Chapter IV

Results

Effects of Russell's viper venom on general circulation (Table 1, Fig 1-2)

Group I : control animals.

Data summarized in Fig 1 show that a slow intravenous injection of 0.05 mg/kg.bw of Russell's viper venom within 10 min depressed mean arterial pressure (MAP) significantly from 122.24 ± 31.59 to 85.62 ± 35.67 mmHg ($p<0.05$). The depression persisted for 30 min then gradually increased to approach the control level by 50 min. At the end of experiment mean arterial pressure rose up significantly to 131.64 ± 30.4 mmHg ($p<0.05$). The marked change in heart rate (HR) was not apparent within 30 min of envenomation but the decline was found significantly ($p<0.05$) in 50 min and sustained throughout the experiment (Fig 2). The significant rising in packed cell volume (PCV) was noted only in 10 min of envenomation from 31.8 ± 1.52 to 34.6 ± 3.1% ($p<0.05$).

Group II : animals treated with 2 mg/kg/min of imidazole after envenomation.

Intravenous injection of Russell's viper venom produced a profound hypotension, which significant value could be obtained

within 10 min from 138.84 ± 48.56 to 103.96 ± 46.24 mmHg ($p<0.01$). The significant decline was sustained for 30 min then increased significantly within 50 and 70 min ($p<0.05$), which these periods thromboxane synthetase inhibitor (imidazole) has been infused via left renal artery. The high mean arterial pressure persisted throughout the experiment. Envenomation produced a significant elevation of packed cell volume (PCV) throughout the experiment ($p<0.05$ to $p<0.01$). A sharp rise of heart rate was seen within 10 min of envenomation then turned down and gradually rose again, however these changes were not significant (Fig 2).

Group III : animals pretreated with 2 mg/kg/min of imidazole

Result in Fig. 1 reveal that after 10 mins of continuous infusion of thromboxane synthetase inhibitor (imidazole) via renal artery, both mean arterial pressure and packed cell volume increased significantly from 142.64 ± 66.77 to 165.96 ± 63.7 mmHg and from 29.1 ± 5.97 to 34.8 ± 9.11% respectively ($p<0.05$). A slightly decrease in mean arterial pressure with respected to control was occurred in 10 min after envenomation (to 136.94 ± 80.63 mmHg) then progressively elevated to significant level by 70 and 90 min (to 168.32 ± 73.25 and 172.32 ± 69.65 mmHg respectively, $p<0.05$). Packed cell volume also increased to a higher significant level after envenomation by approximately 44.1% ($p<0.001$). There was no significant alteration of heart rate throughout the experiment.

