5)					
Control	141.8 ± 1.2	184.61 ± 6.70	5.37 ± 0.14	179.23 ± 6.69	2.9 ± 0.1
AT(IR)	143.2 ± 1.3	210.59 ± 8.38 *	5.67 ± 0.12	204.92 ± 8.25 *	2.7 ± 0.1
AT(IR)+$NaVO_3$(IV)	145.4 ± 2.7	118.31 ± 7.65 *$$	2.73 ± 0.16 ***$$$	115.59 ± 7.54 *$$	2.3 ± 0.1 *$
Recovery	146.4 ± 2.4	201.13 ± 19.35 $$	4.81 ± 0.18 $$	196.32 ± 19.29 $$	2.5 ± 0.2
Group IV (n=5)					
Control	141.2 ± 1.4	193.45 ± 6.82	5.18 ± 0.33	188.27 ± 6.56	2.7 ± 0.1
MK422(v)	138.0 ± 2.2 *	231.80 ± 7.43 *	5.59 ± 0.46	226.21 ± 7.84 *	2.5 ± 0.3
MK422(v)+$NaVO_3$(IV)	147.2 ± 2.3 *$$	129.02 ± 13.50 *$$	3.55 ± 0.19 *$	125.47 ± 13.65 *$$	3.0 ± 0.5
Recovery	150.8 ± 1.8 *	187.17 ± 8.44 $	9.05 ± 1.23 *$	178.12 ± 9.17 $	5.0 ± 0.8
Group V (n=5)					
Control	142.6 ± 1.4	184.70 ± 2.09	4.28 ± 0.06	180.41 ± 2.07	2.3 ± 0.0
ACh(IR)	147.8 ± 1.2	242.17 ± 7.74 **	6.09 ± 0.21 ***	236.07 ± 7.57 **	2.5 ± 0.0 **
ACh(IR)+$NaVO_3$(IV)	144.8 ± 1.5	115.16 ± 1.50 ***$$$	2.28 ± 0.13 ***$$$	112.89 ± 1.53 ***$$$	2.0 ± 0.1 $
Recovery	140.4 ± 1.2	205.60 ± 10.73 $$	3.44 ± 0.16 *$	202.15 ± 10.61 $$	1.7 ± 0.1 ***
Group VI (n=5)					
Control	140.2 ± 1.4	187.30 ± 10.99	5.34 ± 0.43	181.96 ± 11.21	2.9 ± 0.4
Ver(IR)	137.0 ± 1.5 *	228.26 ± 14.43 **	7.20 ± 0.36 *	221.06 ± 14.37 **	3.2 ± 0.2
Ver(IR)+$NaVO_3$(IV)	142.4 ± 1.2	153.59 ± 13.78 $	9.08 ± 0.81 *$	144.51 ± 13.25 $	6.0 ± 0.4 **$$
Recovery	149.2 ± 1.0 *$$	149.58 ± 10.33 *	7.18 ± 0.33 *	142.40 ± 10.32 *	4.9 ± 0.4 ***

Values are the means±SEM. Only one experimental kidney values are presented. Abbreviations : P_{Na}, plasma sodium concentration; $GFR \times P_{Na}$, filtered load of sodium; $U_{Na}V$, urinary sodium excretion; T_{Na}, tubular reabsorption of sodium; FE_{Na}, fractional excretion of sodium.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by \$ $P<0.05$, \$\$ $P<0.01$, \$\$\$ $P<0.001$ different from previous values.

Table 4. Changes in potassium excretionin response to intravenous sodium metavanadate infusion in all groups.

Parameter	P_K (mEq/L)	$GFR \times P_K$ (μEq/min/kg.bw.)	U_KV (μEq/min/kg.bw.)	T_K (μEq/min/kg.bw.)	FE_K (%)
Group I (n=5)					
Control	3.7 ± 0.1	6.02 ± 0.14	1.07 ± 0.05	4.95 ± 0.11	17.8 ± 0.6
NSS(IR)	3.7 ± 0.1	5.95 ± 0.13	1.04 ± 0.04	4.91 ± 0.11	17.5 ± 0.6
NSS(IR)+$NaVO_3$(IV)	5.8 ± 0.1 *** $$$	7.12 ± 0.17 * $	0.64 ± 0.05 *** $$$	6.48 ± 0.16 ** $$	9.05 ± 0.6 *** $$$
Recovery	4.2 ± 0.2 * $$	5.33 ± 0.31 $$	1.02 ± 0.03 $$	4.31 ± 0.31 $$	19.4 ± 1.1 $$
Group II (n=5)					
Control	3.4 ± 0.1	4.73 ± 0.14	0.66 ± 0.06	4.07 ± 0.20	14.1 ± 1.8
Pra(IR)	3.4 ± 0.0	5.50 ± 0.17 ***	0.72 ± 0.04	4.78 ± 0.17 ***	13.1 ± 0.7
Pra(IR)+$NaVO_3$(IV)	4.0 ± 0.2	2.30 ± 0.39 ** $$	0.30 ± 0.06 * $$$	2.00 ± 0.33 * $$	12.9 ± 0.5
Recovery	4.0 ± 0.1 **	4.06 ± 0.39 $$$	0.89 ± 0.10 * $$$	3.17 ± 0.31 $$$	21.9 ± 1.0 ** $$
Group III (n=5)					
Control	3.9 ± 0.1	5.13 ± 0.32	1.04 ± 0.04	4.09 ± 0.29	20.5 ± 0.6
AT(IR)	4.0 ± 0.2	5.92 ± 0.46 *	1.23 ± 0.05 *	4.69 ± 0.47	21.3 ± 1.7
AT(IR)+$NaVO_3$(IV)	4.8 ± 0.1 *** $$	3.93 ± 0.22	0.56 ± 0.03 ** $$$	3.37 ± 0.21	14.3 ± 0.9 *** $
Recovery	4.8 ± 0.2 *	6.59 ± 0.56 $$	0.95 ± 0.03 $$	5.65 ± 0.57 $	14.8 ± 1.3 *
Group IV (n=5)					
Control	3.7 ± 0.1	5.07 ± 0.18	0.96 ± 0.04	4.10 ± 0.16	19.1 ± 0.7
MK422(v)	3.6 ± 0.1	6.11 ± 0.16 *	1.11 ± 0.06 **	5.00 ± 0.19 *	18.2 ± 1.2
MK422(v)+$NaVO_3$(IV)	4.4 ± 0.1 ** $$	3.88 ± 0.40 * $	0.99 ± 0.11	2.89 ± 0.38 * $	26.9 ± 3.4
Recovery	4.7 ± 0.1 ***	5.83 ± 0.34 * $$	1.59 ± 0.09 ** $	4.24 ± 0.33 $	27.7 ± 2.0 *
Group V (n=5)					
Control	3.8 ± 0.1	4.88 ± 0.16	1.02 ± 0.03	3.86 ± 0.15	20.9 ± 0.7
ACh(IR)	3.8 ± 0.1	6.25 ± 0.22 **	1.35 ± 0.03 **	4.90 ± 0.19	21.7 ± 0.4
ACh(IR)+$NaVO_3$(IV)	4.0 ± 0.1 * $	3.22 ± 0.10 *** $$$	1.13 ± 0.10	2.08 ± 0.18 *** $$$	35.7 ± 3.7 * $
Recovery	4.2 ± 0.2 *	6.18 ± 0.49 * $$	0.96 ± 0.07	5.22 ± 0.52 * $$	16.3 ± 2.3 $$
Group VI (n=5)					
Control	3.6 ± 0.1	4.85 ± 0.44	1.07 ± 0.03	3.78 ± 0.43	22.8 ± 1.9
Ver(IR)	3.5 ± 0.1	5.51 ± 0.39 **	1.57 ± 0.08 **	3.93 ± 0.33	28.9 ± 1.4 *
Ver(IR)+$NaVO_3$(IV)	4.1 ± 0.1	4.33 ± 0.28 $	1.61 ± 0.07 **	2.72 ± 0.22 $	37.5 ± 0.9 ** $$
Recovery	4.5 ± 0.1	4.50 ± 0.37	1.27 ± 0.12 $	3.23 ± 0.34	28.6 ± 2.5

Values are the means±SEM. Only one experimental kidney values are presented.

Abbreviations : P_K, plasma potassium concentration; $GFR \times P_K$, filtered load of potassium; U_KV, urinary potassium excretion; T_K, tubular reabsorption of potassium; FE_K, fractional excretion of potassium.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.

Table 5. Changes in chloride excretion in response to intravenous sodium metavanadate infusion in all groups.

Parameter	P_{Cl} (mEq/L)	$GFR \times P_{Cl}$ (μEq/min/kg.bw.)	$U_{Cl}V$ (μEq/min/kg.bw.)	T_{Cl} (μEq/min/kg.bw.)	FE_{Cl} (%)
Group I (n=5)					
Control	108.2 ± 1.4	178.15 ± 5.63	5.16 ± 0.15	173.00 ± 5.50	2.9 ± 0.1
NSS(IR)	108.0 ± 1.1	176.06 ± 5.17	5.16 ± 0.17	170.91 ± 5.03	2.9 ± 0.1
NSS(IR)+$NaVO_3$(IV)	120.2 ± 1.1 ** $$	147.83 ± 4.78 ** $$	2.31 ± 0.09 *** $$$	145.52 ± 4.71 ** $$	1.6 ± 0.0 *** $$$
Recovery	117.6 ± 1.1 * $	148.50 ± 5.95 ***	4.35 ± 0.23 $$	144.15 ± 6.15 ***	3.0 ± 0.3
Group II (n=5)					
Control	104.6 ± 0.9	144.78 ± 4.26	4.56 ± 0.11	140.22 ± 4.33	3.2 ± 0.2
Pra(IR)	106.6 ± 1.3	171.23 ± 4.63 *	4.79 ± 0.13	166.44 ± 4.62 *	2.8 ± 0.1
Pra(IR)+$NaVO_3$(IV)	118.4 ± 3.4 * $	68.31 ± 11.58 ** $$$	2.49 ± 0.10 *** $$$	65.82 ± 11.50 ** $$$	4.0 ± 0.5
Recovery	107.6 ± 0.6 $	107.28 ± 7.20 * $$	3.23 ± 0.38	104.05 ± 6.85 * $$	3.0 ± 0.2
Group III (n=5)					
Control	107.0 ± 0.7	139.39 ± 5.48	3.68 ± 0.21	135.70 ± 5.47	2.7 ± 0.2
AT(IR)	108.4 ± 2.1	159.21 ± 5.95 *	4.33 ± 0.19 **	154.88 ± 5.95 *	2.7 ± 0.2
AT(IR)+$NaVO_3$(IV)	114.6 ± 2.5 * $	93.62 ± 7.03 * $$	2.02 ± 0.11 ** $$	91.60 ± 6.93 * $$	2.2 ± 0.1
Recovery	114.8 ± 3.2	158.12 ± 16.66 $$	3.17 ± 0.35 $	154.94 ± 16.51 $$	2.1 ± 0.2
Group IV (n=5)					
Control	104.4 ± 1.3	143.14 ± 5.74	4.14 ± 0.22	139.00 ± 5.62	2.9 ± 0.1
MK422(v)	108.4 ± 1.8 **	182.12 ± 6.22 **	3.95 ± 0.15	178.18 ± 6.31 **	2.2 ± 0.1 ***
MK422(v)+$NaVO_3$(IV)	116.0 ± 2.1 ** $	101.93 ± 11.05 * $$	2.35 ± 0.08 ** $$	99.58 ± 11.00 * $$	2.4 ± 0.3
Recovery	115.4 ± 1.4 ***	143.52 ± 7.56 $	5.67 ± 0.76 $	137.85 ± 7.95 $	4.1 ± 0.8
Group V (n=5)					
Control	105.2 ± 1.4	136.29 ± 2.46	3.70 ± 0.13	132.59 ± 2.53	2.7 ± 0.1
ACh(IR)	109.4 ± 1.5 *	179.24 ± 6.17 **	4.32 ± 0.08 *	174.93 ± 6.17 **	2.4 ± 0.1
ACh(IR)+$NaVO_3$(IV)	115.4 ± 0.6 ** $	91.85 ± 1.87 *** $$$	1.78 ± 0.14 *** $$$	90.07 ± 1.93 *** $$$	1.9 ± 0.2 *
Recovery	109.4 ± 1.6	159.98 ± 7.75 * $$$	2.49 ± 0.17 *** $	157.49 ± 7.86 * $$$	1.6 ± 0.2 ***
Group VI (n=5)					
Control	104.2 ± 1.0	139.23 ± 8.25	4.17 ± 0.38	135.06 ± 8.56	3.1 ± 0.5
Ver(IR)	108.0 ± 1.0 *	168.12 ± 10.94 **	6.84 ± 0.48 *	161.28 ± 11.12 **	4.2 ± 0.5 *
Ver(IR)+$NaVO_3$(IV)	110.8 ± 1.2 *	119.42 ± 10.54 $	6.74 ± 0.75 *	112.68 ± 10.02 $	5.7 ± 0.5 ** $
Recovery	110.6 ± 2.5	110.63 ± 7.36 *	4.58 ± 0.44 $$	106.04 ± 7.32 *	4.2 ± 0.5 * $$

Values are the means±SEM. Only one experimental kidney values are presented.
Abbreviations : P_{Cl}, plasma chloride concentration; $GFR \times P_{Cl}$, filtered load of chloride; $U_{Cl}V$, urinary chloride excretion; T_{Cl}, tubular reabsorption of chloride; FE_{Cl}, fractional excretion of chloride.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.

Table 6. Changes in bicarbonate excretion in response to intravenous sodium metavanadate infusion in all groups.

Parameter	B_{HCO_3} (mmole/L)	$GFR \times B_{HCO_3}$ (μmole/min/kg.bw.)	$U_{HCO_3}V$ (μmole/min/kg.bw.)	T_{HCO_3} (μmole/min/kg.bw.)	FE_{HCO_3} (%)
Group I (n=5)					
Control	22.5 ± 0.6	37.16 ± 2.12	0.08 ± 0.00	37.08 ± 2.11	0.23 ± 0.01
NSS(IR)	22.6 ± 0.6	36.96 ± 2.18	0.09 ± 0.00	36.87 ± 2.17	0.24 ± 0.01
NSS(IR)+$NaVO_3$(IV)	16.8. ± 0.8 *** $$$	20.72 ± 1.55 *** $$$	0.09 ± 0.01	20.63 ± 1.55 *** $$$	0.46 ± 0.04 ** $$
Recovery	21.7 ± 0.8 $	27.37 ± 1.00 * $	0.08 ± 0.01	27.29 ± 1.00 * $	0.28 ± 0.03 $
Group II (n=5)					
Control	25.3 ± 0.7	34.95 ± 0.59	0.06 ± 0.00	34.88 ± 0.59	0.18 ± 0.01
Pra(IR)	24.7 ± 0.7 **	39.66 ± 1.26 *	0.11 ± 0.01	39.56 ± 1.27 *	0.27 ± 0.04
Pra(IR)+$NaVO_3$(IV)	21.1 ± 0.7 *** $$$	12.24 ± 2.17 ** $$$	0.01 ± 0.00 *** $$	12.23 ± 2.17 ** $$$	0.08 ± 0.01 ** $
Recovery	21.9 ± 1.7	22.05 ± 2.57 * $$	0.06 ± 0.01 $$	21.99 ± 2.57 * $$	0.27 ± 0.03 $
Group III (n=5)					
Control	23.5 ± 0.5	30.53 ± 0.89	0.08 ± 0.01	30.46 ± 0.88	0.25 ± 0.04
AT(IR)	21.7 ± 0.3 *	31.88 ± 1.26	0.10 ± 0.02 **	31.77 ± 1.25	0.32 ± 0.05 *
AT(IR)+$NaVO_3$(IV)	19.4 ± 1.0 *	16.02 ± 1.78 ** $$	0.07 ± 0.01	15.95 ± 1.78 ** $$	0.46 ± 0.10 *
Recovery	20.9 ± 0.6 *	28.86 ± 3.10 $$	0.06 ± 0.00	28.80 ± 3.10 $$	0.21 ± 0.01
Group IV (n=5)					
Control	25.9 ± 0.7	35.41 ± 1.48	0.11 ± 0.01	35.30 ± 1.48	0.30 ± 0.03
MK422(v)	22.6 ± 0.3 *	37.91 ± 0.64	0.11 ± 0.02	37.80 ± 0.65	0.30 ± 0.06
MK422(v)+$NaVO_3$(IV)	24.4 ± 1.1	21.23 ± 2.16 ** $$	0.07 ± 0.01 **	21.17 ± 2.17 * $$	0.35 ± 0.07
Recovery	25.2 ± 0.9	31.20 ± 1.53 $$	0.23 ± 0.03 ** $$	30.96 ± 1.54 $$	0.77 ± 0.11 ** $
Group V (n=5)					
Control	25.8 ± 0.4	33.45 ± 0.95	0.12 ± 0.01	33.33 ± 0.96	0.35 ± 0.03
ACh(IR)	26.4 ± 0.5	43.26 ± 1.35 **	0.15 ± 0.01 *	43.12 ± 1.35	0.34 ± 0.02
ACh(IR)+$NaVO_3$(IV)	22.8 ± 0.6 * $$$	18.20 ± 0.74 *** $$$	0.08 ± 0.01 ** $$	18.12 ± 0.74 *** $$$	0.42 ± 0.05
Recovery	22.7 ± 1.0	33.46 ± 2.93 $$	0.08 ± 0.01 **	33.38 ± 2.93 $$	0.25 ± 0.06
Group VI (n=5)					
Control	25.5 ± 0.2	34.04 ± 2.04	0.19 ± 0.02	33.85 ± 2.05	0.57 ± 0.08
Ver(IR)	28.5 ± 0.3 ***	44.11 ± 2.51 ***	0.27 ± 0.03	43.84 ± 2.53 ***	0.62 ± 0.08
Ver(IR)+$NaVO_3$(IV)	22.4 ± 0.4 ** $$	24.20 ± 2.23 * $$	0.29 ± 0.05	23.91 ± 2.18 * $$	1.16 ± 0.15 * $$
Recovery	23.3 ± 0.4 *	23.26 ± 1.53 **	0.32 ± 0.06	22.95 ± 1.53 **	1.38 ± 0.27 *

Values are the means±SEM. Only one experimental kidney values are presented.
Abbreviations : P_{HCO_3}, plasma bicarbonate concentration; $GFR \times P_{HCO_3}$, filtered load of bicarbonate; $U_{HCO_3}V$, urinary bicarbonate excretion; T_{HCO_3}, tubular reabsorption of bicarbonate; FE_{HCO_3}, fractional excretion of bicarbonate.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.

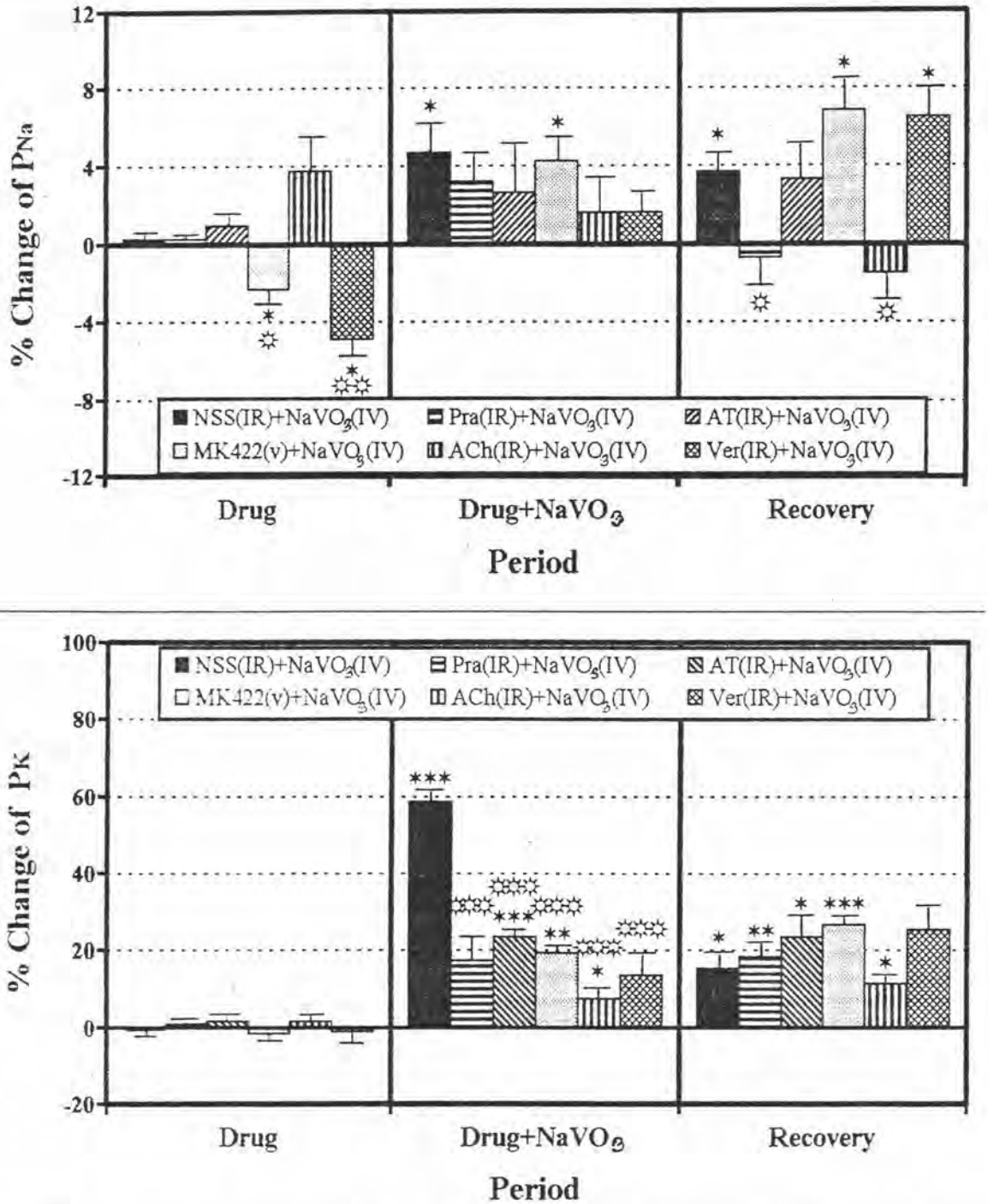


Figure 5 Percentage changes in plasma sodium concentration (P_{Na}) and plasma potassium concentration (P_K) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

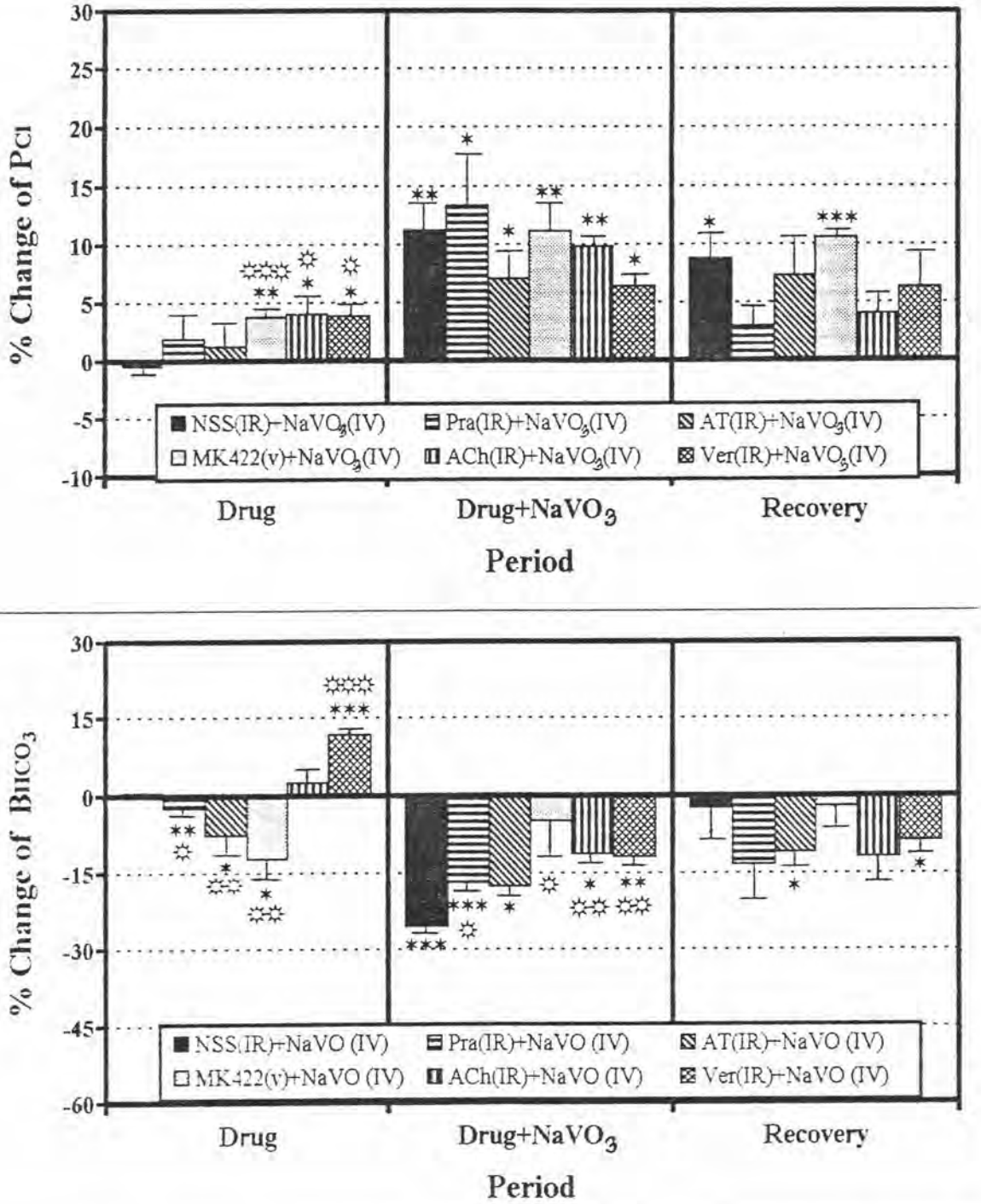


Figure 6 Percentage changes in plasma chloride concentration (P_{Cl}) and blood bicarbonate concentration (B_{HCO_3}) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcoline (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

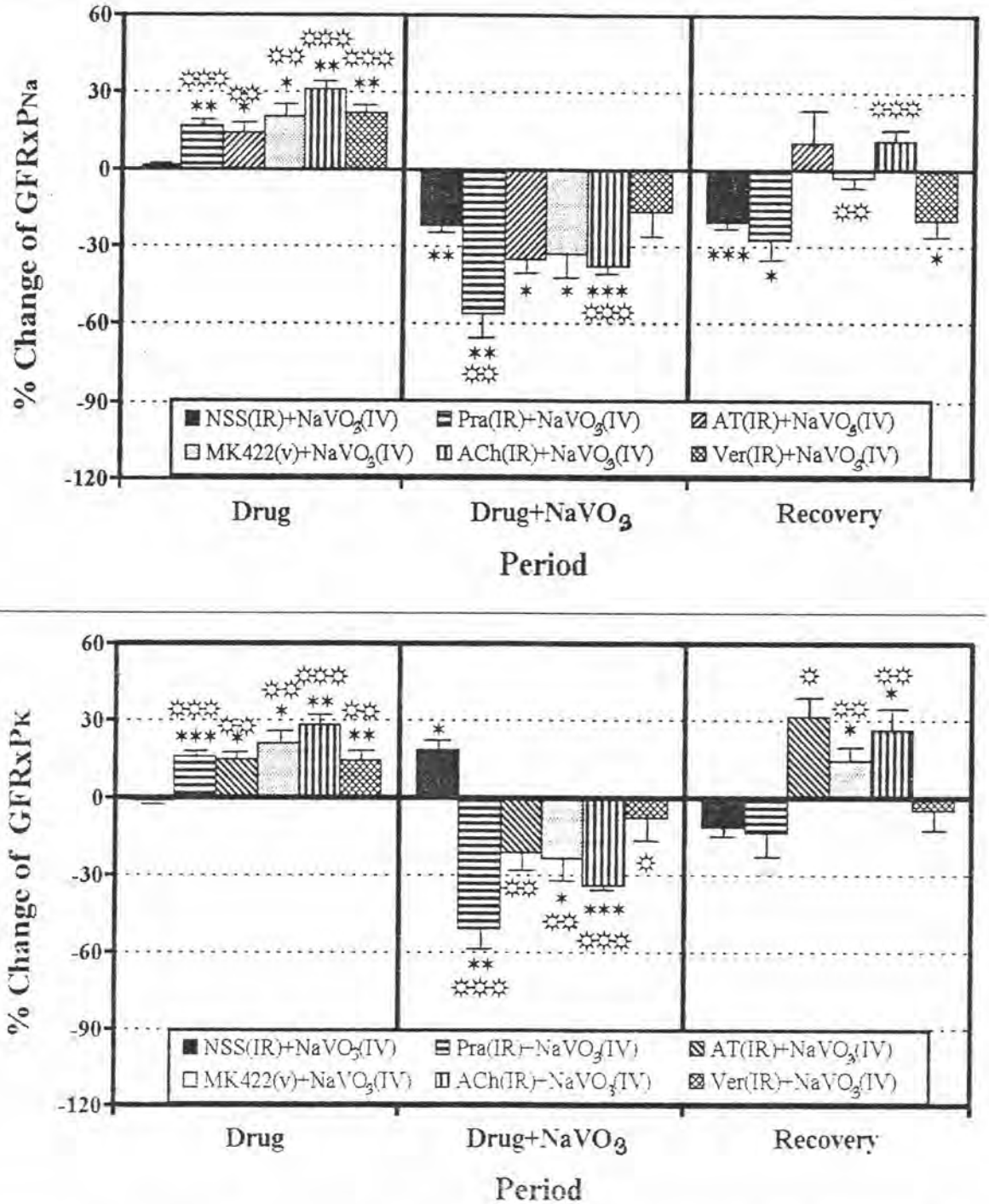


Figure 7 Percentage changes in filter load of sodium ($GFRxP_{Na}$) and potassium ($GFRxP_K$) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).
Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.
Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

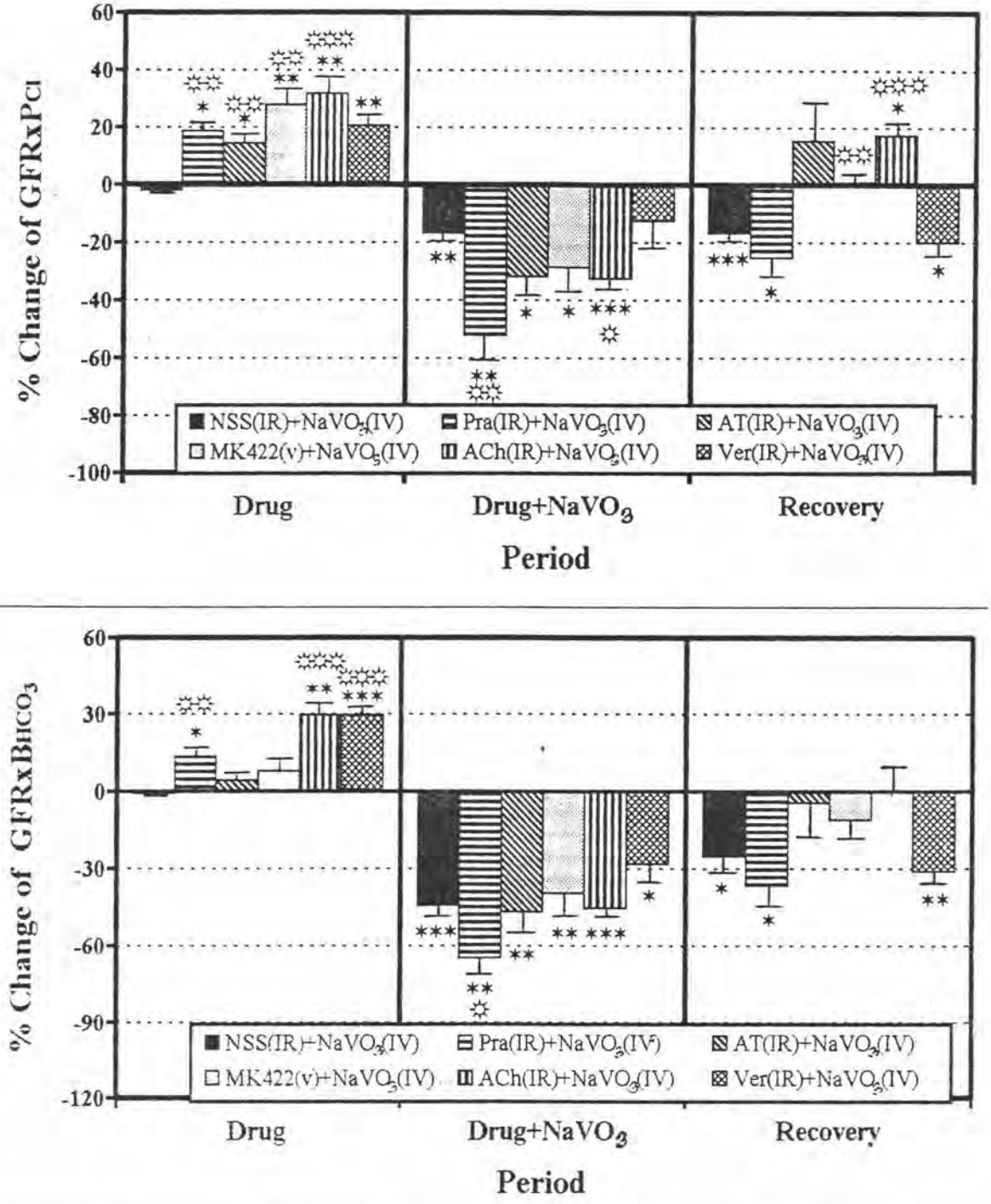


Figure 8 Percentage changes in filter load of chloride (GFRxPCl) and bicarbonate ($GFRxB_{HCO_3}$) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

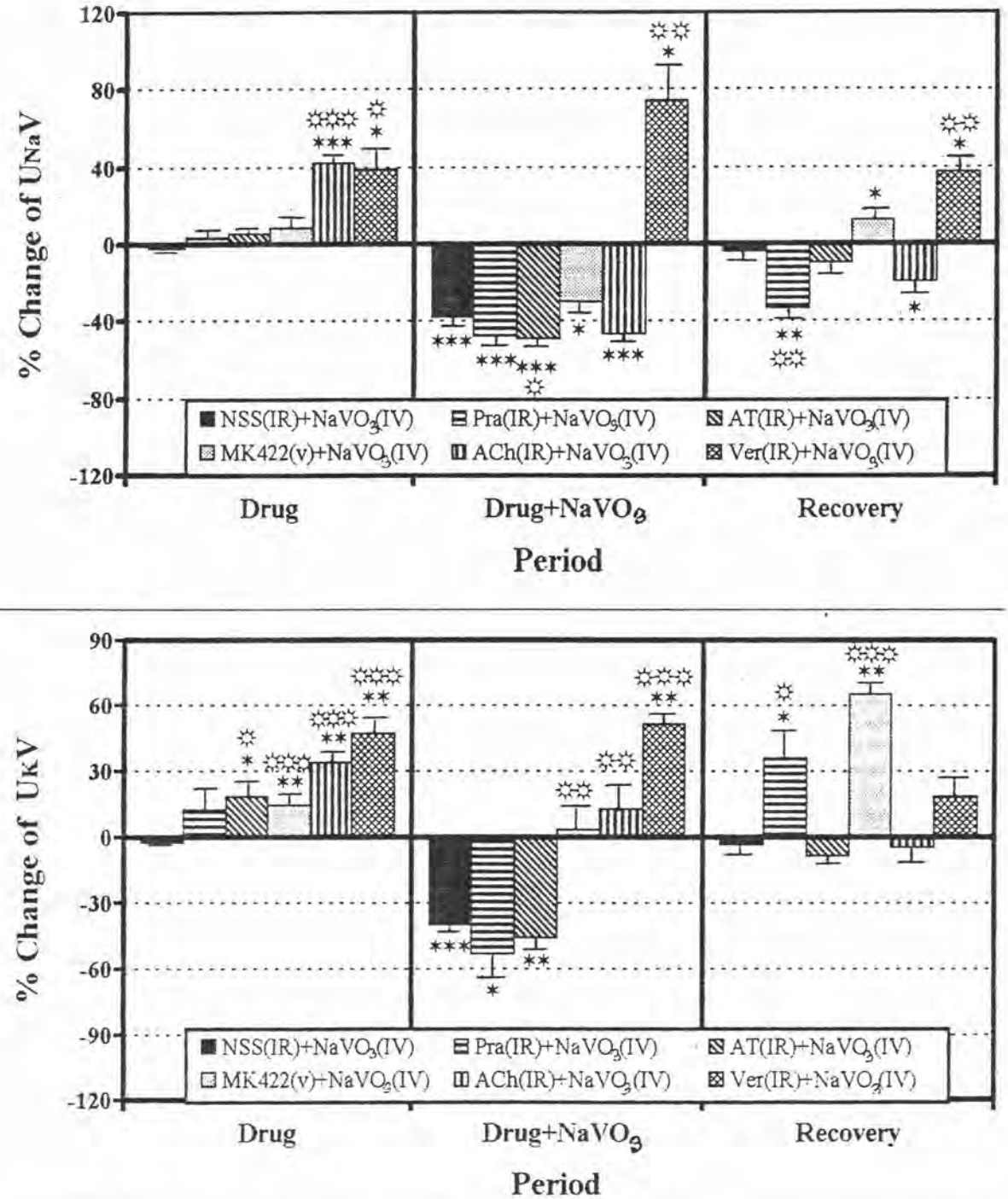


Figure 9 Percentage changes in urinary sodium excretion (U_{NaV}) and urinary potassium excretion (U_{KV}) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$; ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

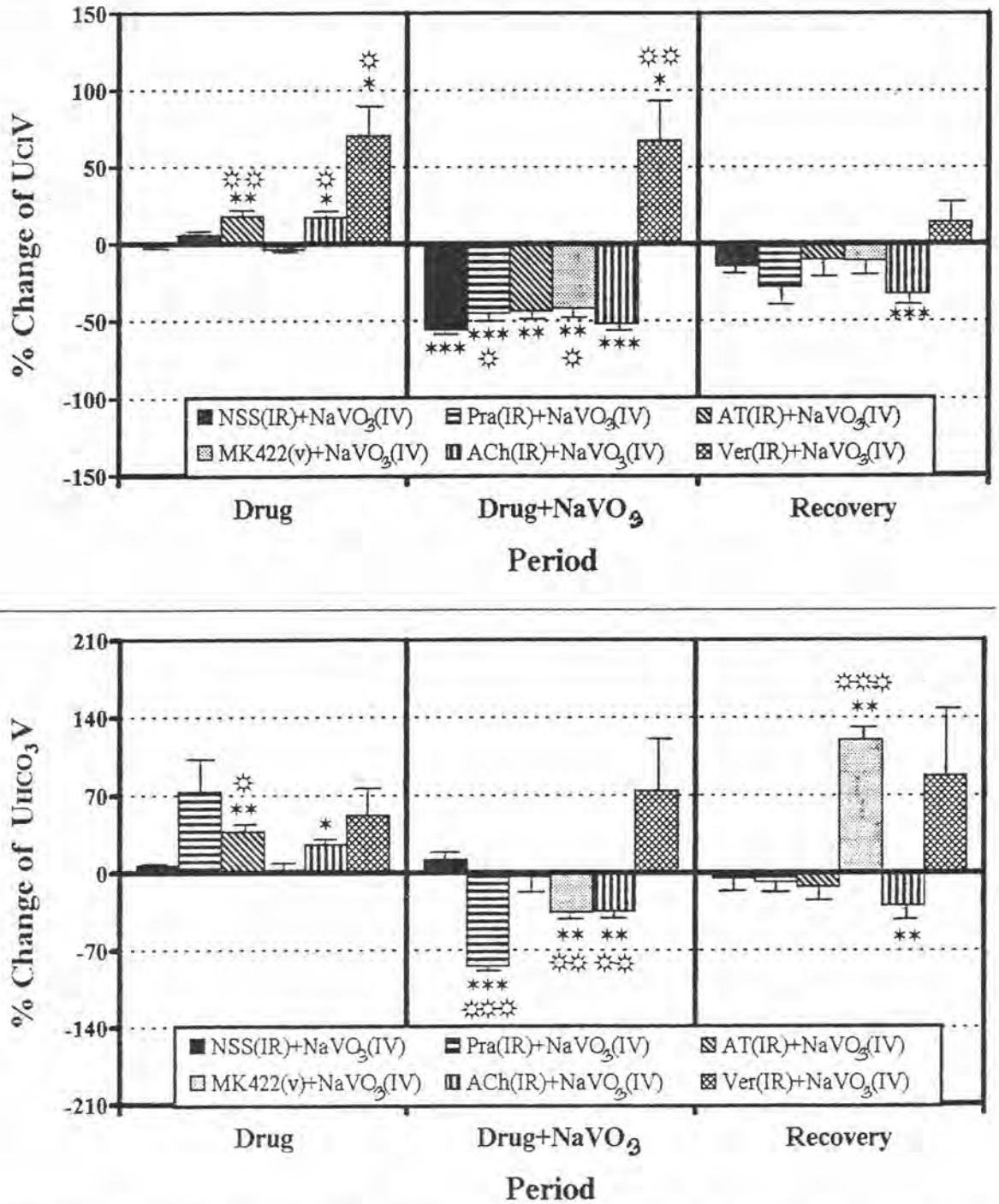


Figure 10 Percentage changes in urinary chloride excretion ($U_{Cl}V$) and urinary bicarbonate excretion ($U_{HCO_3}V$) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (GroupI) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