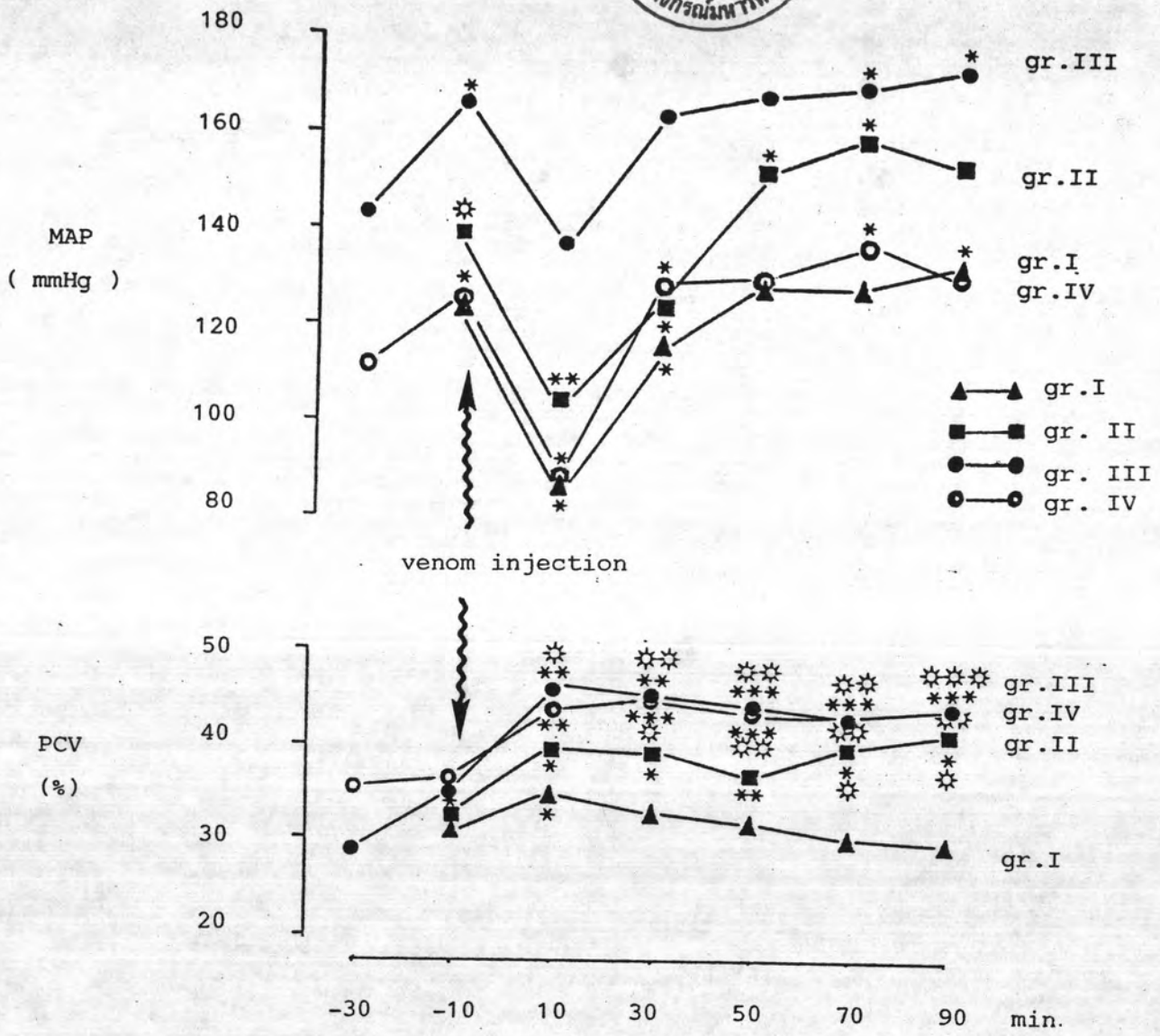

Fig.1; Effects of intravenous injection of Russell's viper venom on mean arterial pressure (MAP) (upper panel) and packed cell volume (PCV) (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Values are statistically significantly different from group I. at the same period, ✡ $p < 0.05$, ✡✡ $p < 0.01$, ✡✡✡ $p < 0.001$.

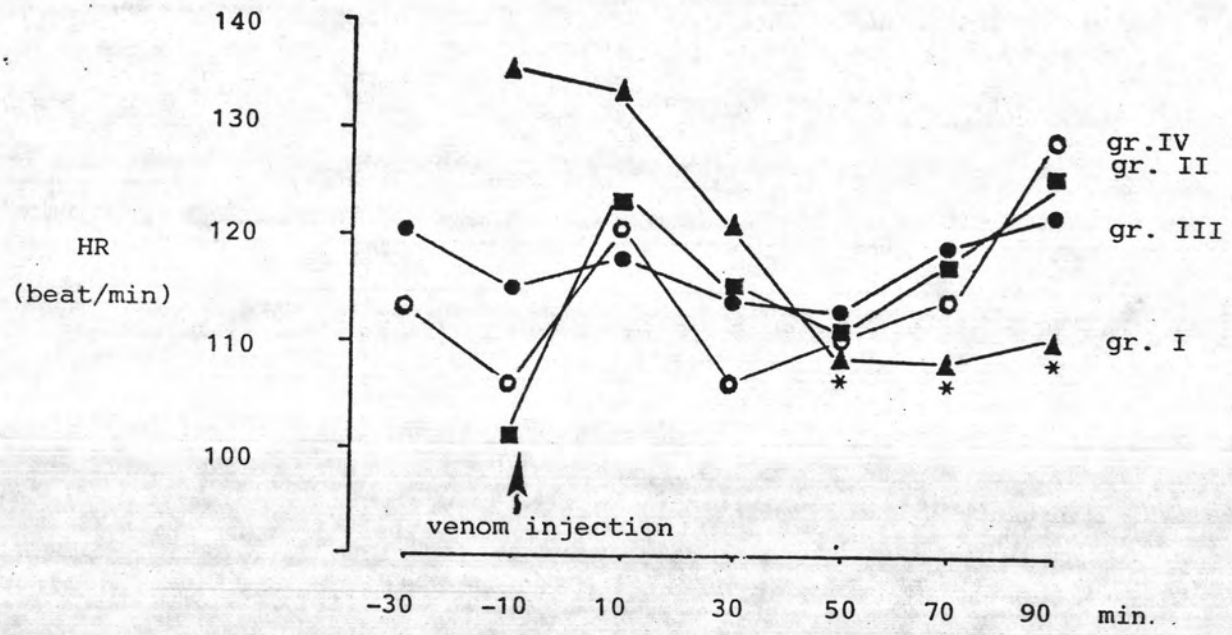

Fig.2: Effects of intravenous injection of Russell's viper venom on heart rate (HR) in group I (control animals). group II (animals treated with 2mg/kg/min of imidazole after envenomation). group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).
Values are statistically significantly different from control period of each group.

* $p < 0.05$.

Table 1 Effect of Russell's viper venom on general circulation in dogs.

Parameter	Group I			Group II			Group III			Group IV	
	Control	Post-envenomation		Control	Post-envenomation (+IMID)		Control	Pre-treated with IMID(2mg) Post-envenomation		Control	Pre-treated with IMID(0.5mg) Post-envenomation
		30 min	90 min		30 min	90 min		30 min	90 min		30 min	90 min
MAP (mmHg)	122.24 ±31.59	114.62 ±30.60 **	131.64 ±30.40 *	138.84 ±48.56 #	122.96 ±54.97 *	153.98 ±40.31 #,*	142.64 ±66.77	162.98 ±75.70 ##,**	172.32 ±69.65 ##,*** *	110.33 ±29.96	129.66 ±21.77 #,*** *	130.66 ±43.56 ##,**
PCV %	31.80 ±1.52	32.90 ±4.26	29.30 ±2.99 **	32.30 ±6.30	39.30 ±8.82	41.70 ±7.94	29.10 ±5.97	45.10 ±5.70	44.10 ±5.59	35.70 ±7.77	45.30 7.25	44.40 ±7.59
HR (beat/ min)	135.00 ±25.36	120.60 ±31.49	109.8 ±18.56	101.14 ±21.14	115.20 ±19.27	125.40 ±20.70	120.60 ±16.34	114.00 ±20.56	122.40 ±16.62	112.60 ±15.94	105.60 ±11.69	129.60 ±27.11

Group I : control animals recieved the venom alone; Group II : animal treated with 2 mg/kg/min of imidazole after envenomation; Group III : animals pretreated with 2 mg/kg/min of imidazole and group IV : animals pretreated with 0.5 mg/kg/min of imidazole. Values are mean±SD.

* $p<0.05$; ** $p<0.01$; *** $p<0.001$ with respect to control period of each group.

# $p<0.05$; ## $p<0.01$; ### $p<0.001$ with respect to group I at the same period .

Group IV : animals pretreated with 0.5 mg/kg/min of imidazole.

After 10 min of intrarenal arterial continuous infusion of imidazole, mean arterial pressure rose significantly from 110.33 to 122.3 mmHg ($p<0.05$). However, intravenous injection of Russell's viper venom also produced profound hypotension in this group (Fig 1 upper panel) within10 mins of envenomation. After 30 min mean arterial pressure roseagain to the level higher than that of control period. The significant difference was seen in 30,50 and 70 min peroid respectively. Packed cell volume was slightly increased by the effect of imidazole and strikingly elevation throughout the experiment after the venom injection. The more time lasted, the more significant difference was apparent which was similar to group III. Heart rate was affacted in a minor extent by both imidazole and envenomation.

In comparison, although the initial mean arterial pressure of group II was significantly higher than group I ($p<0.05$), intravenous injection of the same dosage of Russell's viper venom produced a marked hypotension similarly to group I. After continuous infusion of imidazole, mean arterial pressure was more increase in group II. However no significant difference between groups in these period were seen. While in group III which imidazole has been continuously infused prior to envenomation showed a mild decrease of mean arterial pressure from the control level (Fig. 1, upper panel). After envenomation, the increase in mean arterial pressure in this group was similar to group II. Imidazole caused a markedly persistent elevation of packed cell volume in both group II and III whereas group I

revealed a decline to approach the control level in 30 min (Fig.1,lower panel). These differences among group were more pronounced in group III ($p < 0.001$). Heart rate showed no significant differences among groups, however imidazole treated groups (II and III) showed a slight increase in heart rate whereas a marked decrease was found in group I (Fig. 2).

Effects of Russell's viper venom on renal hemodynamics (Table 2, Fig 3-7)

Group I : control animals.

The results summarized in Fig 3-7 show effective renal plasma flow (ERPF), effective renal blood flow (ERBF) and glomerular filtration rate (GFR) fell immediately to the lowest level within 10 mins after venom injection in both right and left kidney. These lowering data were not significant. Filtration fraction (FF) was suddenly increased within 10 min in both kidney. In the right kidney the significant elevation was seen in 30 and 70 min ($p<0.05$) after envenomation. A slight increase of filtration fraction was occurred in theleft kidney throughout the experiment. An alteration of renal vascular resistance in response to envenomation was variable, the divergent response between right and left kidney occurred in 10 min. The former was increased while the latter was decreased. Both of them were no significant difference from the control level. At the end of experiment renal vascular resistance was increased in both kidney.

Group II : animals treated with 2 mg/kg/min of imidazole after envenomation.

There were marked decrease in effective renal plasma flow, effective renal blood flow and glomerular filtration rate within 10 min of both kidney ($p < 0.05$). At 30 min all these data became to rise again. When imidazole was infused via left renal artery, all of these parameters were suppressed again. Especially in left kidney the depression of effective renal plasma flow and effective renal blood flow were presented in 70 and 90 min ($p<0.05$). The marked lowering of glomerular filtration rate was occurred at the end of experiment ($p <0.05$). Filtration fraction significantly increased in 10 min in right kidney ($p<0.05$), similar elevation but not significant was found in the left kidney. When intrarenal continuouse infusion of imidazole was performed, progressive lowering of filtration fraction was occurred. Renal vascular resistance was sharply increased in 10 min in both kidney. Although the rising was variable, it sustained high level throughout the experiment.