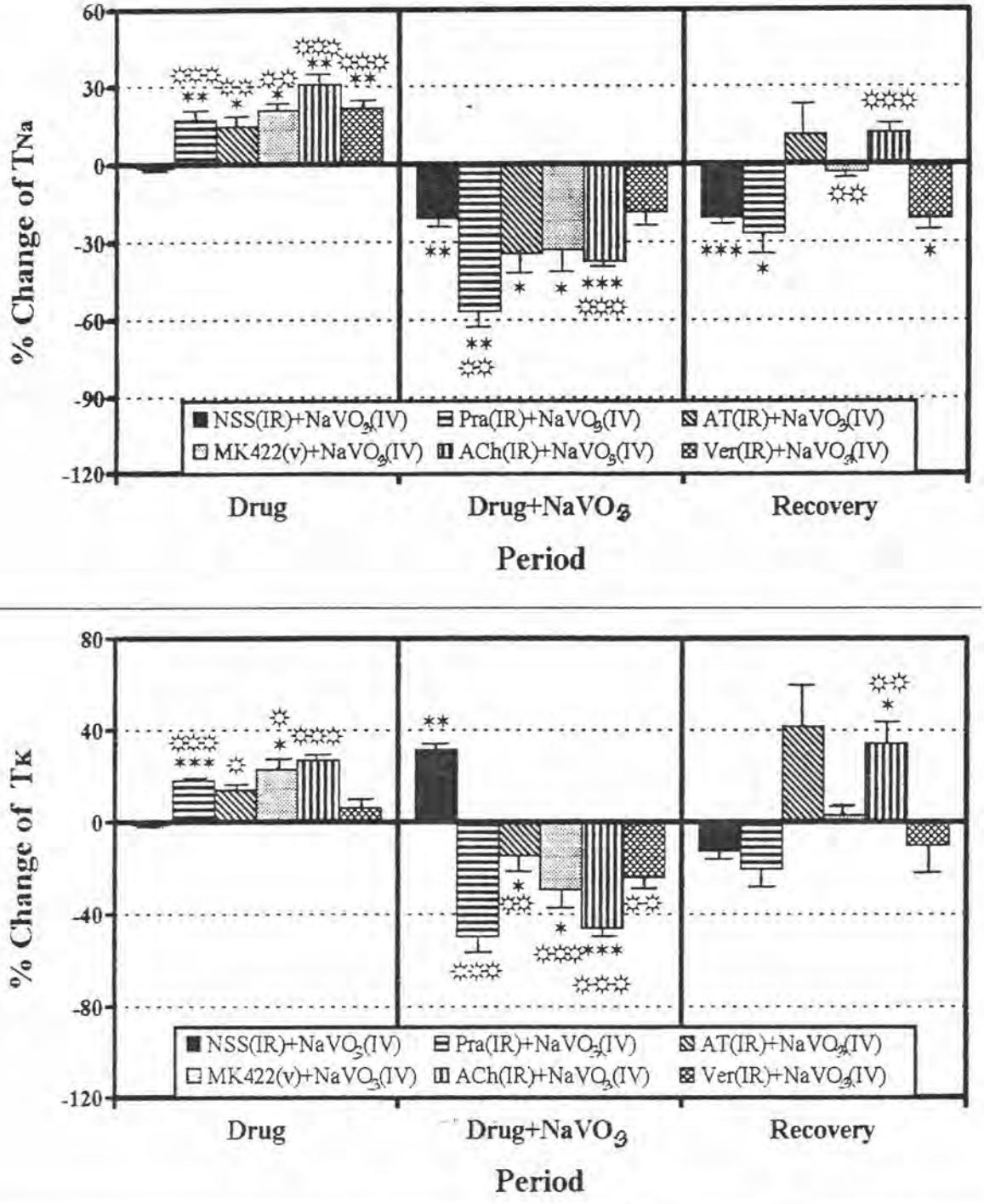


Figure 11 Percentage changes in tubular reabsorption of sodium (T_{Na}) and potassium (T_K) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), Verapamil (Ver), and verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

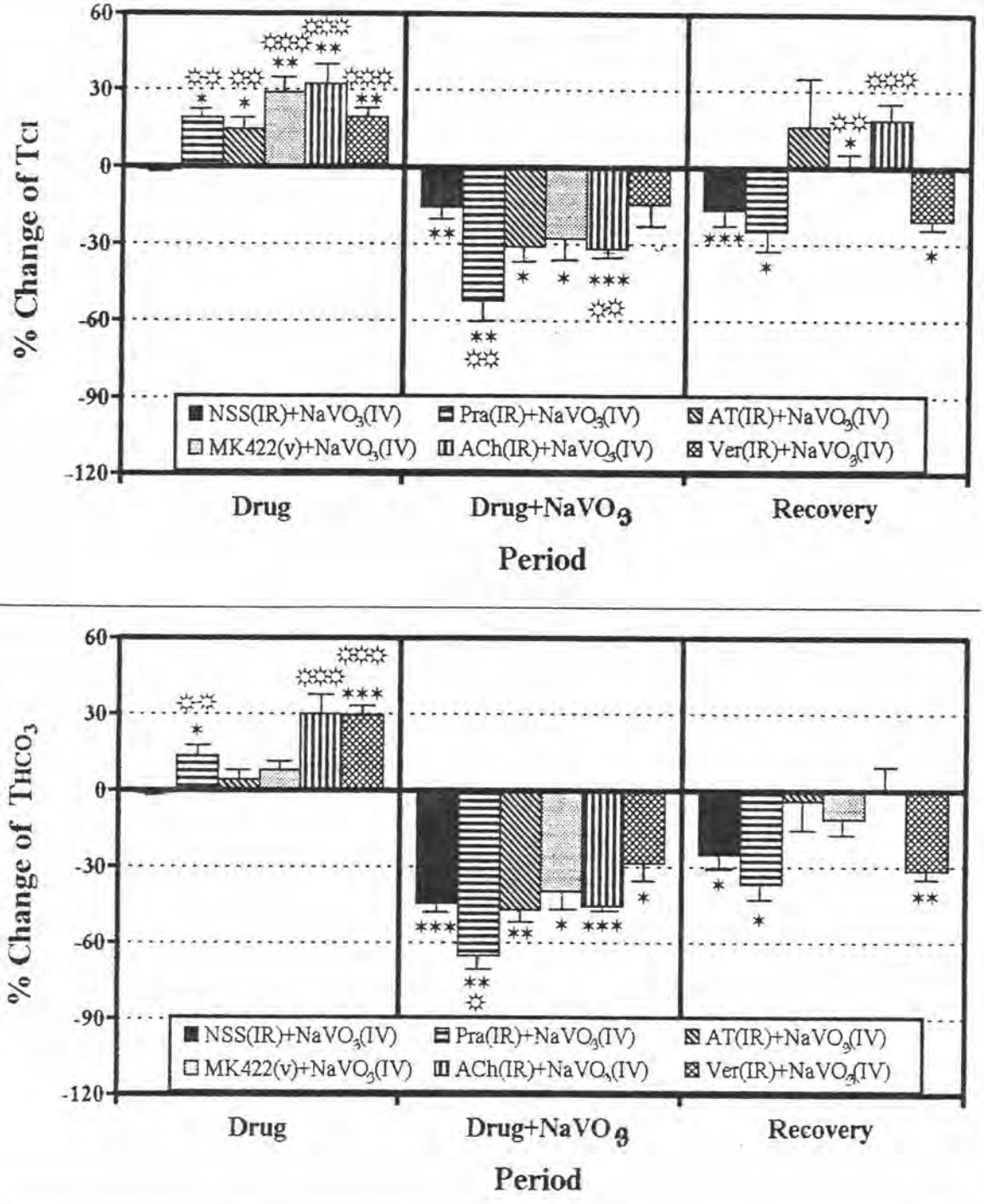


Figure 12 **Percentage changes in tubular reabsorption of chloride (T_{Cl}) and bicarbonate (T_{HCO_3}) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).**
Significant difference values using paired t'test are indicated by * P<0.05, **P<0.01, *** P<0.001 compaired to the control value of each group.
Significant difference values using unpaired t'test are indicated by ☼ P<0.05, ☼☼P<0.01,☼☼☼ P<0.001 compaired to group I at the same time interval.

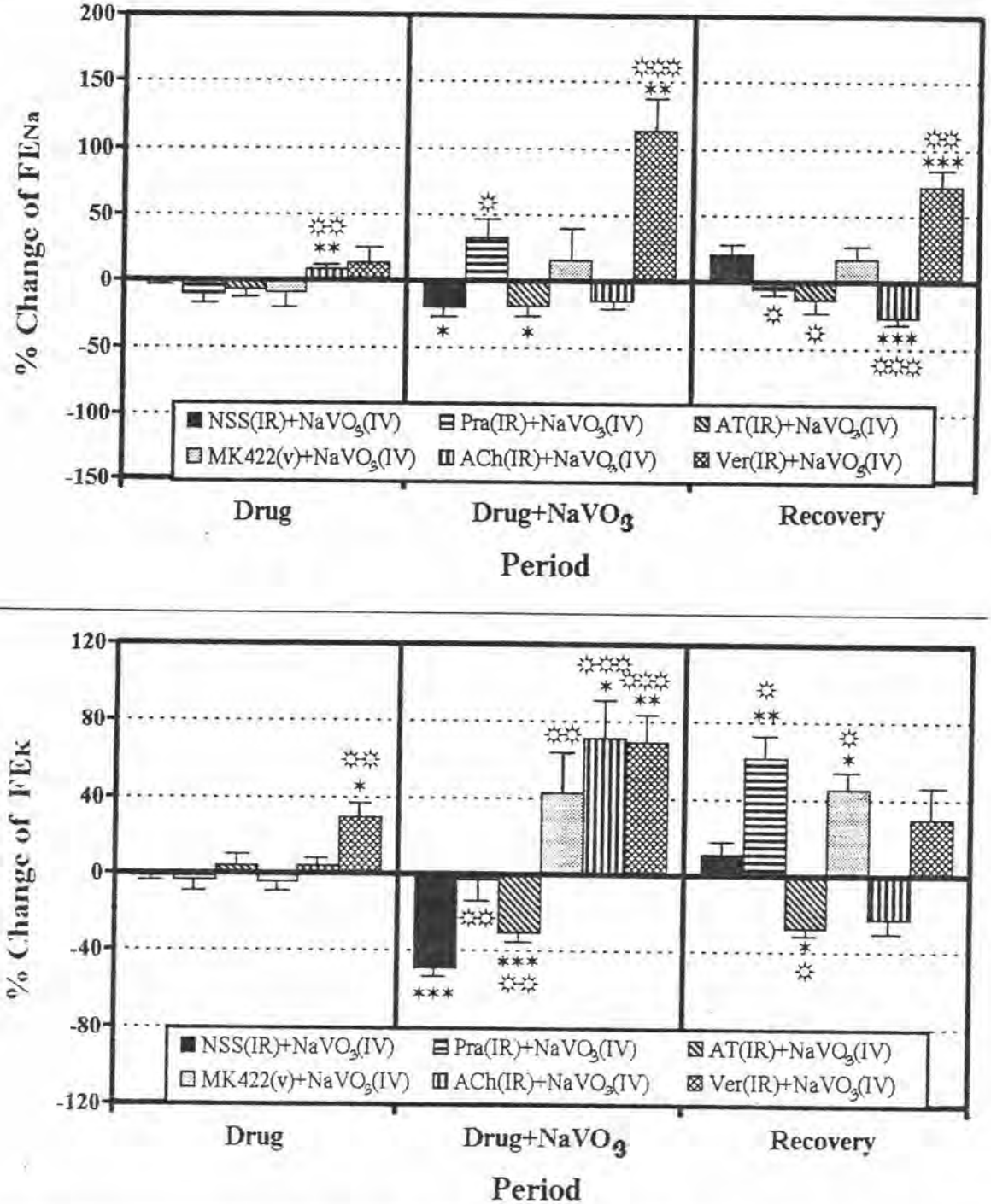


Figure 13 Percentage changes in fractional reabsorption of sodium (FE_{Na}) and potassium (FE_K) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

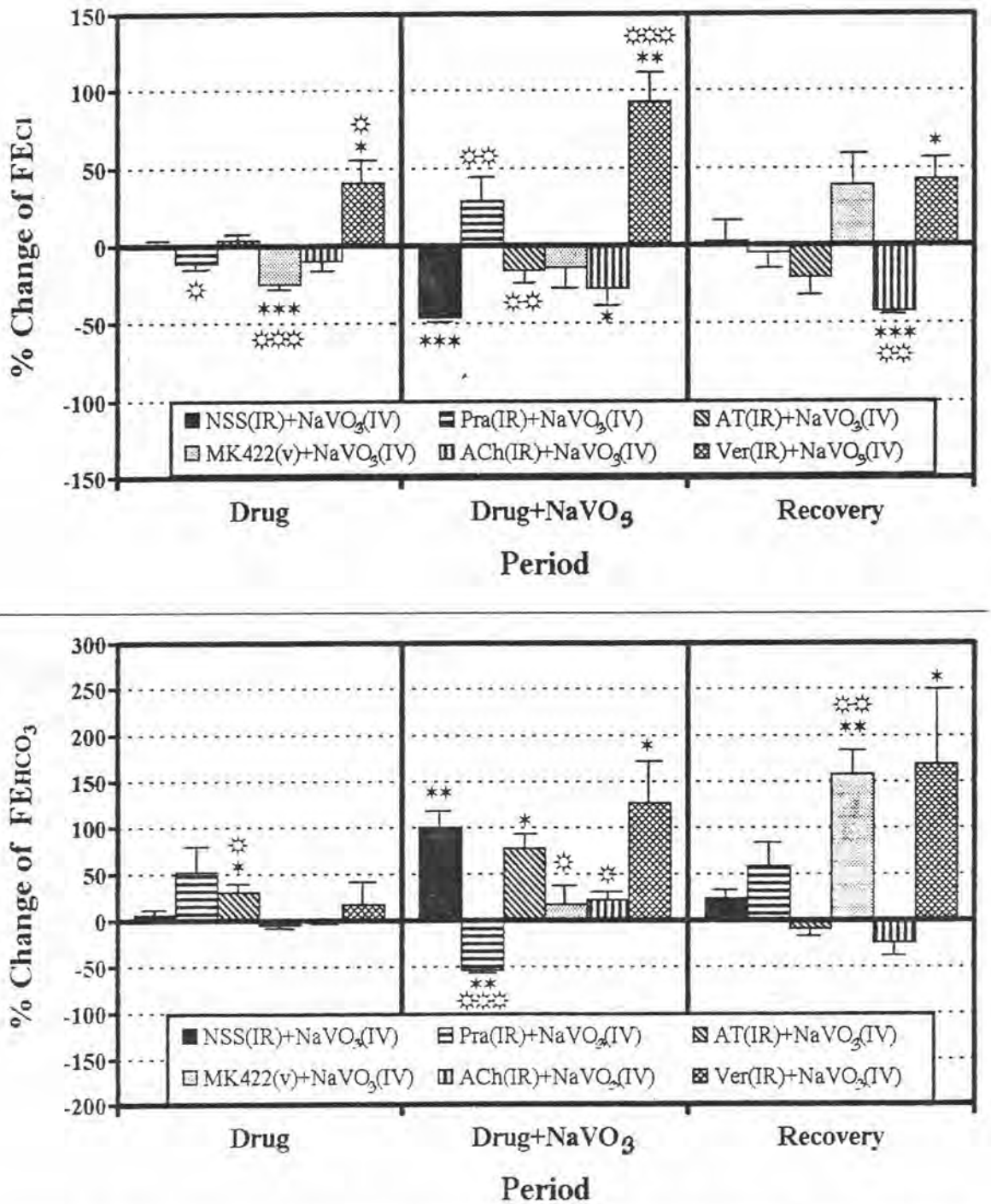


Figure 14 Percentage changes in fractional reabsorption of chloride (FE_{Cl}) and bicarbonate (FE_{HCO_3}) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼$P<0.05$, ☼☼$P<0.01$, ☼☼☼$P<0.001$ compaired to group I at the same time interval.

Table 7. Changes in plasma and urine anion gap in response to intravenous sodium metavanadate infusion in six groups.

Parameter	Plasma anion gap (mEq/L)		Urine anion gap (mEq/L)	
Group I (n=5)				
Control	9.93 ± 0.76		59.68 ± 4.42	
NSS(IR)	10.44 ± 0.31		57.16 ± 5.93	
NSS(IR)+NaVO3(IV)	10.25 ± 2.36		119.72 ± 4.40	** $$
Recovery	6.45 ± 2.14		88.16 ± 3.87	* $
Group II (n=5)				
Control	11.87 ± 1.40		75.56 ± 11.76	
Pra(IR)	10.89 ± 2.13		44.87 ± 4.39	
Pra(IR)+NaVO3(IV)	6.92 ± 2.75		114.48 ± 23.07	
Recovery	11.28 ± 1.04		72.43 ± 22.66	
Group III (n=5)				
Control	11.30 ± 0.76		74.38 ± 7.22	
AT(IR)	13.12 ± 1.05		49.88 ± 7.38	**
AT(IR)+NaVO3(IV)	11.39 ± 2.23		43.76 ± 4.05	**
Recovery	10.69 ± 1.41		66.82 ± 12.21	
Group IV (n=5)				
Control	10.94 ± 1.11		57.70 ± 6.17	
MK422(v)	7.00 ± 1.25	*	64.00 ± 7.75	
MK422(V)+NaVO3(IV)	6.82 ± 0.75	*	86.28 ± 7.48	
Recovery	10.20 ± 0.98		80.98 ± 11.02	
Group V (n=5)				
Control	11.61 ± 2.09		48.74 ± 4.94	
ACh(IR)	11.98 ± 2.03		68.26 ± 3.62	*
ACh(IR)+NaVO3(IV)	6.58 ± 1.94		70.26 ± 9.13	
Recovery	8.34 ± 1.81		73.18 ± 15.20	
Group VI (n=5)				
Control	10.52 ± 0.51		49.78 ± 8.42	
Ver(IR)	10.33 ± 0.85		25.88 ± 5.99	*
Ver(IR)+NaVO3(IV)	9.16 ± 1.16		44.6 ± 7.94	$$
Recovery	15.35 ± 1.87		46.58 ± 7.76	

Values are means±SEM. Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 different from control and by $ P<0.05, $$ P<0.01, $$$ P<0.001 different from previous values.