Group III : animals pretreated with 2 mg/kg/min of imidazole

Continuous intrarenal arterial infusion of thromboxane synthetase inhibitor (TSI imidazole) produced a mild increase in effective renal plasma flow, effective renal blood flow and glomerular filtration rate in 10 min. Intravenous injection of Russell's viper venom caused a marked reduction of these parameters within 10 and 30 min ($p<0.01$ and $p< 0.05$ respectively) in the right kidney. The left

kidney showed a significant decline of effective renal plasma flow only within 10 min ($p<0.05$). However, marked but not significant reduction of both effective renal blood flow and glomerular filtration rate were also appeared at this time. The significant reduction of glomerular filtration rate was higher ($p<0.01$) at 30 min and persisted at this level throughout the experiment. The significant reduction of both effective renal plasma flow and effective renal blood flow were increased ($p<0.01$) at 30 min then decreased to the previous value ($p<0.05$) throughout the experiment. Filtration fraction was slightly decreased after imidazole infusion. Envenomation produced a marked increase in filtration fraction in both kidneys. The significant increase was apprent only in the left kidney 30 min after the venom injection. After 30 min of envenomation filtration fraction gradually decreased near the control level. Renal vascular resistance was increased after imidazole had been infused alone. Envenomation during intrarenal infusion of imidazole induced progressive elevation of renal vascular resistance throughout the experiment. In the right kidney, a significant elevation of renal vascular resistance was seen in 10 mins after the venom injection.

Group IV : animals pretreated with 0.5 mg/kg/min of imidazole

Continuous intrarenal arterial infusion of imidazole produced a mild increase in effective renal plasma flow, renal blood flow and glomerular filtration rate in the right and a mild decrease in the left kidney within 10 min. Envenomation depressed all of these parameters throughout the experimental period (Fig 3-5). Significant

difference of the renal hemodynamic from the control group was more apparent in the left kidney. Renal vascular resistance was slightly increased by the effect of imidazole, after envenomation it progressively elevated throughout the experiment in the left kidney as same as group III.

Filtration fraction slightly altered by imidazole infusion. After envenomation filtration fraction suddenly increased in left the kidney which was greatly extendible than the right kidney. Then it gradually declined to the level under the pre-envenomation period in left kidney.

In comparison (Fig 3-5) effects of Russell's viper venom on renal hemodynamics in three groups of dog revealed that intravenous injection of 0.05 mg/kg bw. of the venom alone did not cause any significant change in effective renal plasma flow, effective renal blood flow and glomerular filtration rate from control period. Where as Intrarenal arterial continuous infusion of thromboxane synthetase inhibitor, produced profound depression of these parameters. These suppression of the group II and III were significantly different from group I which recieved the venom alone and the severity was more pronounced in the left kidney than the right kidney. Filtration fraction (Fig. 6) was found higher in both group II and group III than group I . There were increase in filtration fraction during 30 min suddenly after envenomation in all groups. Renal vascular resistance in group III revealed a sharp rise and persisted at the high level throughout the experiment. This elevation was dominant in