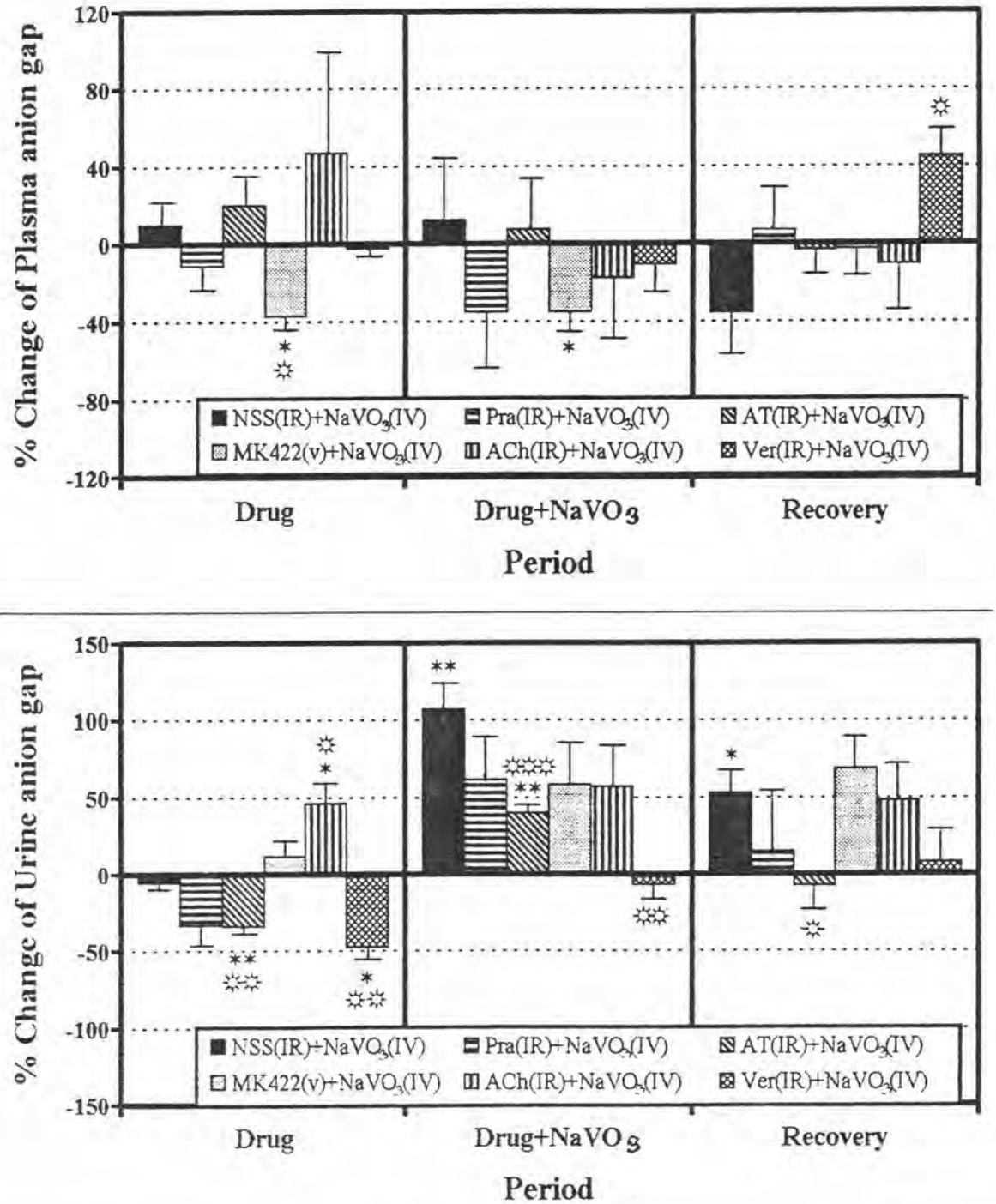


Figure 15 Percentage changes in plasma anion gap and urine anion gap in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and inravenous injection with enalapril maleate (MK422).
Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.
Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

Effects of Intravenous Sodium Metavanadate Infusion on Urinary Acid-Base Excretion.

The results of changes in urinary acid-base excretion in dogs given intravenous sodium metavanadate infusion without pretreatment of various drugs (group I) and pretreatment of intrarenal arterial infusion with prazosin (group II), atenolol (group III), acetylcholine (group V), verapamil (group VI), and intravenous injection with MK422 (group IV) are summerized in Table 8-9 and Figure 16-20 .

Group I : Animals Pretreated With Isotonic Normal Saline Solution Before Sodium Metavanadate Infusion

After intrarenal arterial saline infusion caused no change in any of the measurements made. The intravenous sodium metavanadate infusion developed hyperkalemic hyperchloremic metabolic acidosis with a significant decrease in blood pH from the control value of 7.43±0.01 to 7.20±0.05 ($P<0.05$), whereas urine pH was unable to lower urine pH below 5.5 significantly from the control value of 6.30±0.02 to 6.63±0.09 ($P<0.05$), so that nonbicarbonate buffer wuold not be expected to contribute to the urine P_{CO_2} above systemic arterial blood levels, though blood P_{CO_2} and urine P_{CO_2} rose up without statistically significance. Therefore, no significant decrease in the difference between urine and blood (U-B P_{CO_2}) was observed (Table 8). Urinary excretion of titratable acidity ($U_{TA}V$) significantly decreased to 54.44±7.38 % of the control value ($P<0.05$), as for urinary excretion of ammonium ($U_{NH_4}V$) significantly decreased to 62.37±5.16 % of the control value ($P<0.05$), while urinary excretion of bicarbonate remained unchanged, so that fractional net acid excretion (NAE/GFR) significantly reduced to 62.94±5.99 % of the control value ($P<0.05$).

Stopping the sodium metavanadate infusion, blood pH returned to basal control value and significantly increased from the the experimental period value ($P<0.01$). Urine pH returned to basal control value without significant difference from the experimental period value. Blood P_{CO_2} and urine P_{CO_2} returned to basal control value and significantly increased from the experimental period value ($P<0.05$). Thus, the U-B P_{CO_2} difference remained reduced without statistically significance. Urinary excretion of titratable acidity returned to basal control value and significantly raised form the experimental period value ($P<0.05$). Urinary excretion of ammonium insignificantly decreased from the control value, while it insignificantly increased from the experimental period value. No significant change in urinary excretion of bicarbonate was observed. Therefore, fractional net acid excretion returned to basal control value and significantly elevated from the experimental period value ($P<0.05$).

Group II : **Animals Pretreated With Prazosin (Pra) Before Sodium Metavanadate Infusion**

After intrarenal infusion of prazosin alone, there were no different in any of the measurements made. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of prazosin caused no developed metabolic acidosis. However, blood pH significantly decreased from the control value of 7.50 ± 0.02 to 7.47 ± 0.01 ($P<0.05$) and from the given prazosin alone value ($P<0.05$), whereas urine pH insignificantly fell from the control value and from the given prazosin alone value ($P<0.01$). No significant increase in blood P_{CO_2} was observed, while urine P_{CO_2} significantly increased from the control value of 36.03 ± 0.72 to 40.83 ± 0.89 ($P<0.05$) and from the given prazosin alone value ($P<0.001$). Thus, no significant decrease in the difference between urine and blood (U-B P_{CO_2}) was observed. There were no significant change in urinary excretion of titratable acidity and ammonium,

while urinary excretion of bicarbonate markedly significantly decreased from the control value ($P<0.001$) and from the given prazosin alone value ($P<0.01$), so that no significant change in fractional net acid excretion was observed.

Withdrawal of sodium metavanadate and prazosin infusion, there were no significant alteration in blood pH, urine pH, and blood P_{CO_2}, while urine P_{CO_2} significantly increased from the control value ($P<0.05$) without significant from the experimental period value. Therefore, the U-B P_{CO_2} difference and remained reduced without statistically significance. Urinary excretion of titratable acidity and ammonium insignificantly decreased from the control value, while it insignificantly increased from the experimental period value, while urinary excretion of bicarbonate returned to basal control value and significantly elevated from the experimental period value ($P<0.01$). Thus, no significant rose up in fractional net acid excretion was observed.

Group III : **Animals Pretreated With Atenolol (AT) Before Sodium Metavanadate Infusion.**

After intrarenal infusion of atenolol alone, although there was no significant change from the control value in urinary excretion of titratable, urinary excretion of ammonium and bicarbonate significantly increased from the control value ($P<0.01$), so that fractional net acid excretion significantly rose up from the control value ($P<0.01$). The another of the measurements made remained changed from the control value. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of atenolol caused no developed metabolic acidosis. However, blood pH significantly decreased from the control value of 7.48 ± 0.02 to 7.36 ± 0.01 ($P<0.05$) without significant from the given atenolol alone value, whereas there was no significant change in urine pH and blood P_{CO_2}, though urine P_{CO_2} insignificantly increased

from the control value but significantly raised from the given atenolol alone value ($P<0.05$). Thus, no significant increase in the difference between urine and blood (U-B P_{CO_2}) was observed. Urinary excretion of titratable acidity and ammonium significantly decreased to 30.47±4.43 % of the control value ($P<0.01$), 21.89±3.21 % of the control value ($P<0.01$), respectively, and from the given atenolol alone value ($P<0.01$), there were no significant change in urinary excretion of bicarbonate, so that fractional net acid excretion significantly decreased to 26.45±3.61 % of the control value ($P<0.01$) and from the given atenolol alone value ($P<0.001$).

Withdrawal of sodium metavanadate and atenolol infusion, blood pH significantly remained decreased from the control value ($P<0.05$) without significant from the experimental period value, whereas there was no significant change in urine pH. Blood P_{CO_2} significantly increased from the control value ($P<0.05$) without significant from the experimental period value, while there was no significant rose up in urine P_{CO_2}. Thus, no significant decrease in the difference between urine and blood (U-B P_{CO_2}) was observed. Urinary excretion of titratable acidity significantly increased from the control value ($P<0.001$) and from the experimental period value ($P<0.001$). Urinary excretion of ammonium, although it insignificantly decreased from the control value, significantly decreased from the experimental period value ($P<0.01$). No significant change in urinary excretion of bicarbonate was observed, so that fractional net acid excretion significantly increased to 36.96±8.62 % of the control value ($P<0.05$) and from the experimental period value ($P<0.001$).

Group IV : **Animals Pretreated With Enalapril Maleate (MK 422) Before Sodium Metavanadate Infusion.**

Single dose intravenous injection of MK422 alone, there was no significant change from the control value in blood pH, whereas urine pH significantly decreased from the control value ($P<0.05$). No significant change in blood P_{CO_2}, urine P_{CO_2}, the U-B P_{CO_2} difference were observed. Urinary excretion of titratable significantly increased from the control value ($P<0.01$), urinary excretion of ammonium and bicarbonate remained unchanged, so that fractional net acid excretion significantly rose up from the control value ($P<0.05$). When intravenous infusion of sodium metavanadate caused no developed metabolic acidosis. Blood pH, although it insignificantly decreased from the control value, significantly fell from the given MK422 alone value ($P<0.05$). Urine pH significantly decreased from the control value of 6.33 ± 0.07 to 6.15 ± 0.07 ($P<0.05$) without significant change from the given MK422 alone value. Blood P_{CO_2}, although it insignificantly changed from the control value, significantly rose up from the given MK422 alone value ($P<0.05$). Urine P_{CO_2} significantly increased from the control value of 35.77 ± 0.94 to 40.96 ± 1.07 mmHg ($P<0.01$) and from the given MK422 alone value ($P<0.01$). Thus, no significant increase in the difference between urine and blood (U-B P_{CO_2}) was observed. Urinary excretion of titratable acidity significantly increased to 28.71 ± 5.35 % of the control value ($P<0.05$) without difference from the given MK422 alone value, while there were no significant change in urinary excretion of ammonium, however, Urinary excretion of bicarbonate significantly decreased from the control value ($P<0.01$) without difference from the given MK422 alone value, so that no significant increase in fractional net acid excretion was observed.

Withdrawal of sodium metavanadate and MK422 infusion, there was no significant change in plasma pH, whereas urine pH significantly increased from the control value ($P<0.001$) and from the experimental period value ($P<0.01$). Blood P_{CO_2} significantly decreased from the control value ($P<0.05$) without significant from the experimental period value, while urine P_{CO_2} significantly decreased from the experimental period value ($P<0.05$) without significant from the control value. Thus, no significant alteration in the difference between urine and blood (U-B P_{CO_2}) was observed. Urinary excretion of titratable acidity significantly remained increased from the control value ($P<0.01$) and from the experimental period value ($P<0.05$), whereas no significant change in urinary excretion of ammonium was observed, while urinary excretion of bicarbonate significantly increased from the control value ($P<0.01$), and from the experimental period value ($P<0.01$). Thus, no significant increase in fractional net acid excretion was observed.

Group V : Animals Pretreated With Acetylcholine (ACh) Before Sodium Metavanadate Infusion

Intrarenal infusion of acetylcholine alone, blood pH and urine pH significantly decreased from the control value ($P<0.01$), blood P_{CO_2} and urine P_{CO_2} significantly increased from the control value ($P<0.01$), so that the U-B P_{CO_2} difference significantly decreased from the control value ($P<0.01$). Urinary excretion of titratable significantly increased from the control value ($P<0.05$), urinary excretion of ammonium remained unchanged, while urinary excretion of bicarbonate significantly increased from the control value ($P<0.05$) so that no significant change in fractional net acid excretion was observed.

When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of acetylcholine, caused no developed metabolic acidosis but reduced acid excretion. However, blood pH significantly fell from the control value of 7.55±0.02 to 7.37±0.03 ($P<0.01$) without significant change from the given acetlycholine alone value. No significant change in urine pH was observed. Blood P_{CO_2} and urine P_{CO_2} significantly increased from the control value of 29.27±1.09 to 39.75±3.35 mmHg ($P<0.05$), 33.95±1.46 to 43.15±1.86 mmHg ($P<0.01$), respectively, without significant change from the given acetlycholine alone value, thus, there was also no significant difference in the U-B P_{CO_2} difference. Urinary excretion of titratable acidity, ammonium, and bicarbonate significantly decreased to 20.48±3.51 % of the control value ($P<0.01$), 66.23±2.82 % of the control value ($P<0.001$), and 34.64±4.44 % of the control value ($P<0.01$), respectively, and from the given acetylcholine alone value ($P<0.01$, $P<0.001$, $P<0.01$, respectively), so that fractional net acid excretion significantly decreased to 51.85±2.38 % of the control value ($P<0.001$) and from the given acetylcholine alone value ($P<0.001$).

Withdrawal of sodium metavanadate and acetylcholine infusion, blood pH significantly remained decreased from the control value ($P<0.05$) without significant from the experimental period value. There was no significant change in urine pH, blood P_{CO_2}, urine P_{CO_2}, and the U-B P_{CO_2} difference. Urinary excretion of titratable acidity returned to basal value and significantly increased from the experimental period value ($P<0.01$), whereas urinary excretion of ammonium and bicarbonate significantly remained decreased from the control value ($P<0.01$) without significant change from the experimental period value. Therefore, fractional net acid excretion significantly remained decreased from the control value ($P<0.001$) without significant change from the experimental period value.

Group VI : **Animals Pretreated With Verapamil (Ver) Before Sodium Metavanadate Infusion**

Intrarenal infusion of verapamil alone, Urine pH significantly decreased from the control value ($P<0.01$). There were no different in any other of the measurements made. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of verapamil caused no developed metabolic acidosis. No significant alterations in any of the measurements made were observed. Withdrawal of sodium metavanadate and verapamil caused no change difference in any measurements made.

Comparison, the intravenous infusion of sodium metavanadate produced the hyperkalemic hyperchlorimic renal tubular acidosis, these effects which were totally blocked by verapamil and patially by prazosin, atenolol, enalapril maleate, acetylcholine. Blood pH (Figure 16, upper panel) in group II-VI decreased in the same manner after intravenous infusion of sodium metavanadate alone (Group I) which significantly higher than group I at the same time interval in group IV ($P<0.05$). Urine pH (Figure 16, lower panel) in group III insignificantly increased in the same manner as group I, however, in another group decreased in the opposite manner of group I which were significantly lower than group I at the same time interval in group II ($P<0.01$), group IV ($P<0.01$), group V ($P<0.01$), and group VI ($P<0.01$). Blood P_{CO_2} (Figure 17, upper panel) and urine P_{CO_2} (Figure 17, lower panel) in group II-VI increased in the same manner as group I which no significant change from group I at the same time interval. No significant difference in the difference between urine and blood P_{CO_2} (Figure 18) was observed. Urinary excretion of titratable acidity (Figure 119, upper panel) in group II, III, V decreased in the same manner as group I, however, in group IV and VI increased in the opposite manner of group I which were significantly higher than group I at the same time interval in group II ($P<0.05$), group III ($P<0.05$), group IV

($P<0.001$), group V ($P<0.01$) and group VI ($P<0.01$). Urinary excretion of ammonium (Figure 19, lower panel) in group II-VI decreased in the opposite manner of group I which was significantly higher than group I at the same time interval in group II ($P<0.01$), group III ($P<0.001$), group IV ($P<0.001$), and group VI ($P<0.05$). Fractional net acid excretion (Figure 20) in group III ,V, VI decreased in the same manner as group I, however, in group II and IV increased in the opposite manner of group I which were significantly higher than group I at the same time interval in group II ($P<0.01$), group III ($P<0.01$), group IV ($P<0.001$), and group VI ($P<0.05$).

Effects of Intravenous Sodium Metavanadate Infusion on Urinary water Excretion.

The results of changes in urinary water excretion in dogs given intravenous sodium metavanadate infusion without pretreatment of various drugs (group I) and pretreatment of intrarenal arterial infusion with prazosin (group II), atenolol (group III), acetylcholine (group V), verapamil (group VI), and intravenous injection with MK422 (group IV) are summerized in Table 10 and Figure 21-22 .

Group I : **Animals Pretreated With Isotonic Normal Saline Solution Before Sodium Metavanadate Infusion**

After intrarenal arterial saline infusion caused no change in any of the measurements made. The intravenous sodium metavanadate infusion, fractional water excretion (V/GFR) significantly decreased to 24.81±4.41 % of the control value ($P<0.01$), whereas fractional osmolar clearance (C_{osm}/GFR) slighly increased to 19.21±8.40 % of the control value without statistically significance, so that fractional free water clearance (C_{H_2O}/GFR) markedly significantly decreased to 163.12±10.52 % of the control value ($P<0.01$). Stopping the sodium metavanadate infusion, fractional

water excretion returned to basal control value and significantly increased from the the experimental period value ($P<0.05$), whereas fractional osmolar clearance significantly increased from the control value ($P<0.01$) and from the the experimental period value ($P<0.05$), therefore fractional free water clearance markedly significantly still decreased to from the control value ($P<0.001$) without significant change from the the experimental period value.

Group II : **Animals Pretreated With Prazosin (Pra) Before Sodium Metavanadate Infusion**

After intrarenal infusion of prazosin alone caused mildly diuresis, fractional water excretion significantly increased from the control value ($P<0.05$), whereas no significant increase in fractional osmolar clearane was observed, thus, fractional free water clearance significantly rose up from the control value ($P<0.05$). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of prazosin, fractional water excretion significantly decreased to 49.57±6.41 % of the control value ($P<0.01$) and from the given prazosin alone value ($P<0.01$), whereas fractional osmolar clearance markedly significantly decreased to 50.65±6.93 % of the control value and from the given prazosin alone value ($P<0.01$), so that there was no significant decrease in fractional free water clearance. Withdrawal of sodium metavanadate and prazosin infusion, fractional water excretion and fractional osmolar clearance significantly increased from the control value ($P<0.05$) and from the experimental period value ($P<0.01$), therefore fractional free water clearance significantly reduced from the control value ($P<0.05$) and from the experimental period value ($P<0.01$).

Group III : **Animals Pretreated With Atenolol (AT) Before Sodium Metavanadate Infusion.**

After intrarenal infusion of atenolol alone caused mildly diuresis, fractional water excretion significantly increased from the control value ($P<0.05$), whereas no significant increase in fractional osmolar clearane was observed, thus, fractional free water clearance remained unchanged from control value. When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of atenolol caused no significant increase in fractional water excretion and fractional osmolar clearance, so that fractional free water clearance significantly decreased to 263.27 ± 135.11 % of the control value ($P<0.05$) and from the given atenolol alone value ($P<0.05$). Withdrawal of sodium metavanadate and atenolol infusion, fractional water excretion and fractional osmolar clearance returned to the basal value without significant change from the experimental period value, therefore fractional free water clearance significantly remained reduced from the control value ($P<0.05$) without significant change from the experimental period value.

Group IV : **Animals Pretreated With Enalapril Maleate (MK 422) Before Sodium Metavanadate Infusion.**

Single dose intravenous injection of MK422 alone caused no change in any of the measurements made. When intravenous infusion of sodium metavanadate, caused no significant increase in fractional water excretion and fractional osmolar clearance, so that no significant decrease in fractional free water clearance was observed. Withdrawal of sodium metavanadate and MK422, fractional water excretion and fractional osmolar clearance significantly increased from the control value ($P<0.05$) without significant

change from the experimental period value, therefore no significant decrease in fractional free water clearance was observed.

Group V : **Animals Pretreated With Acetylcholine (ACh) Before Sodium Metavanadate Infusion**

Intrarenal infusion of acetylcholine alone caused mildly diuresis, no significant increase in fractional water excretion and fractional osmolar clearane was observed, thus, fractional free water clearance significantly rose up from the control value ($P<0.05$). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of acetylcholine, there was no significant increase in fractional water excretion and fractional osmolar clearance, so that fractional free water clearance significantly decreased to 125.71±7.71 % of the control value ($P<0.01$) and from the given acetylcholine alone value ($P<0.01$). Withdrawal of sodium metavanadate and acetylcholine infusion, fractional water excretion significantly reduced from the control value ($P<0.05$) and from the experimental period value ($P<0.05$), as for fractional osmolar clearance significantly fell from the experimental period value ($P<0.01$) without significant change from the control value, therefore fractional free water clearance significantly reduced from the control value ($P<0.001$) and elevated from the experimental period value ($P<0.05$).

Group VI : **Animals Pretreated With Verapamil (Ver) Before Sodium Metavanadate Infusion**

Intrarenal infusion of verapamil alone produced diuresis, fractional water excretion and fractional osmolar clearane significantly rose up from the control value ($P<0.05$), therefore fractional free water clearance significantly reduced from the

control value ($P<0.05$). When intravenous infusion of sodium metavanadate and sustaining intrarenal infusion of verapamil, fractional water excretion and fractional osmolar clearance significantly rose up to 155.50±30.54 % of the control value ($P<0.01$), 164.78±32.38 % of the control value ($P<0.01$), respectively, and the given verapamil alone value ($P<0.01$). Thus, fractional free water clearance, although insignificantly decreased to 43.26±131.23 % of the control value, significantly decreased from the given verapamil alone value ($P<0.001$). Withdrawal of sodium metavanadate and verapamil infusion, fractional water excretion and fractional osmolar clearance significantly rose up from the control value ($P<0.01$), without significant change from the given verapamil alone value, so that no significant increase to the basal value in fractional free water clearance was observed.

Comparison, the intravenous infusion of sodium metavanadate did not produced diuresis, these effects which were totally blocked by verapamil and patially by atenolol, enalapril maleate, acetylcholine. Fractional water excretion (Figure 21) in group II decreased in the same manner after intravenous infusion of sodium metavanadate alone (Group I) which significantly lower than group I at the same time interval ($P<0.05$), however, in another group increased in the opposite manner of group I which were significantly higher than group I at the same time interval in group III ($P<0.05$), group IV ($P<0.05$), group V ($P<0.05$), and group VI ($P<0.001$). Fractional osmolar clearance (Figure 20, upper panel) in group III-VI increased in the same manner as group I which was significantly higher than group I at the same time interval in group VI ($P<0.01$), however, in group II decreased in the opposite manner of group I which were significantly higher than group I at the same time interval ($P<0.001$). Fractional free water clearance (Figure 22, lower panel) in group III-VI decreased in the same manner as group I, but in group II increased in the opposite manner and significantly higher than group I in group II ($P<0.01$), and group V ($P<0.05$).

Table 8. Changes in blood pH, blood P_{CO_2}, urine pH, urine P_{CO_2} and urine-blood P_{CO_2} in response to intravenous sodium metavanadate infusion in all groups.

Parameter	Blood pH	Urine pH	Blood P_{CO_2} (mmHg)	Urine P_{CO_2} (mmHg)	U-B P_{CO_2} (mmHg)
Group I (n=5)					
Control	7.43 ± 0.01	6.30 ± 0.02	33.32 ± 0.80	37.10 ± 0.52	3.78 ± 1.17
NSS(IR)	7.44 ± 0.01	6.35 ± 0.02	32.94 ± 1.34	36.69 ± 0.73	3.74 ± 1.83
NSS(IR)+$NaVO_3$(IV)	7.20 ± 0.05 *$	6.63 ± 0.09 *$	41.96 ± 3.56	43.06 ± 2.34	1.10 ± 2.70
Recovery	7.45 ± 0.04 $$	6.43 ± 0.03	31.65 ± 2.57 $	32.29 ± 2.52 $	0.64 ± 1.13
Group II (n=5)					
Control	7.50 ± 0.02	6.53 ± 0.03	32.49 ± 1.75	36.03 ± 0.72	3.54 ± 1.67
Pra(IR)	7.47 ± 0.01	6.52 ± 0.06	33.63 ± 1.39	35.70 ± 1.34	2.07 ± 1.10
Pra(IR)+$NaVO_3$(IV)	7.34 ± 0.02 *$	6.27 ± 0.07 $$	38.50 ± 2.82	40.83 ± 0.89 *$$$	2.33 ± 2.33
Recovery	7.34 ± 0.04	6.33 ± 0.07	39.77 ± 4.25	41.81 ± 1.15 *	2.03 ± 3.79
Group III (n=5)					
Control	7.48 ± 0.02	5.94 ± 0.18	31.71 ± 1.21	34.34 ± 1.03	2.64 ± 1.47
AT(IR)	7.43 ± 0.03	5.89 ± 0.18	32.30 ± 1.97	34.12 ± 1.45	1.83 ± 2.16
AT(IR)+$NaVO_3$(IV)	7.36 ± 0.01 *	5.95 ± 0.21	33.89 ± 1.88	38.34 ± 1.96 $	4.45 ± 3.23
Recovery	7.35 ± 0.02 *	5.52 ± 0.13	37.03 ± 1.55 *	37.32 ± 1.55	0.30 ± 1.95
Group IV (n=5)					
Control	7.51 ± 0.01	6.33 ± 0.07	32.07 ± 0.22	35.77 ± 0.94	3.70 ± 0.97
MK422(v)	7.51 ± 0.02	6.14 ± 0.12 *	28.15 ± 1.49	36.76 ± 1.16	8.61 ± 2.29
MK422(v)+$NaVO_3$(IV)	7.47 ± 0.02 $	6.15 ± 0.07 *	33.68 ± 2.02 $	40.96 ± 1.07 **$$	7.28 ± 1.83
Recovery	7.54 ± 0.01	6.55 ± 0.06 ***$$	29.49 ± 0.65 *	33.11 ± 1.66 $	3.63 ± 1.71
Group V (n=5)					
Control	7.55 ± 0.02	6.47 ± 0.05	29.27 ± 1.09	33.95 ± 1.46	4.68 ± 0.56
ACh(IR)	7.43 ± 0.03 **	6.28 ± 0.05 **	39.33 ± 2.49 **	41.70 ± 2.52 *	2.36 ± 1.12 *
ACh(IR)+$NaVO_3$(IV)	7.37 ± 0.03 **	6.35 ± 0.04	39.75 ± 3.35 *	43.15 ± 1.86 **	3.40 ± 1.67
Recovery	7.45 ± 0.04 *	6.19 ± 0.20	33.33 ± 3.80	37.90 ± 4.03	4.57 ± 2.63
Group VI (n=5)					
Control	7.48 ± 0.05	6.48 ± 0.02	34.83 ± 3.68	38.29 ± 2.08	3.46 ± 1.69
Ver(IR)	7.53 ± 0.04	6.35 ± 0.04 **	34.58 ± 3.02	38.92 ± 2.76	4.34 ± 1.05
Ver(IR)+$NaVO_3$(IV)	7.39 ± 0.08	6.15 ± 0.15	39.18 ± 6.32	43.58 ± 5.81	4.39 ± 0.52
Recovery	7.38 ± 0.08	6.16 ± 0.21	41.88 ± 6.82	46.60 ± 4.85	4.72 ± 2.21

Values are the means±SEM. Abbreviation : P_{CO_2}, carbon dioxide tension. Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.

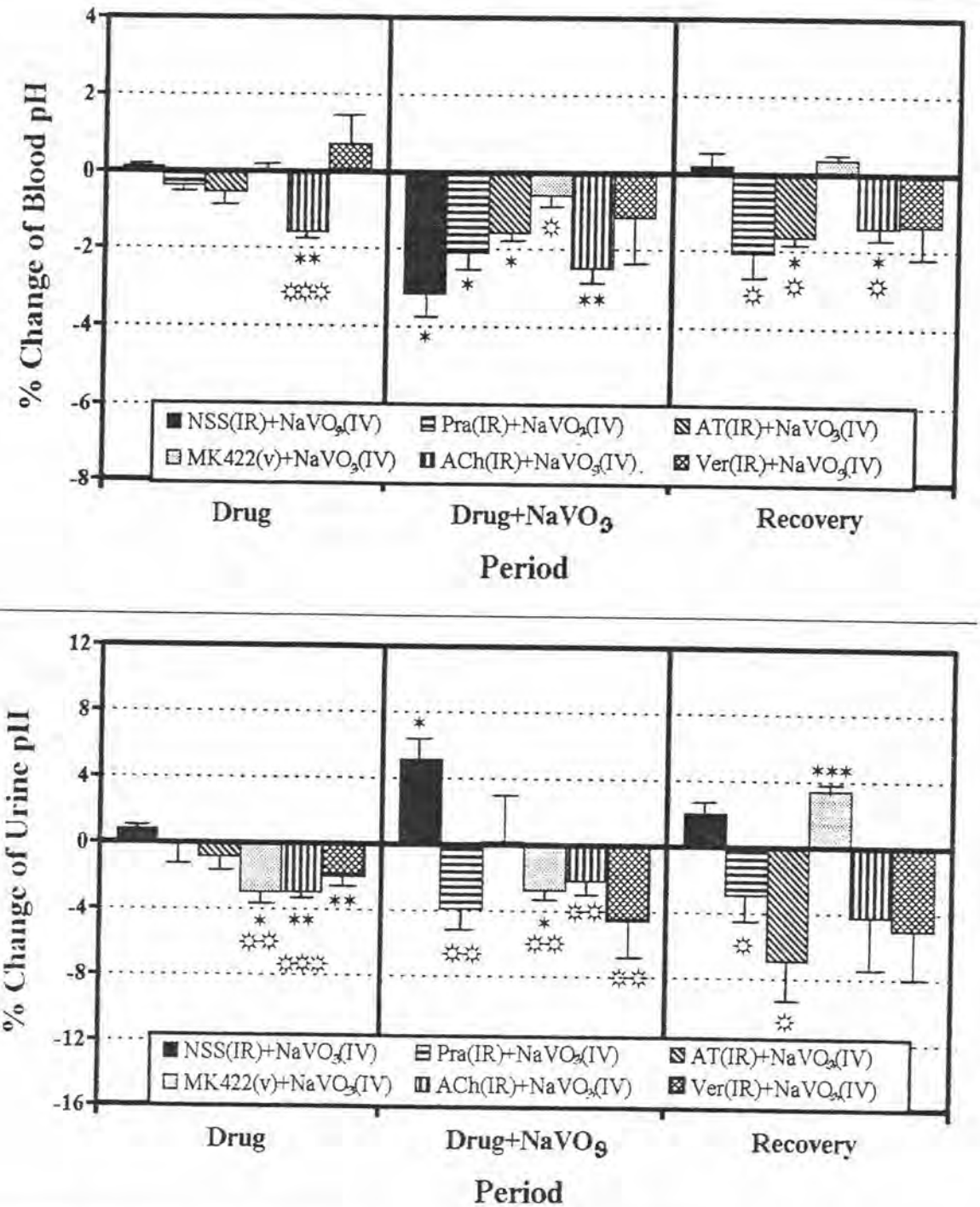


Figure 16 Percentage changes in blood pH and urine pH in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422).

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.

Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

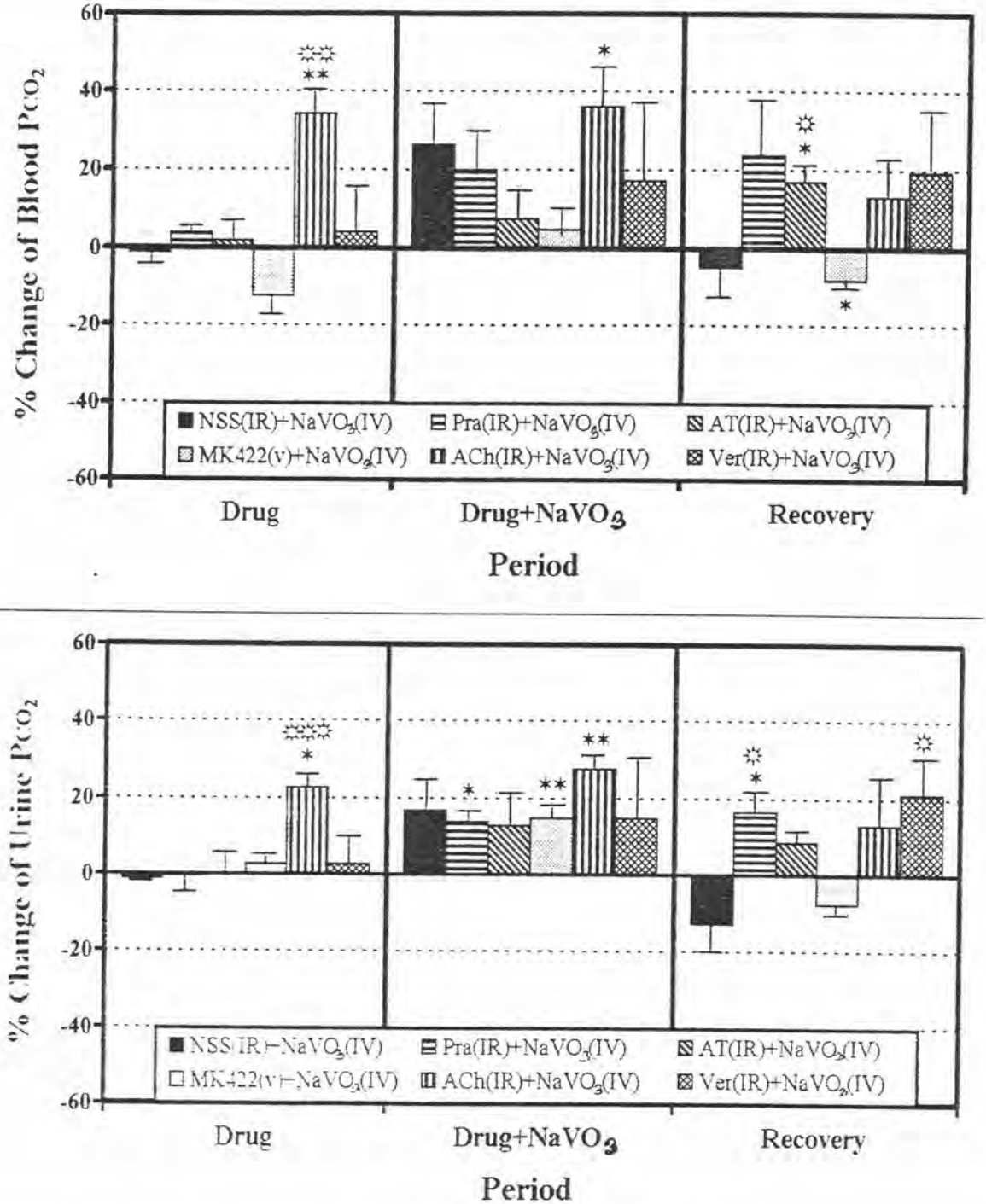


Figure 17 Percentage changes in blood P_{CO_2} and urine P_{CO_2} in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).

Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 compaired to the control value of each group.

Significant difference values using unpaired t'test are indicated by ☼P<0.05, ☼☼P<0.01,☼☼☼P<0.001 compaired to group I at the same time interval.

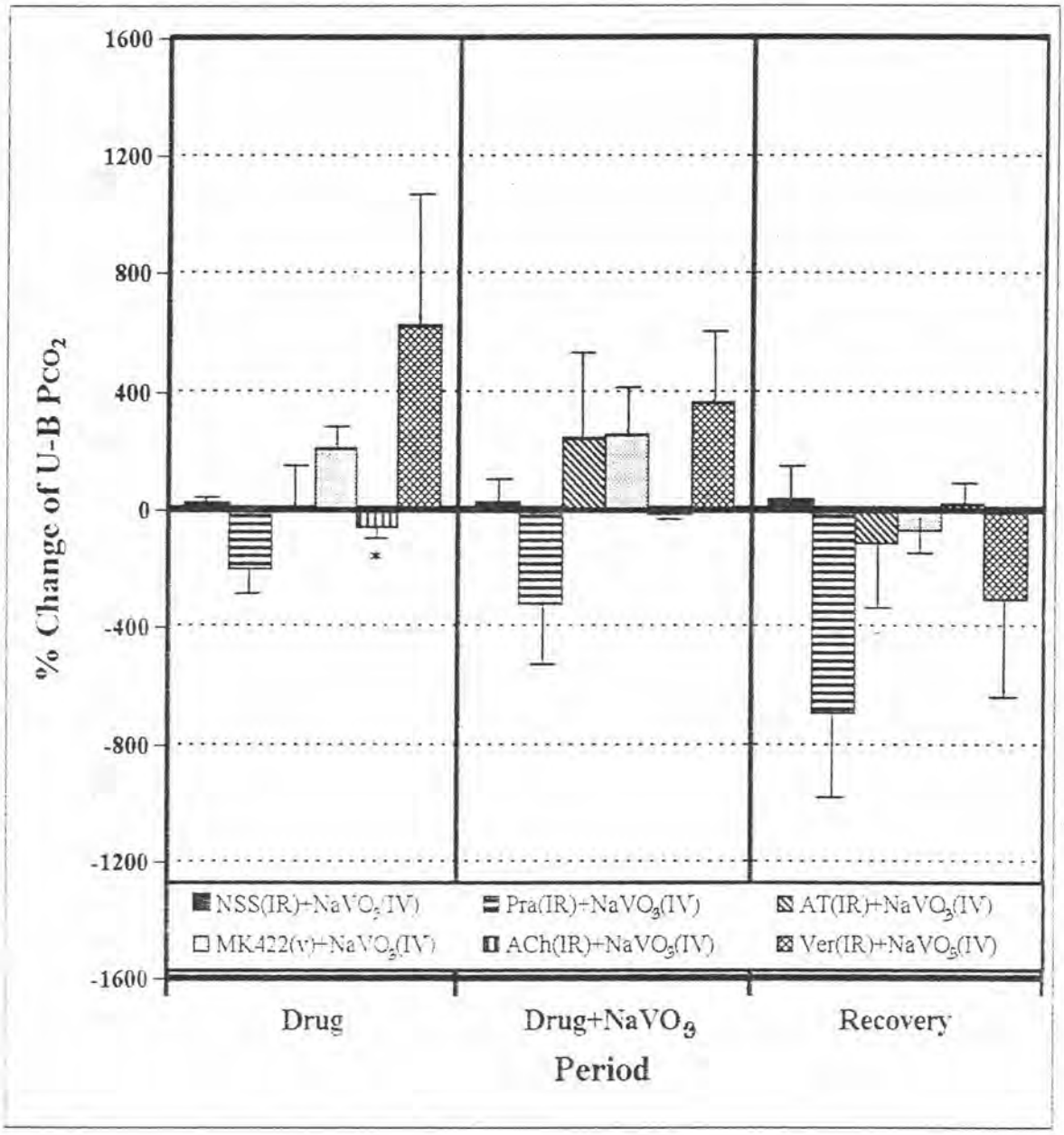


Figure 18 Percentage changes in urine-blood P_{CO_2} in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver), and intravenous injection with enalapril maleate (MK422).

Significant difference values using paired t'test indicated by * P<0.05, ** P<0.01, *** P<0.001 compaired to the control value of each group.

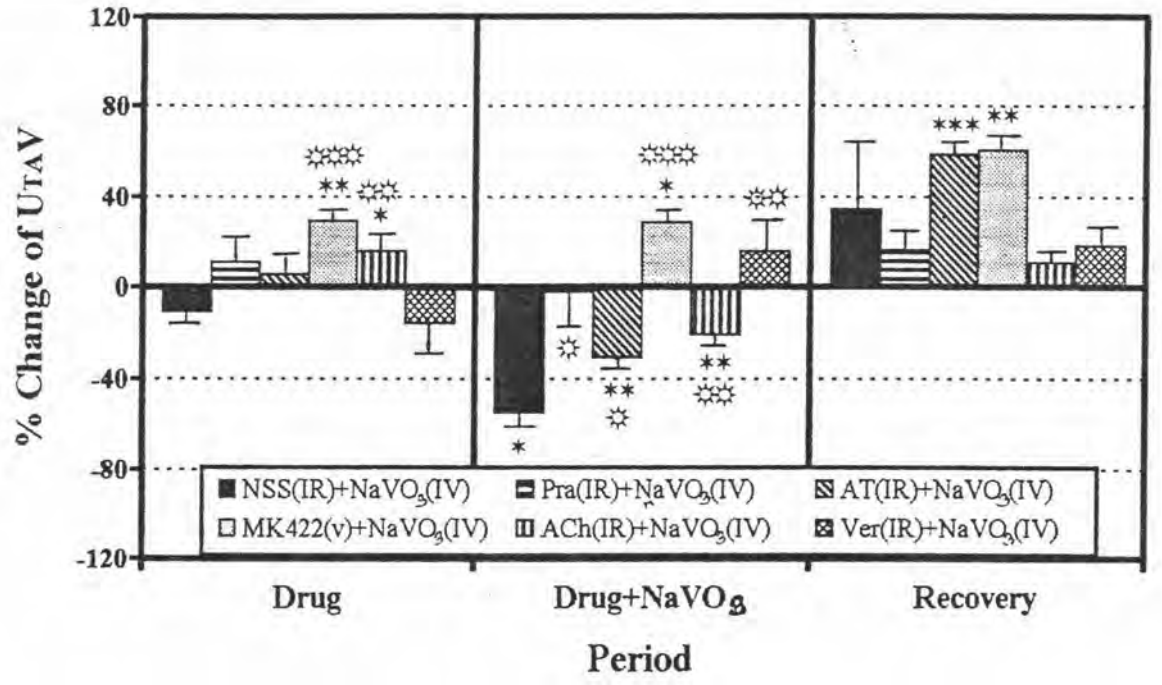
Significant difference values using unpaired t'test indicated by ☼ P<0.05, ☼☼P<0.01,☼☼☼P<0.001 compaired to group I at the same time interval.