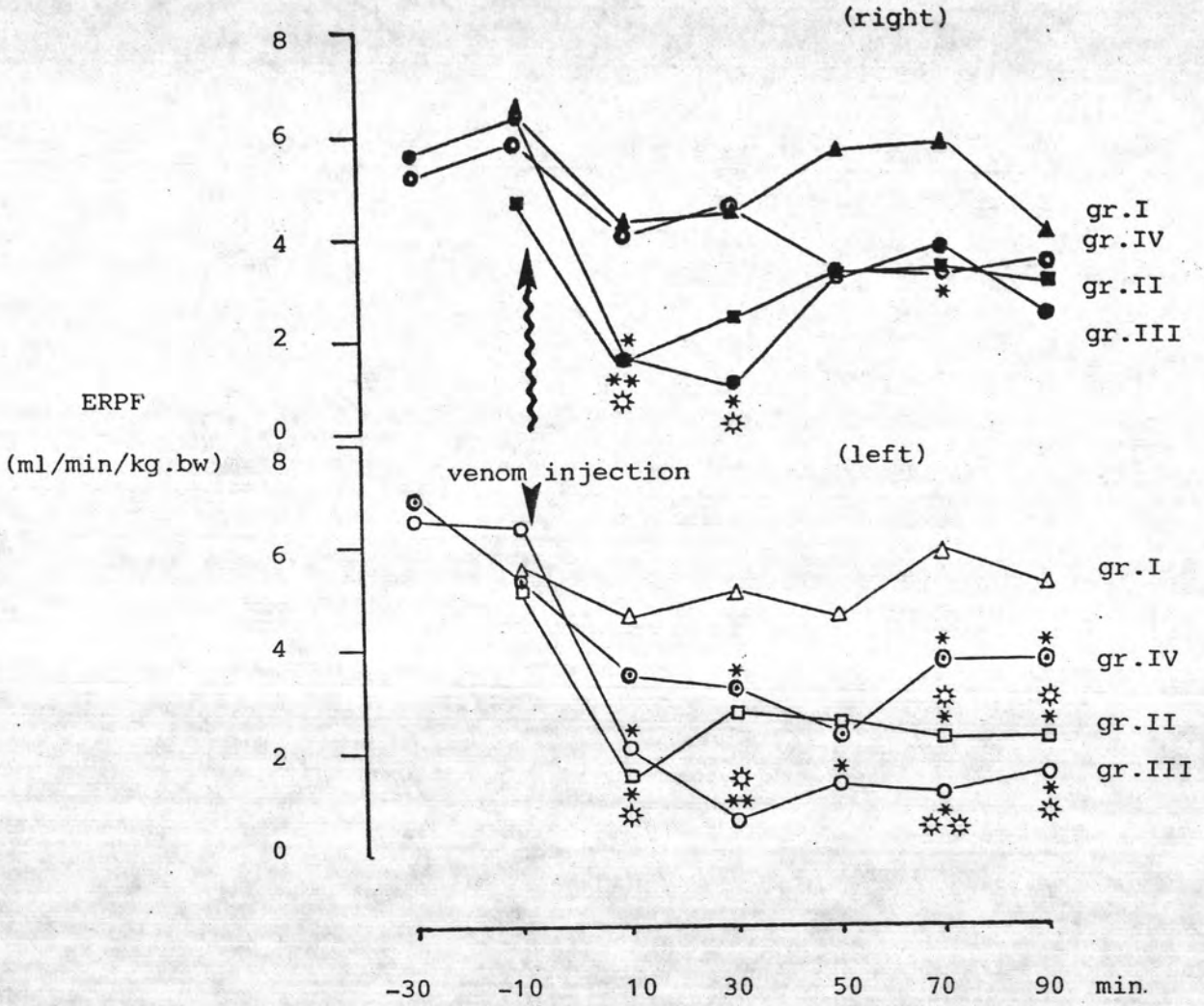

Fig.3: Effects of intravenous injection of Russell's viper venom on effective renal plasma flow (ERPF) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$,

Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$, ✡✡ $p < 0.01$.

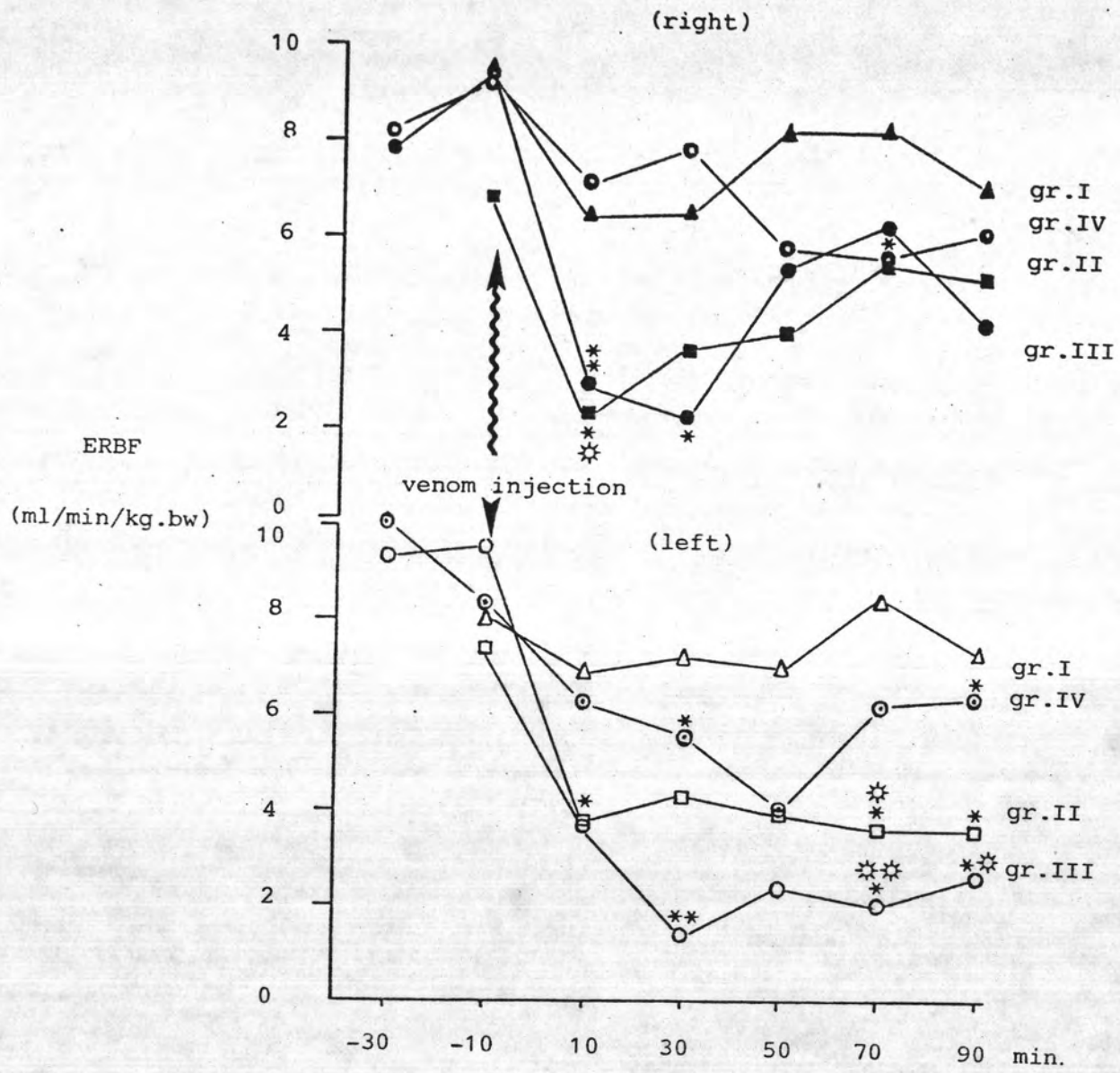

Fig.4: Effects of intravenous injection of Russell's viper venom on effective renal blood flow (ERBF) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.

Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$, ✡✡ $p < 0.01$.

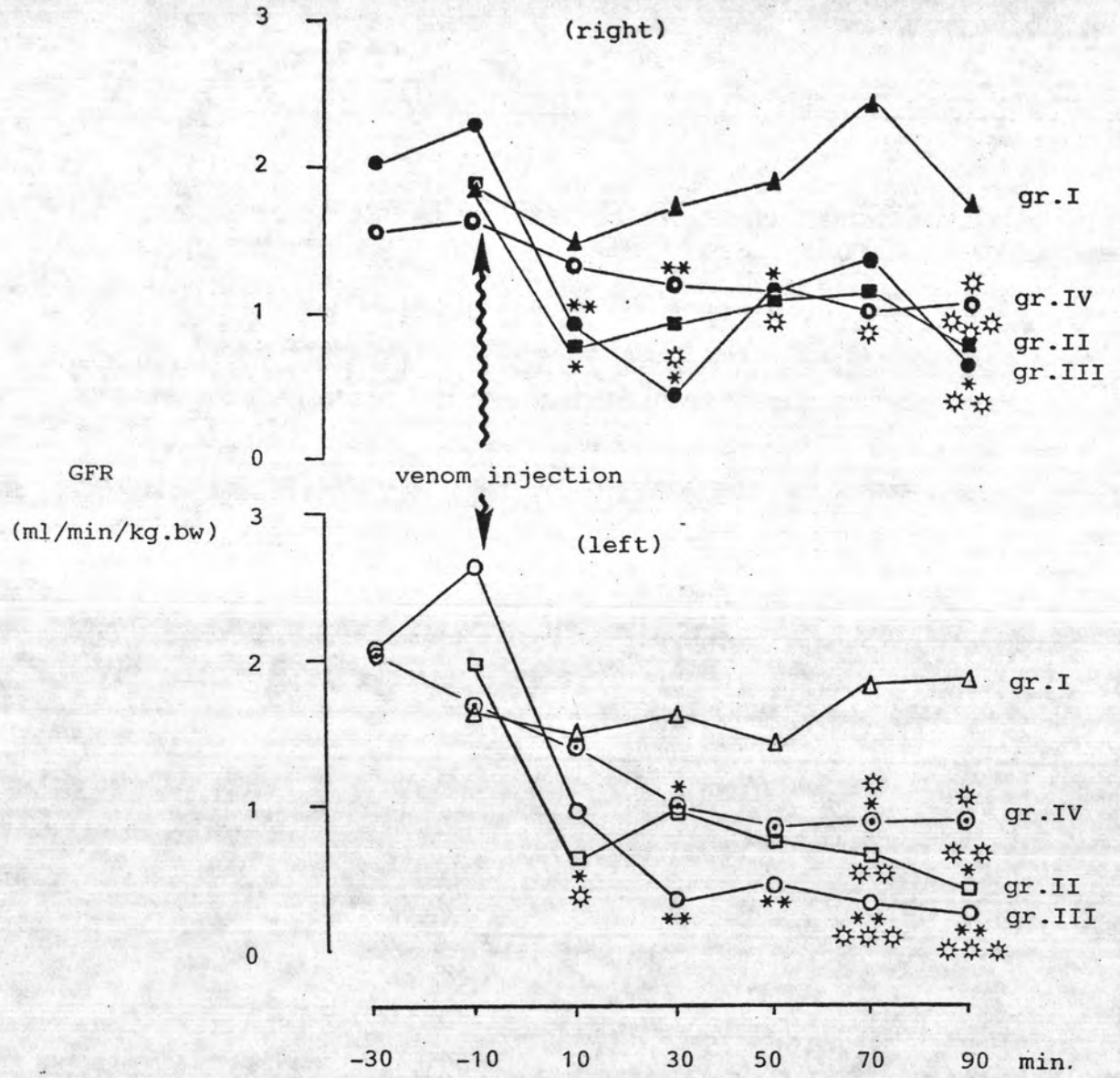

Fig.5: Effects of intravenous injection of Russell's viper venom on glomerular filtration rate (GFR) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation) group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole). Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$. Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$, ✡✡ $p < 0.01$, ✡✡✡ $p < 0.001$.