Table 9. Changes in acid-base excretion in response to intravenous sodium metavanadate infusion in all groups.

Parameter	$U_{TA}V$ (μmole/min/kg bw.)	$U_{NH_4}V$ (μmole/min/kg bw.)	$U_{HCO_3}V$ (μmole/min/kg bw.)	NAE/GFR (mEq/ml)
Group I (n=5)				
Control	0.81 ± 0.16	1.75 ± 0.44	0.08 ± 0.00	2.48 ± 0.57
NSS(IR)	0.73 ± 0.14	1.63 ± 0.40	0.09 ± 0.00	2.27 ± 0.53
NSS(IR)+$NaVO_3$(IV)	0.34 ± 0.05 * $	0.61 ± 0.15 * $	0.09 ± 0.01	0.86 ± 0.18 * $
Recovery	0.91 ± 0.14 $	1.12 ± 0.23	0.08 ± 0.01	1.95 ± 0.29 $
Group II (n=5)				
Control	0.82 ± 0.07	0.89 ± 0.05	0.06 ± 0.00	1.65 ± 0.11
Pra(IR)	0.93 ± 0.13	1.04 ± 0.10	0.11 ± 0.01	1.86 ± 0.23
Pra(IR)+$NaVO_3$(IV)	0.78 ± 0.09	0.84 ± 0.10	0.01 ± 0.00 *** $$	1.62 ± 0.16
Recovery	0.93 ± 0.06	1.25 ± 0.14	0.06 ± 0.01 $$	2.12 ± 0.18
Group III (n=5)				
Control	0.63 ± 0.04	0.93 ± 0.03	0.08 ± 0.01	1.49 ± 0.07
AT(IR)	0.65 ± 0.04	1.22 ± 0.04 **	0.10 ± 0.02 **	1.77 ± 0.03 **
AT(IR)+$NaVO_3$(IV)	0.44 ± 0.04 ** $$	0.73 ± 0.03 ** $$	0.07 ± 0.01	1.09 ± 0.07 ** $$$
Recovery	0.99 ± 0.03 *** $$$	1.08 ± 0.04 $$	0.06 ± 0.00	2.01 ± 0.05 * $$$
Group IV (n=5)				
Control	0.72 ± 0.07	0.97 ± 0.11	0.11 ± 0.01	1.58 ± 0.16
MK422(v)	0.91 ± 0.07 **	1.22 ± 0.18	0.11 ± 0.02	2.02 ± 0.24 *
MK422(v)+$NaVO_3$(IV)	0.92 ± 0.09 *	0.90 ± 0.08	0.07 ± 0.01 **	1.75 ± 0.14
Recovery	1.15 ± 0.12 ** $	1.00 ± 0.13	0.23 ± 0.03 ** $$	1.91 ± 0.25
Group V (n=5)				
Control	0.80 ± 0.02	1.57 ± 0.09	0.12 ± 0.01	2.26 ± 0.09
ACh(IR)	0.93 ± 0.04 *	1.45 ± 0.08	0.15 ± 0.01 *	2.23 ± 0.07
ACh(IR)+$NaVO_3$(IV)	0.63 ± 0.01 ** $$	0.52 ± 0.03 *** $$$	0.08 ± 0.01 ** $$	1.08 ± 0.03 *** $$$
Recovery	0.89 ± 0.04 $$	0.52 ± 0.03 ***	0.08 ± 0.01 **	1.33 ± 0.06 ***
Group VI (n=5)				
Control	0.72 ± 0.03	0.88 ± 0.05	0.19 ± 0.02	1.41 ± 0.07
Ver(IR)	0.60 ± 0.09	0.74 ± 0.09	0.27 ± 0.03	1.07 ± 0.19
Ver(IR)+$NaVO_3$(IV)	0.81 ± 0.09	0.67 ± 0.05	0.29 ± 0.05	1.18 ± 0.16
Recovery	0.83 ± 0.05	0.84 ± 0.05	0.32 ± 0.06	1.36 ± 0.10

Values are the means±SEM. Only one experimental kidney values are presented. Abbreviations : $U_{TA}V$, urinary titratable acid excretion; $U_{NH_4}V$, urinary ammonium excretion; $U_{HCO_3}V$, urinary bicarbonate excretion; NAE/GFR, fractional net acid excretion.

Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ different from control and by $ $P<0.05$, $$ $P<0.01$, $$$ $P<0.001$ different from previous values.



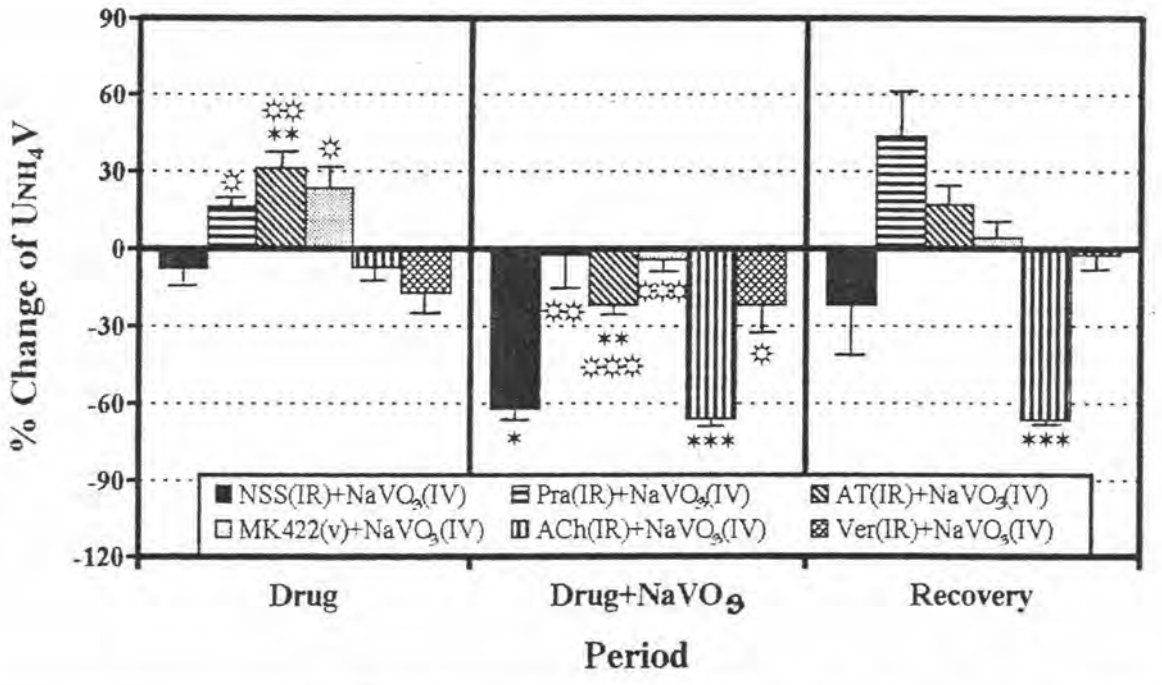


Figure 19 **Percentage changes in urinary titratable acid excretion ($U_{TA}V$) and urinary ammonium excretion ($U_{NH_4}V$) in dogs response to sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and verapamil (Ver) and intravenous injection with enalapril maleate (MK422). Significant difference values using paired t'test are indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group. Significant difference values using unpaired t'test are indicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.**

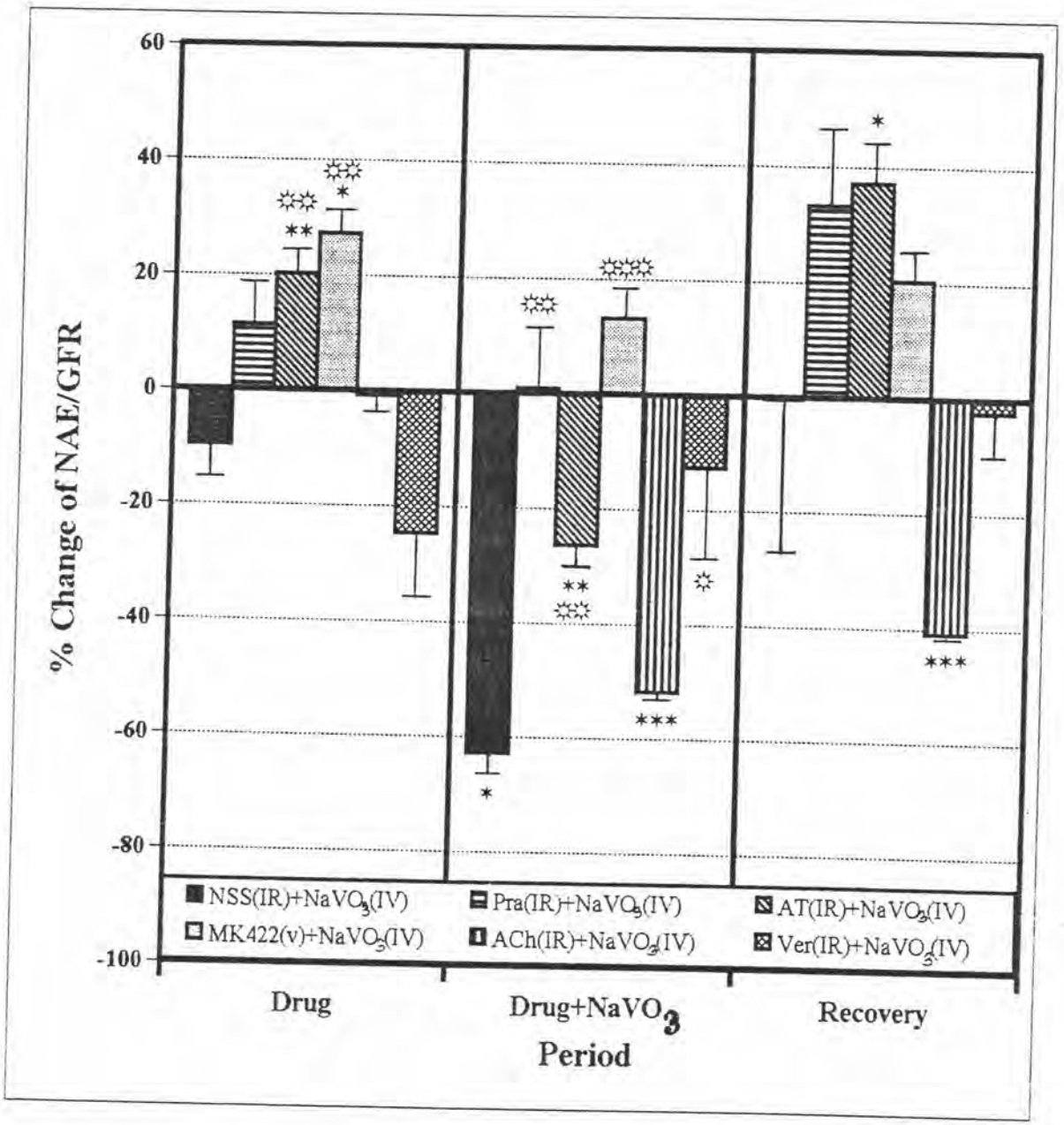


Figure 20 Percentage changes in fractional net acid excretion (NAE/GFR) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422).
Significant difference values using paired t'test indicated by * P<0.05, **P<0.01, *** P<0.001 compaired to the control value of each group.
Significant difference values using unpaired t'test indicated by ☼ P<0.05, ☼☼P<0.01, ☼☼☼P<0.001 compaired to group I at the same time interval.

Table10. Changes in water excretion in response to intravenous sodium metavanadate infusion in six groups.

Parameter	V/GFR (%)		Cosm/GFR (%)		CH_2O/GFR (%)	
Group I (n=5)						
Control	1.75 ± 0.05		1.31 ± 0.04		0.44 ± 0.08	
NSS(IR)	1.77 ± 0.07		1.23 ± 0.06		0.54 ± 0.11	
NSS(IR)+$NaVO_3$(IV)	1.32 ± 0.09	** $$	1.56 ± 0.11		-0.24 ± 0.02	** $$
Recovery	1.98 ± 0.11	$	2.28 ± 0.13	** $	-0.30 ± 0.04	***
Group II (n=5)						
Control	1.16 ± 0.08		1.27 ± 0.11		-0.12 ± 0.05	
Pra(IR)	1.66 ± 0.11	*	1.60 ± 0.06		0.05 ± 0.08	*
Pra(IR)+$NaVO_3$(IV)	0.58 ± 0.07	** $$	0.61 ± 0.07	** $$	-0.03 ± 0.01	
Recovery	1.65 ± 0.09	* $$	1.93 ± 0.09	** $$$	-0.28 ± 0.04	* $$
Group III (n=5)						
Control	2.92 ± 0.25		2.80 ± 0.31		0.31 ± 0.12	
AT(IR)	3.72 ± 0.35	*	3.47 ± 0.40	*	0.24 ± 0.15	
AT(IR)+$NaVO_3$(IV)	3.59 ± 0.21		3.95 ± 0.33		-0.36 ± 0.13	* $
Recovery	2.95 ± 0.07		3.24 ± 0.11		-0.29 ± 0.15	*
Group IV (n=5)						
Control	2.60 ± 0.16		2.83 ± 0.29		-0.23 ± 0.14	
MK422(v)	2.59 ± 0.26		2.72 ± 0.36		-0.13 ± 0.10	
MK422(V)+$NaVO_3$(IV)	3.06 ± 0.41		3.37 ± 0.48		-0.31 ± 0.11	
Recovery	5.01 ± 0.58	*	5.47 ± 0.67	*	-0.46 ± 0.13	
Group V (n=5)						
Control	2.57 ± 0.13		2.05 ± 0.12		0.52 ± 0.04	
ACh(IR)	2.79 ± 0.08		2.20 ± 0.05		0.59 ± 0.04	*
ACh(IR)+$NaVO_3$(IV)	2.76 ± 0.28		2.90 ± 0.30		-0.14 ± 0.04	** $$
Recovery	1.85 ± 0.19	* $	1.79 ± 0.16	$$	0.07 ± 0.03	*** $
Group VI (n=5)						
Control	3.81 ± 0.61		3.62 ± 0.55		0.20 ± 0.14	
Ver(IR)	5.37 ± 0.66	*	6.39 ± 0.83	**	-1.03 ± 0.18	*
Ver(IR)+$NaVO_3$(IV)	9.00 ± 0.86	** $$	8.93 ± 0.94	** $	0.07 ± 0.12	$$$
Recovery	8.97 ± 1.13	**	8.81 ± 1.10	**	0.16 ± 0.25	

Values are means±SEM. Only one experimental kidney values are presented. Abbreviations : V/GFR, fractional water excretion; C_{osm}/GFR, fractional osmolar clearance; C_{H_2O}/GFR, fractional free water clearance.

Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 different from control and by $ P<0.05, $$ P<0.01, $$$ P<0.001 different from previous values.

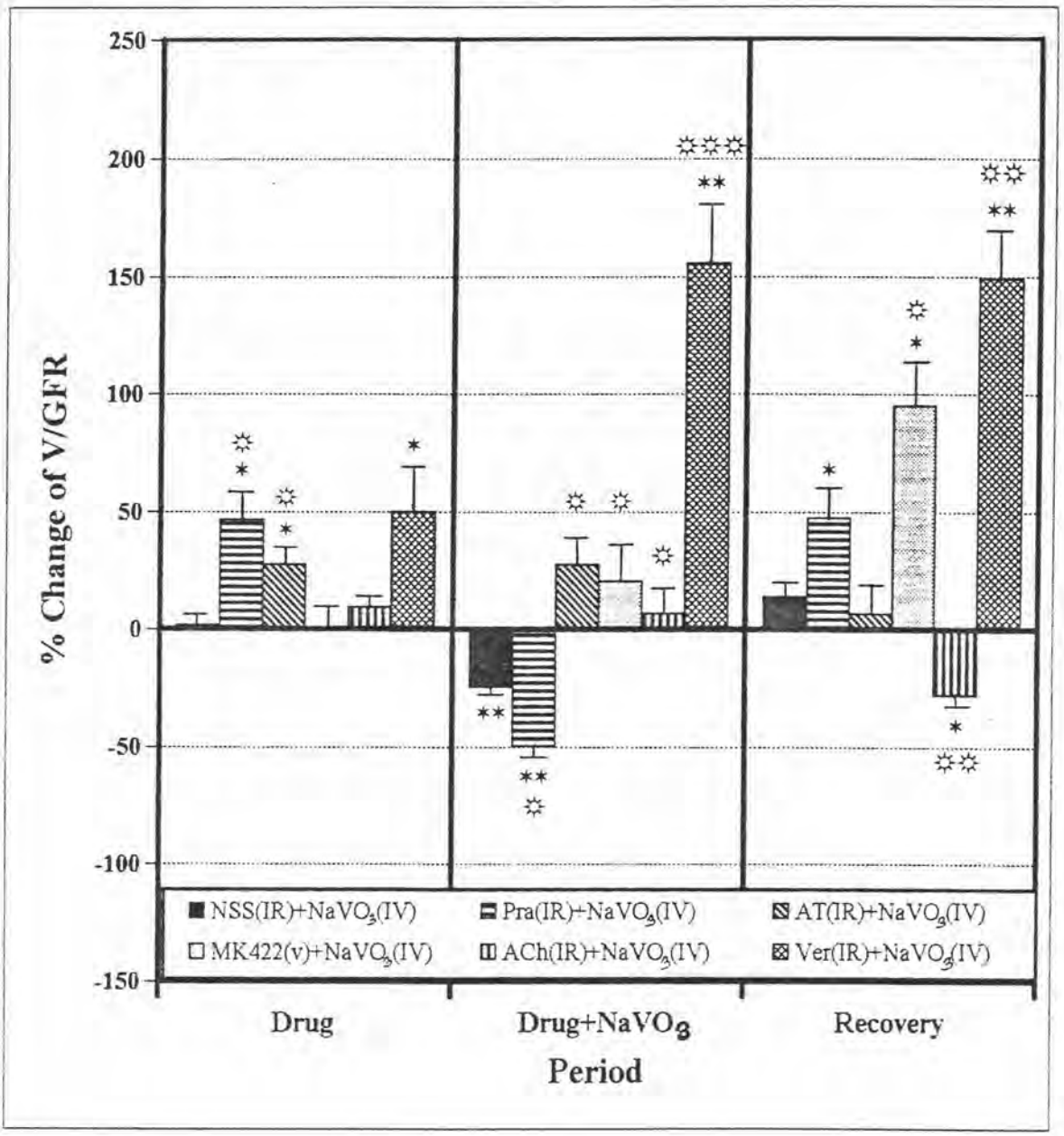


Figure 21 Percentage changes in fractional water excretion (V/GFR) in dogs response to intravenous infusion of sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal arterial infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422).

Significant difference values using paired t'test indicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.

Significant difference values using unpaired t'test indicated by ☼$P<0.05$, ☼☼$P<0.01$, ☼☼☼$P<0.001$ compaired to group I at the same time interval.

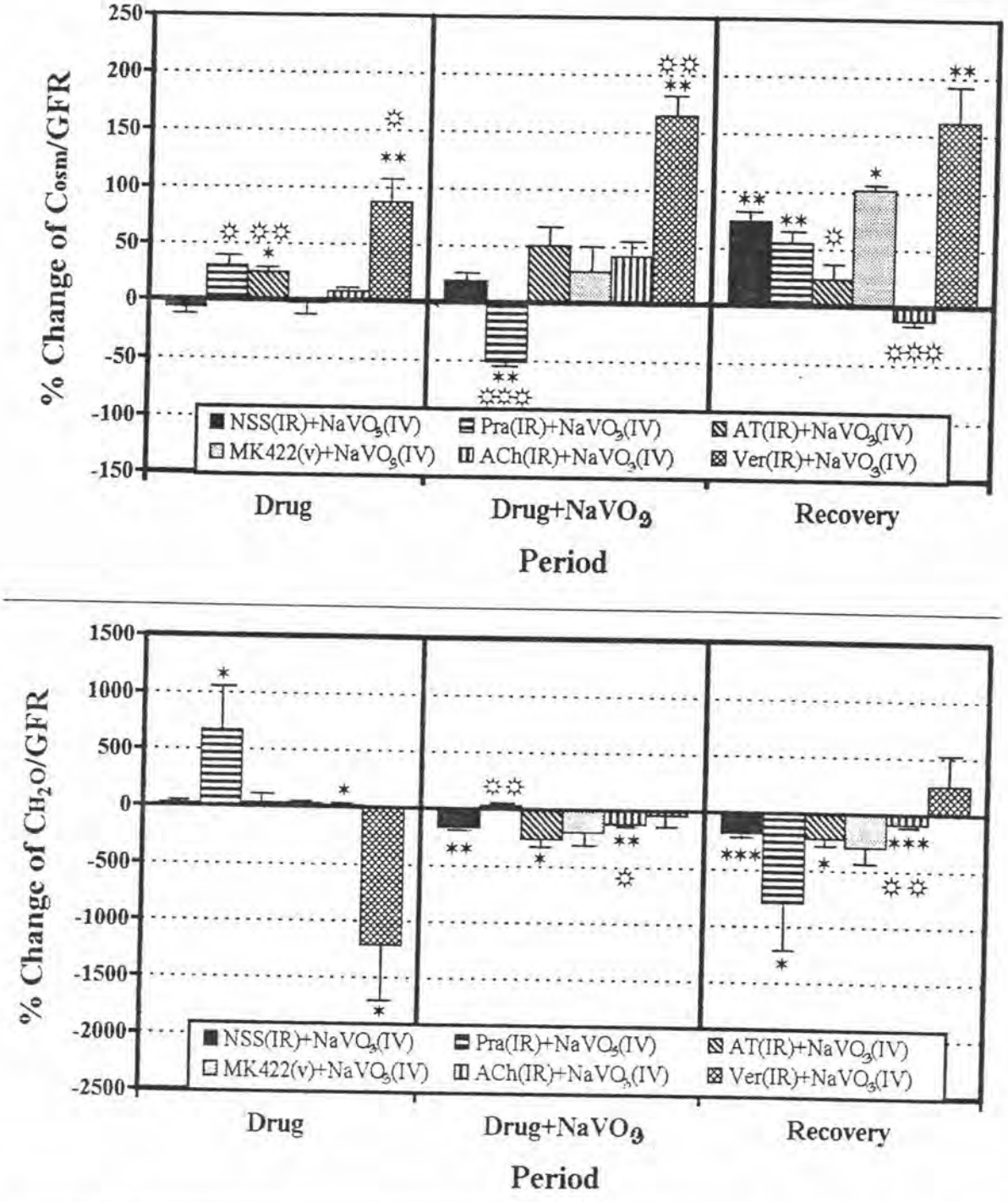


Figure 22 Percentage changes in fractional osmolar clearance (C_{osm}/GFR) and fractional free water clearance (C_{H_2O}/GFR) in dogs response to sodium metavanadate ($NaVO_3$) alone (Group I) and pretreated intrarenal infusion with prazosin (Pra), atenolol (AT), acetylcholine (ACh), verapamil (Ver) and intravenous injection with enalapril maleate (MK422).
Significant difference values using paired t'test are ndicated by * $P<0.05$, ** $P<0.01$, *** $P<0.001$ compaired to the control value of each group.
Significant difference values using unpaired t'test are ndicated by ☼ $P<0.05$, ☼☼ $P<0.01$, ☼☼☼ $P<0.001$ compaired to group I at the same time interval.

Effects of Intravenous Sodium Metavanadate Infusion on Renal Tubular Transport.

Glucose reabsorption :

The results from this experimental are summarized in Table 11 and Figure 23. The intravenous infusion of sodium metavanadate caused a marked depression in glomerular filtration rate before glucose loading from the control value of 1.70±0.04 to 0.94±0.11 ml/min/kg.bw. ($P<0.001$) and after glucose loading from the control value of 1.77±0.03 to 1.26±0.10 ml/min/kg.bw. ($P<0.01$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.05$), and urine flow rate before glucose loading from the control value of 58.30±13.63 to 30.19±9.96 µl/min/kg.bw. ($P<0.05$) but after glucose loading unalteration from the control value which insignificantly rose with glucose loading in vanadate-infused dogs. Stopping infusion of sodium metavanadate, glomerular filtration rate before glucose loading returned to the basal value and significantly increased from the experimental period value ($P<0.01$), while it after glucose loading returned to the basal value and insignificantly increased from the experimental period value which insignificantly rose with glucose loading in vanadate-infused dogs. Urine flow rate before glucose loading returned to the basal value and insignificantly increased from the experimental period value, while it after glucose loading returned to the basal value and significantly increased from the experimental period value ($P<0.05$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.01$). No significant decrease in fractional excretion of sodium before and after glucose loading from the control value were observed, whereas it significantly rose with glucose loading in vanadate-infused dogs ($P<0.01$). No significant decrease in fractional excretion of potassium before and after glucose loading from the control value were observed, whereas it insignificantly rose with glucose loading in vanadate-

infused dogs. Stopping infusion of sodium metavanadate, no significant change in the fractional sodium and potassium before and after glucose loading were observed which insignificantly rose with glucose loading in vanadate-infused dogs. Plasma glucose concentration significantly depressed before glucose loading from the control value of 90.00±3.04 to 68.14±4.87 mg/dl ($P<0.001$) and after glucose loading from the control value of 557.72±19.48 to 447.43±11.20 mg/dl ($P<0.001$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, plasma glucose concentration before glucose loading significantly increased from the control value ($P<0.01$) and from the experimental period ($P<0.001$), while it returned to basal value and significantly rose from the experimental period ($P<0.001$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.001$). Figure 23 (upper panel) clearly illustrates the significant striking depression in tubular reabsorption of glucose per millilitre of GFR (T_G/GFR) seen in vanadate-infused dogs both at low concentration of plasma glucose from the control value of 0.90 ±0.03 to 0.60±0.04 mg/ml ($P<0.001$) and elevated concentration of plasma glucose from the control value of 4.87±0.18 to 3.71±0.07 mg/ml ($P<0.01$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, T_G/GFR before and after glucose loading returned to the basal value and significantly increased from the experimental period ($P<0.01$) which significantly rose with glucose loading in vanadate-infused dogs ($P<0.001$). During intravenous infusion of sodium metavanadate period show a further almost linear in increase in T_G/GFR as blood glucose is raised ($y = 0.01x+0.14$, $r = 0.988$, $P<0.001$) and it did not differ from that obtained in control period ($y = 0.01x+0.17$, $r = 0.999$, $P<0.001$) and in recovery period ($y = 0.01x+0.36$, $r = 0.952$, $P<0.001$). Thus, dogs with intravenous infusion of sodium metavanadate exhibited a marked depression of the renal threshold for glucose at low plasma glucose concentration, whereas the marked depression in maximal tubular glucose reabsorption per millilitre of GFR was reflected

by glycusuria at elevated plasma glucose concentration. However, the difference in T_G/GFR during intravenous infusion of sodium metavanadate period did not correlated with the differences in fractional sodium excretion ($y = 0.57x+0.42$, $r = 0.353$), whereas the T_G/GFR during control period and recovery period correlated with the differences in fractional sodium excretion ($y = 2.50x+5.02$, $r = 0.606$, $P<0.01$), ($y = 0.89x-0.67$, $r = 0.479$, $P<0.05$), respectively (Figure 23, lower panel).

Bicarbonate reabsorption :

The results from this experimental are summarized in Table 12 and Figure 24. The intravenous infusion of sodium metavanadate caused a marked depression in glomerular filtration rate before bicarbonate loading and after bicarbonate loading when comparable to the control value ($P<0.01$) which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.05$), and urine flow rate before bicarbonate loading ($P<0.05$) but after bicarbonate loading unalteration from the control value which insignificantly rose with bicarbonate loading in vanadate-infused dogs. Stopping infusion of sodium metavanadate, glomerular filtration rate before bicarbonate loading returned to the basal value and significantly increased from the experimental period value ($P<0.01$), while it after bicarbonate loading returned to the basal value and insignificantly increased from the experimental period value, which insignificantly rose with bicarbonate loading in vanadate-infused dogs. Urine flow rate before bicarbonate loading returned to the basal value and insignificantly increased from the experimental period value while it after bicarbonate loading returned to the basal value and significantly increased from the experimental period value ($P<0.05$), which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.01$). No significant decrease in blood pH and urine pH before and after bicarbonate loading from the control value were observed, whereas they significantly rose with bicarbonate loading

in vanadate-infused dogs ($P<0.01$). No significant decrease in blood P_{CO_2} before and after bicarbonate loading from the control value were observed, whereas it insignificantly rose with bicarbonate loading in vanadate-infused dogs. No significant decrease in urine P_{CO_2} before bicarbonate loading from the control value was observed but it after bicarbonate loading significantly reduced from the control value of 68.19± 9.29 to 52.65±9.15 mmHg ($P<0.05$), whereas it insignificantly rose with bicarbonate loading in vanadate-infused dogs. Therfore, no significant decrease in U-B P_{CO_2} before bicarbonate loading from the control value was observed but it after bicarbonate loading significantly reduced from the control value of 30.68±10.70 to 12.68±8.39 mmHg ($P<0.05$), whereas it insignificantly rose with bicarbonate loading in vanadate-infused dogs. Stopping infusion of sodium metavanadate, blood P_{CO_2} before bicarbonate loading significantly reduced from control value ($P<0.05$) and from the experimental period value ($P<0.05$), while no significant change in the plasma P_{CO_2} after bicarbonate loading was observed which insignificantly rose with bicarbonate loading in vanadate-infused dogs, whereas no significant change in the urine P_{CO_2} before and after bicarbonate loading were observed, which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.05$). Thus, no significant change in the U-B P_{CO_2} before and after bicarbonate loading were observed, which insignificantly rose with bicarbonate loading in vanadate-infused dogs. Fractional chloride excretion before bicarbonate loading significantly decreased from the control value of 2.67±0.32 to 1.60±0.08 % ($P<0.05$) but it after bicarbonate loading insignificantly reduced from the control value which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, no significant change in the fractional chloride excretion before and after bicarbonate loading were observed which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.01$). Blood bicarbonate concentration significantly depressed before bicarbonate loading from the control value of 23.47±0.36 to 22.52±0.33 mmole/L ($P<0.05$) and after bicarbonate

loading from the control value of 42.85±0.48 to 37.56±0.55 mmole/L ($P<0.001$) which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, blood bicarbonate concentration before bicarbonate loading significantly increased from the control value ($P<0.05$) and from the experimental period ($P<0.01$), while blood bicarbonate concentration after bicarbonate loading significantly increased from the experimental period ($P<0.001$) without significant change from the control value which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.001$). Figure 24 (upper panel) clearly illustrates the significant striking depression in tubular reabsorption of bicarbonate per millilitre of GFR (T_{HCO_3}/GFR) seen in vanadate-infused dogs both at low concentration of blood bicarbonate from the control value of 23.39±0.34 to 22.46±0.31 mmole/L ($P<0.05$) and elevated concentration of blood bacarbonate from the control value of 39.86±0.25 to 34.87±0.32 mmole/L ($P<0.001$) which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, T_{HCO_3}/GFR before bicarbonate loading significantly increased from the control value ($P<0.05$) and from the experimental period value ($P<0.01$), while T_{HCO_3}/GFR after bicarbonate loading significantly decreased from the control value ($P<0.05$) and significantly increased from the experimental period value ($P<0.01$) which significantly rose with bicarbonate loading in vanadate-infused dogs ($P<0.001$). During intravenous infusion of sodium metavanadate period show a further almost linear in increase in T_{HCO_3}/GFR as blood bicarbonate is raised ($y = 0.81x+4.24$, $r = 0.987$, $P<0.001$) and it did not differ from that obtained in control period ($y = 0.85x+3.38$, $r = 0.998$, $P<0.001$) and in recovery period ($y = 0.72x+7.23$, $r = 0.949$, $P<0.001$). Thus, dogs with intravenous infusion of sodium metavanadate exhibited a marked depression of the renal threshold for bicarbonate at low plasma bicarbonate concentration, whereas the marked depression in maximal tubular bicarbonate reabsorption per millilitre of GFR at elevated plasma bicarbonate

concentration. This marked depression in T_{HCO_3}/GFR during intravenous infusion of sodium metavanadate period correlated closely with the attendant decrease in fractional chloride excretion ($y = 2.36x+18.26$, $r = 0.977$, $P<0.001$) and it did not differ from that obtained during control period and recovery period correlated with the attendant decrease in fractional chloride excretion ($y = 1.71x+20.65$, $r = 0.668$, $P<0.01$), ($y = 2.01x-21.93$, $r = 0.872$, $P<0.001$), respectively (Figure 24, lower panel).

PAH secretion :

The results from this experimental are summarized in Table 13 and Figure 25. The intravenous infusion of sodium metavanadate caused a marked depression in glomerular filtration rate before PAH loading and after PAH loading when comparable to the control value ($P<0.01$) which significantly rose with PAH loading in vanadate-infused dogs ($P<0.05$), and urine flow rate before PAH loading ($P<0.05$) but after PAH loading unalteration from the control value which insignificantly rose with PAH loading in vanadate-infused dogs. Stopping infusion of sodium metavanadate, glomerular filtration rate before PAH loading returned to the basal value and significantly increased from the experimental period value ($P<0.01$) while it after PAH loading returned to the basal value and insignificantly increased from the experimental period value, which insignificantly rose with PAH loading in vanadate-infused dogs. Urine flow rate before PAH loading returned to the basal value and insignificantly increased from the experimental period value while it after PAH loading returned to the basal value and significantly increased from the experimental period value ($P<0.05$), which significantly rose with PAH loading in vanadate-infused dogs ($P<0.01$). Free plasma PAH concentration significantly raised before PAH loading from the control value of 9.80 ± 0.44 to 17.54 ± 1.52 mg/dl ($P<0.05$) and after PAH loading from the control value of 186.66 ± 6.09 to 279.96 ± 16.23 mg/dl ($P<0.01$) which significantly rose with PAH

loading in vanadate-infused dogs ($P<0.001$). Stopping infusion of sodium metavanadate, free plasma PAH concentration before and after PAH loading significantly increased from the control value ($P<0.01$, $P<0.01$, respectively) without significant change from the experimental period which significantly rose with PAH loading in vanadate-infused dogs ($P<0.001$). Urinary excretion of PAH significantly fell before PAH loading from the control value of 0.64±0.12 to 0.26±0.08 mg/min/kg.bw. ($P<0.05$) and after PAH loading from the control value of 5.95±0.74 to 4.30±0.54 mg/min/kg.bw. ($P<0.05$) which significantly rose with PAH loading in vanadate-infused dogs ($P<0.01$). Stopping infusion of sodium metavanadate, urinary excretion of PAH before and after PAH loading returned to the basal value and significantly increased from the experimental period value ($P<0.05$) which significantly rose with PAH loading in vanadate-infused dogs ($P<0.01$). The significant striking decrease in tubular reabsorption of PAH per millilitre of GFR (T_{PAH}/GFR) seen in vanadate-infused dogs both at low concentration of free plasma PAH from the control value of 0.28±0.07 to 0.08±0.05 mg/ml ($P<0.05$) and high concentration of plasma PAH from the control value of 1.46±0.42 to 0.59±0.31 mg/ml ($P<0.05$) which insignificantly rose with PAH loading in vanadate-infused dogs. Stopping infusion of sodium metavanadate, T_{PAH}/GFR before PAH loading returned to the basal value without significant from the experimental period value, while T_{PAH}/GFR after PAH loading returned to the basal value and significantly increased from the experimental period ($P<0.05$) which significantly rose with PAH loading in vanadate-infuse dogs ($P<0.05$). The difference in T_{PAH}/GFR did not result from differences in free plasma PAH concentration (Figure 25). The clearance of PAH significantly fell before PAH loading from the control value of 6.54±1.29 to 1.42±0.37 ml/min/kg.bw. ($P<0.05$) and after PAH loading from the control value of 3.25±0.48 to 1.62±0.27 ml/min/kg.bw. ($P<0.01$). No significant change in the clearance of PAH with PAH loading in vanadate-infused dogs was observed. Stopping infusion of

the clearance of PAH before PAH loading significantly remained reduced from the control value ($P<0.05$) and significantly rose up from the experimental period value ($P<0.05$), while it after PAH loading returned to the basal value and significantly increased from the experimental period value ($P<0.01$) which insignificantly rose with PAH loading in vanadate-infused dogs. The PAH extraction fraction significantly fell before PAH loading from the control value of 381.44±69.93 to 145.39±29.65 % ($P<0.05$) and after PAH loading from the control value of 181.71±24.67 to 123.97±12.94 % ($P<0.05$). No significant change in the PAH extraction fraction with PAH loading in vanadate-infused dogs was observed. Stopping infusion of sodium metavanadate, the PAH extraction fraction before PAH loading significantly remained reduced from the control value ($P<0.05$) without significant rose up from the experimental period value, while it after PAH loading returned to the basal value and significantly increased from the experimental period value ($P<0.05$) which insignificantly rose with PAH loading in vanadate-infused dogs.

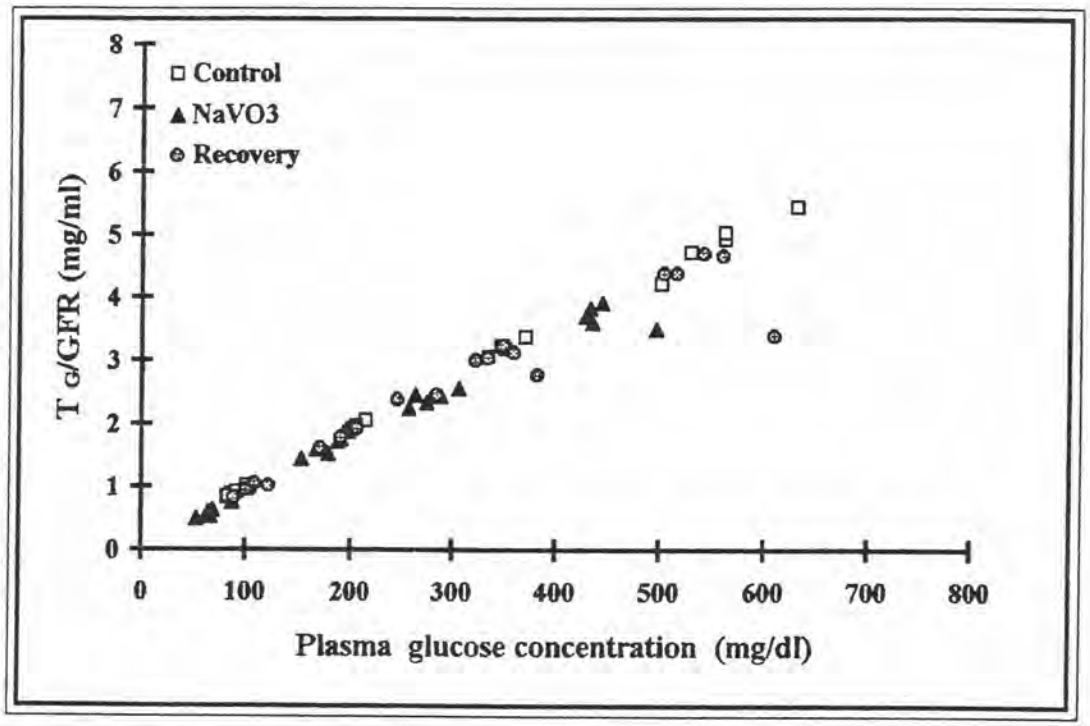
Table 11. Changes in glucose reabsorption in response to intravenous sodium metavanadate infusion.