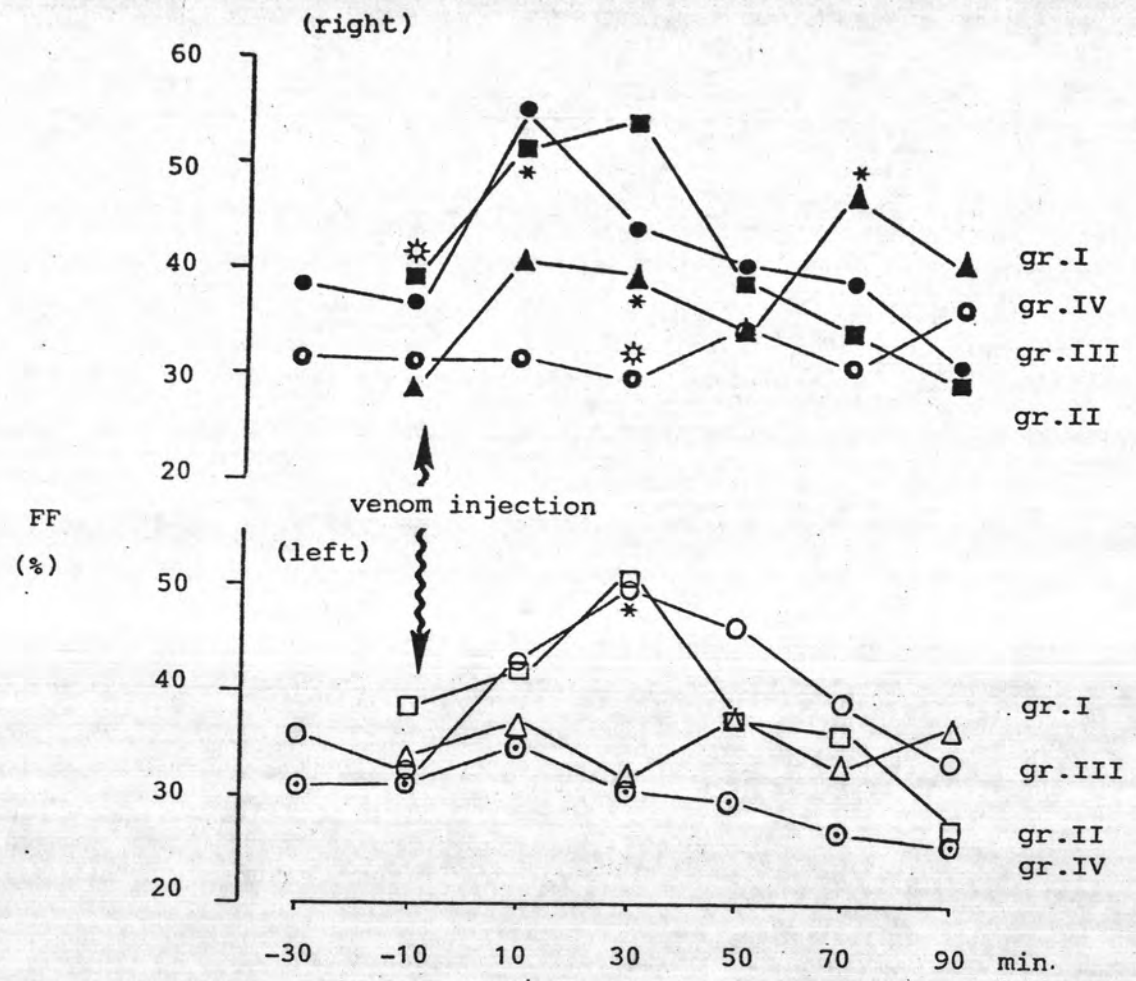

Fig.6: Effects of intravenous injection of Russell's viper venom on filtration fraction (FF) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).
Values are statistically significantly different from control period of each group, * $p < 0.05$.
Values are statistically significantly different from group I at the same period, ☼ $p < 0.05$.