Parameter	Experimental period	Before glucose loading (A)		Glucose loading (B)		AVsB
GFR (ml/min/kg.bw.)	Control	1.70 ± 0.04		1.77 ± 0.33		*NS*
	$NaVO_3$	0.94 ± 0.11	***	1.26 ± 0.10	**	*P<0.05*
	Recovery	1.46 ± 0.09	$$	1.68 ± 0.10		*NS*
V (µl/min/kg.bw.)	Control	58.30 ± 13.63		98.11 ± 13.39		*P<0.01*
	$NaVO_3$	30.19 ± 9.96	*	70.94 ± 23.10		*NS*
	Recovery	58.90 ± 25.01		127.15 ± 33.87	$	*P<0.01*
P_G (mg/dl)	Control	90.00 ± 3.04		557.72 ± 19.48		*P<0.001*
	$NaVO_3$	68.14 ± 4.87	***	447.43 ± 11.20	***	*P<0.001*
	Recovery	105.27 ± 4.88	** $$$	546.72 ± 16.82	$$$	*P<0.001*
U_G (mg/ml)	Control	12.14 ± 2.00		1326.30 ± 65.41		*P<0.001*
	$NaVO_3$	303.19 ± 16.35	***	1529.01 ± 72.28	***	*P<0.001*
	Recovery	264.86 ± 12.25	*** $$	1426.09 ± 73.21	* $	*P<0.001*
T_G/GFR (mg/ml)	Control	0.90 ± 0.03		4.87 ± 0.18		*P<0.001*
	$NaVO_3$	0.60 ± 0.04	***	3.71 ± 0.07	**	*P<0.001*
	Recovery	0.96 ± 0.03	$$$	4.40 ± 0.14	$$	*P<0.001*
FE_{Na} (%)	Control	2.88 ± 0.17		3.38 ± 0.08		*NS*
	$NaVO_3$	2.36 ± 0.16		3.05 ± 0.11		*P<0.01*
	Recovery	3.45 ± 0.21	$	4.29 ± 0.36		*NS*
FE_K (%)	Control	23.14 ± 2.32		31.11 ± 2.38		*P<0.05*
	$NaVO_3$	18.71 ± 1.73		26.53 ± 1.68		*NS*
	Recovery	26.02 ± 3.85		36.41 ± 6.48		*NS*

Values are the means±SEM. Only experimental kidney values are presented.
Abbreviations : T_G/GFR, tubular glucose reabsorption per mililitre GFR.

Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 different from control; $ P<0.05, $$ P<0.01, $$$ P<0.001 different from previous values; NS, not significant.

PANEL A



PANEL B

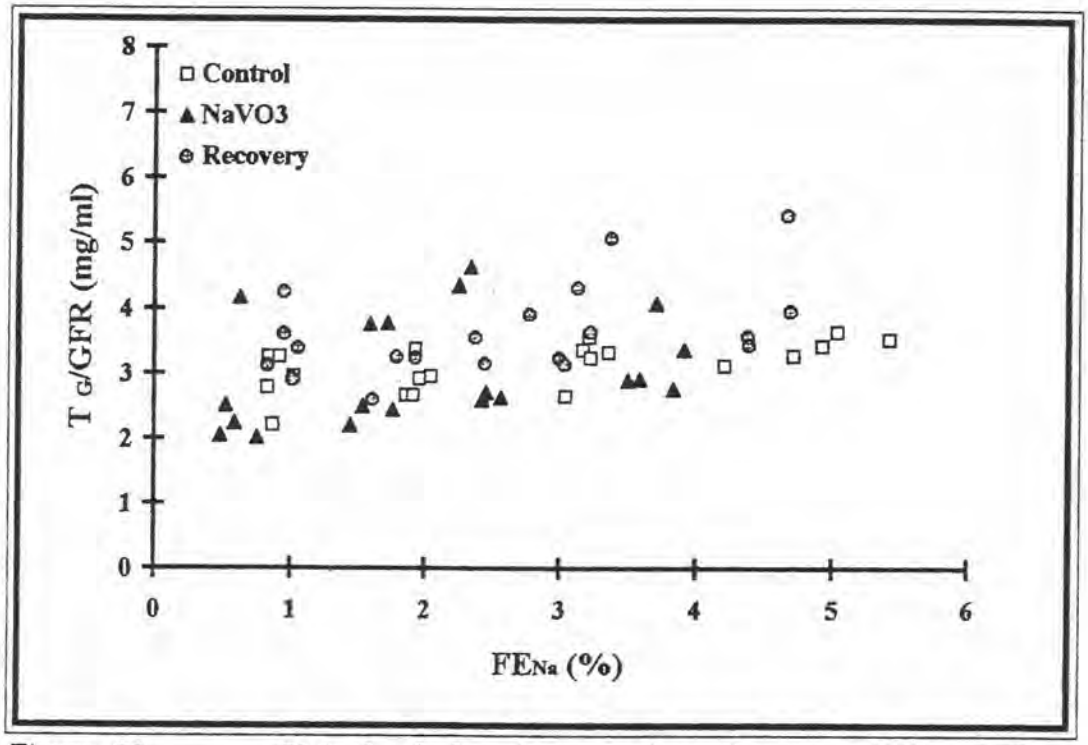


Figure 23 **Plot of tubular glucose reabsorption per millilitre GFR against plasma glucose concentration (PANEL A) or fractional sodium excretion (PANEL B) before (squares), during (triangles) and after (circles) intravenous infusion of sodium metavanadate in dogs.**

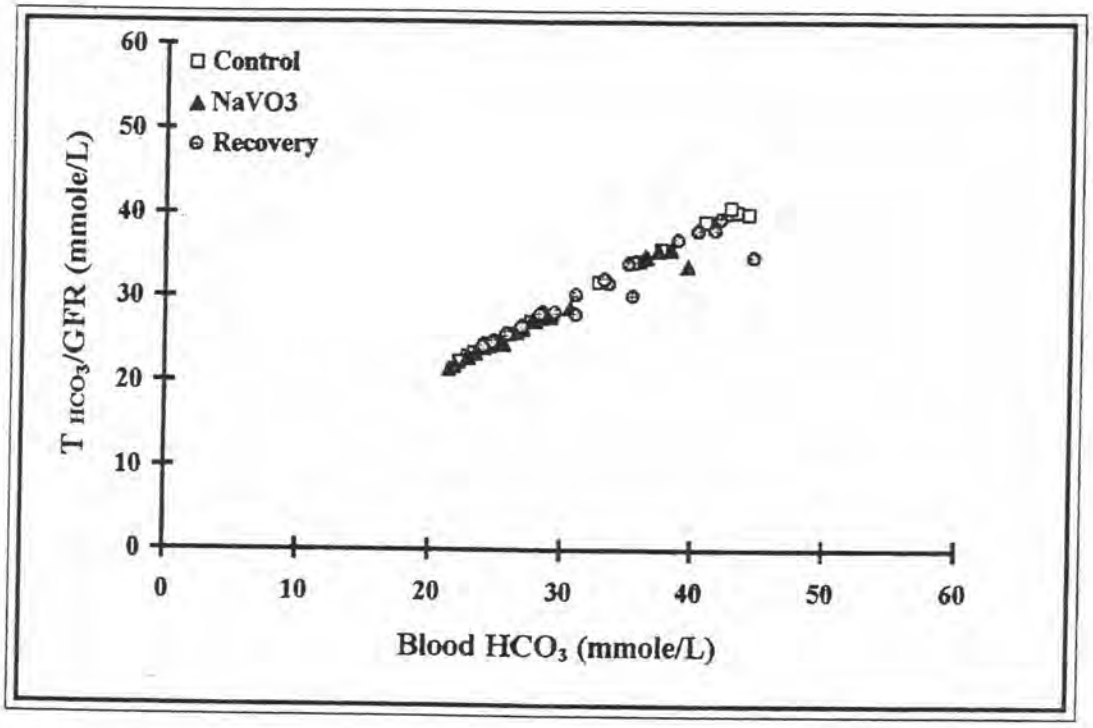
Table 12. Changes in bicarbonate reabsorption in response to intravenous sodium metavanadate infusion.

Parameter	Experimental period	Before HCO_3^- loading (A)		Bicarbonate loading (B)		AVsB
GFR	Control	1.70 ± 0.04		1.77 ± 0.33		*NS*
(ml/min/kg.bw.)	NaVO3	0.94 ± 0.11	***	1.26 ± 0.10	**	*P<0.05*
	Recovery	1.46 ± 0.09	$$	1.68 ± 0.10		*NS*
V	Control	58.30 ± 13.63		98.11 ± 13.39		*P<0.01*
(µl/min/kg.bw.)	NaVO3	30.19 ± 9.96	*	70.94 ± 23.10		*NS*
	Recovery	58.90 ± 25.01		127.15 ± 33.87	$	*P<0.01*
Blood pH	Control	7.39 ± 0.01		7.69 ± 0.07		*P<0.05*
	NaVO3	7.37 ± 0.01		7.58 ± 0.02		*P<0.01*
	Recovery	7.49 ± 0.02	** $$	7.64 ± 0.02		*P<0.05*
Urine pH	Control	5.61 ± 0.09		7.24 ± 0.19		*P<0.01*
	NaVO3	5.72 ± 0.07		7.33 ± 0.18	*	*P<0.01*
	Recovery	6.15 ± 0.17	* $	7.46 ± 0.04		*P<0.01*
Blood P_{CO_2}	Control	37.85 ± 0.84		37.50 ± 4.24		*NS*
(mmHg)	NaVO3	38.25 ± 0.34		39.97 ± 1.83		*NS*
	Recovery	33.09 ± 1.33	* $	39.02 ± 2.70		*NS*
Urine P_{CO_2}	Control	42.26 ± 6.94		68.19 ± 9.29		*P<0.01*
(mmHg)	NaVO3	38.79 ± 6.46		52.65 ± 9.15	*	*NS*
	Recovery	38.50 ± 8.93		63.45 ± 14.15		*P<0.05*
U-B P_{CO_2}	Control	4.41 ± 7.51		30.68 ± 10.70		*P<0.01*
(mmHg)	NaVO3	0.54 ± 6.37		12.68 ± 8.39	*	*NS*
	Recovery	5.40 ± 7.77		29.26 ± 13.09		*NS*
Blood HCO_3	Control	23.47 ± 0.36		42.85 ± 0.48		*P<0.001*
(mmole/L)	NaVO3	22.52 ± 0.33	*	37.56 ± 0.55	***	*P<0.001*
	Recovery	25.28 ± 0.44	* $$	41.51 ± 0.86	$$$	*P<0.001*
Urine HCO_3	Control	2.10 ± 0.20		54.36 ± 1.13		*P<0.001*
(mmole/L)	NaVO3	2.04 ± 0.19	**	50.44 ± 0.90		*P<0.001*
	Recovery	4.00 ± 0.34	*** $$$	52.06 ± 0.71		*P<0.001*
T_{HCO_3}/GFR	Control	23.39 ± 0.34		39.86 ± 0.25		*P<0.001*
(mmole/L)	NaVO3	22.46 ± 0.31	*	34.87 ± 0.32	***	*P<0.001*
	Recovery	25.11 ± 0.37	* $$	37.34 ± 0.68	* $$	*P<0.001*
FE Cl	Control	2.67 ± 0.32		7.87 ± 0.58		*P<0.01*
(%)	NaVO3	1.60 ± 0.08	*	6.78 ± 0.15		*P<0.001*
	Recovery	1.81 ± 0.08		6.74 ± 0.54		*P<0.01*

Values are the means±SEM. Only experimental kidney values are presented. Abbreviations : P_{CO_2}, carbon dioxide tension; HCO_3, bicarbonate; T_{HCO_3}/GFR, tubular bicarbonate reabsorption per mililitre GFR.

Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 different from control; $ P<0.05, $$ P<0.01, $$$ P<0.001 different from previous values; NS, not significant.

PANEL A



PANEL B

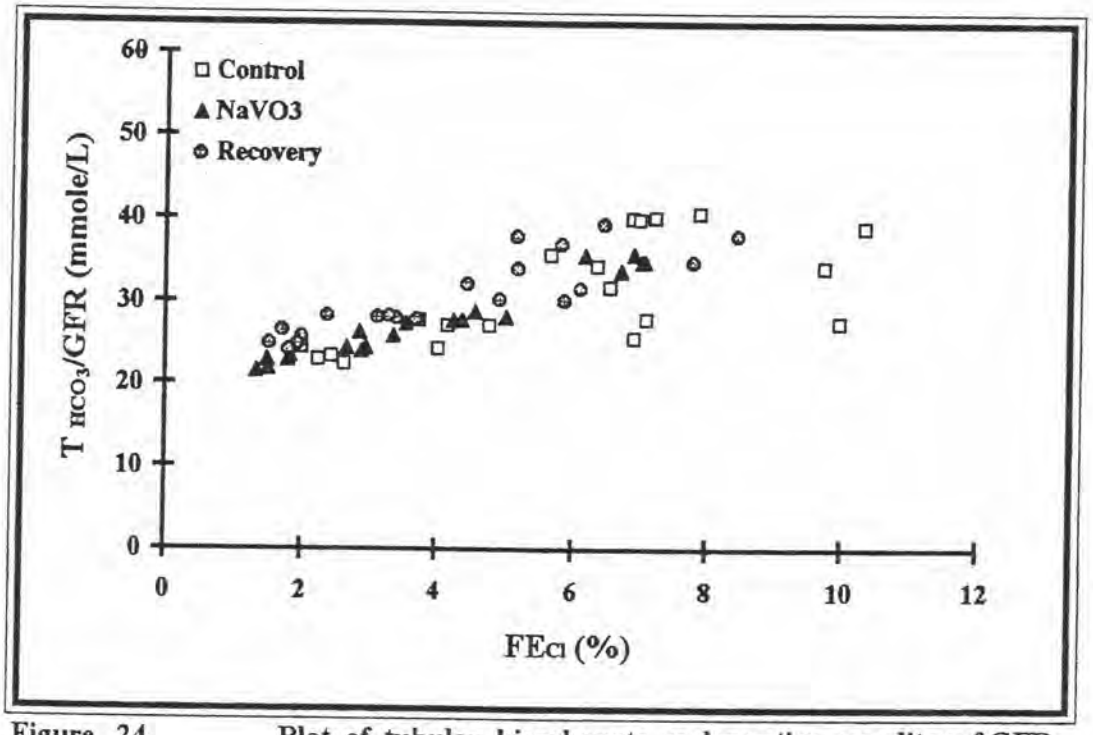


Figure 24 Plot of tubular bicarbonate reabsorption per litre of GFR against blood bicarbonate concentration (PANEL A) or fractional chloride excretion (PANEL B) before (squares), during (triangles) and after (circles) intravenous infusion of sodium metavanadate in dogs.

Table 13. Changes in PAH secretion in response to intravenous sodium metavanadate infusion.

Parameter	Experimental period	Before PAH loading (A)		PAH loading (B)		AVsB
GFR (ml/min/kg.bw.)	Control	1.70 ± 0.04		1.77 ± 0.33		*NS*
	$NaVO_3$	0.94 ± 0.11	***	1.26 ± 0.10	**	*P<0.05*
	Recovery	1.46 ± 0.09	$$	1.68 ± 0.10		*NS*
V (µl/min/kg.bw.)	Control	58.30 ± 13.63		98.11 ± 13.39		*P<0.01*
	$NaVO_3$	30.19 ± 9.96	*	70.94 ± 23.10		*NS*
	Recovery	58.90 ± 25.01		127.15 ± 33.87	$	*P<0.01*
Free plasma PAH (mg/dl)	Control	9.80 ± 0.44		186.66 ± 6.09		*P<0.001*
	$NaVO_3$	17.54 ± 1.52	*	279.96 ± 16.23	**	*P<0.001*
	Recovery	16.24 ± 0.97	**	277.08 ± 14.24	**	*P<0.001*
$U_{PAH}V$ (mg/min/kg.bw.)	Control	0.64 ± 0.12		5.95 ± 0.74		*P<0.01*
	$NaVO_3$	0.26 ± 0.08	*	4.30 ± 0.54	*	*P<0.01*
	Recovery	0.40 ± 0.08	$	8.68 ± 0.99	$$	*P<0.01*
T_{PAH}/GFR (mg/ml)	Control	0.28 ± 0.08		1.46 ± 0.42		*NS*
	$NaVO_3$	0.08 ± 0.05	*	0.59 ± 0.31	*	*NS*
	Recovery	0.11 ± 0.05		1.73 ± 0.77	$	*P<0.05*
C_{PAH} (ml/min/kg.bw.)	Control	6.54 ± 1.29		3.25 ± 0.48		*P<0.05*
	$NaVO_3$	1.42 ± 0.37	*	1.62 ± 0.27	**	*NS*
	Recovery	2.53 ± 0.53	* $	3.15 ± 0.43	$$	*NS*
FE_{PAH} (%)	Control	381.44 ± 69.93		181.71 ± 24.67		*P<0.05*
	$NaVO_3$	145.39 ± 29.68	*	123.97 ± 12.94	*	*NS*
	Recovery	170.81 ± 31.67	*	193.93 ± 32.66	$	*NS*

Values are the means±SEM. Only experimental kidney values are presented.
Abbreviation : T_{PAH}/GFR, tubular p-aminohippuric acid secretion per mililitre GFR.

Significant difference values using paired t'test are indicated by * P<0.05, ** P<0.01, *** P<0.001 different from control; $ P<0.05, $$ P<0.01, $$$ P<0.001 different from previous values; NS, not significant.

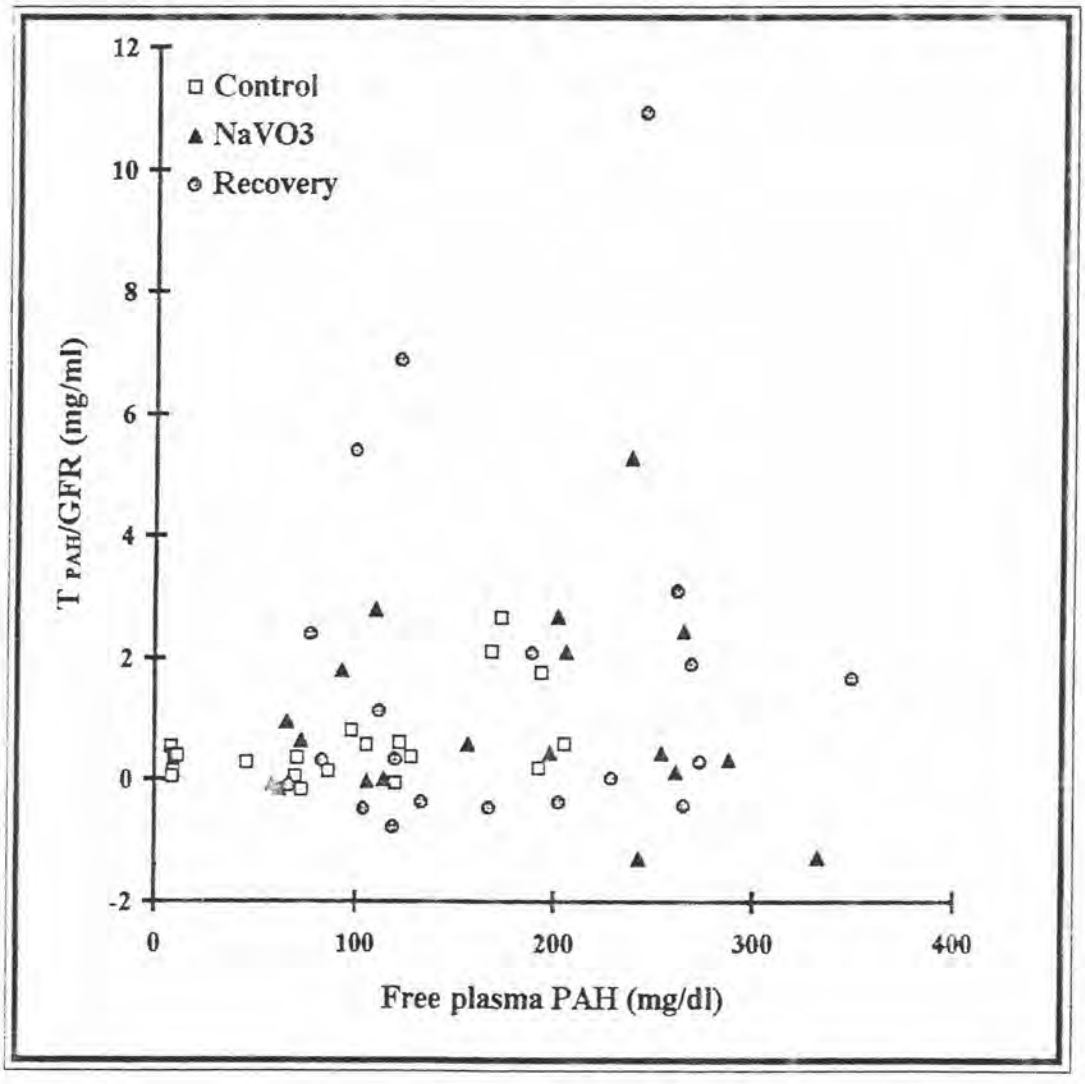


Figure 25 Plot of tubular PAH secretion per millilitre of GFR against free plasma PAH concentration bofore (squares), during (triangles) and after (circles) intravenous infusion of sodium metavanadate in dogs.