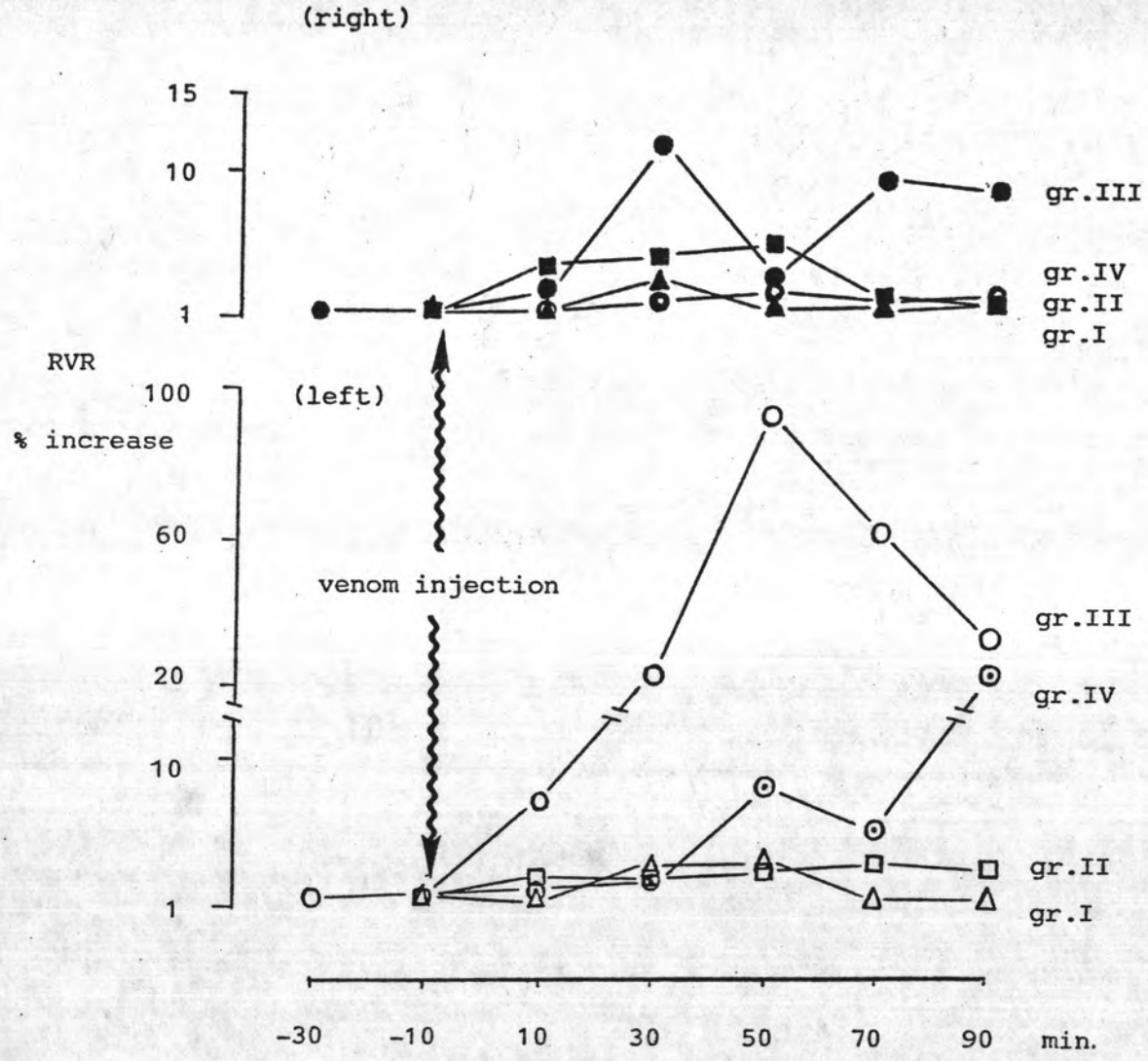

Fig.7 Effects of intravenous injection of Russell's viper venom on renal vascular resistance (RVR) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Table 2 Effect of Russell's viper venom on renal hemodyamic of the right (Rt) and the left (Lt) kidney in dogs.

Parameter		Group I			Group II			Group III			Group IV		
								Pre-treated with IMID(2mg)			Pre-treated with IMID(0.5mg)		
		Control	Post-envenomation		Control	Post-envenomation		Control	Post-envenomation		Control	Post-envenomation	
			30 min	90 min		30 min	(+IMID) 90 min		30 min	90 min		30 min	90 min
RBF (ml/ min/ kg bw)	Rt	9.48 ±2.15	6.37 ±3.94	6.96 ±3.04	6.77 ±2.71	3.54 ±3.01	5.12 ±2.13 *	7.92 ±2.37	2.21 ±2.85 **	4.22 ±3.63 #,*	8.15 ±0.73	7.91 ±4.38 *	6.09 ±3.10 *
	Lt	9.79 ±2.85	7.17 ±4.81	7.27 ±2.69	7.35 ±3.16	4.24 ±1.97	3.53 ±2.51 ###	9.37 ±3.64	1.45 ±1.44 #,*	2.64 ±2.68 ##,*	10.23 ±3.41	5.47 ±3.33 **	6.10 ±3.29 #
GFR (ml/ min/ kg bw)	Rt	1.78 ±0.31	1.68 ±1.05	1.73 ±0.35	1.81 ±0.90	0.89 ±0.47	0.72 ±0.14 ##,*	2.00 ±0.68	0.43 ±0.60 **	0.62 ±0.55 ###,**	1.62 ±0.61	1.22 ±0.64 *	1.08 ±0.28 #
	Lt	1.61 ±0.47	1.60 ±1.04	1.79 ±0.63	1.98 ±1.04	0.91 ±0.62	0.48 ±0.32	2.08 ±0.52	0.35 ±0.29	0.27 ±0.23	2.05 ±0.96	0.96 ±0.68	0.91 ±46.00
FF %	Rt	28.49 ±6.73	38.96 * ±5.83	40.14 ±16.43	38.42 # ±5.11	53.14 ±27.77	28.82 ±13.93	38.33 ±16.94	43.51 ±19.56 *	30.14 ±13.56	31.37 ±10.85	29.69 # ±6.11	37.64 ±16.93
	Lt	33.34 ±17.01	31.88 ±6.84	36.06 ±9.21	38.39 ±7.06	50.26 ±24.15	26.53 ±10.96	35.79 ±17.71	49.77 ±17.15	34.32 ±20.93	31.13 ±10.87	30.50 ±6.06	26.78 ±6.16
RVR %	Rt	100	325.00 ±462.59	177.12 ±133.31	100	439.02 ±442.36	179.12 ±111.30	100	1235.99 ±1410.77	930.53 ±1165.42	100	166.46 ±115.76	191.39 ±108.82
	Lt	100	343.05 ±601.20	125.33 ±52.41	100	186.37 ±125.94	303.74 ±149.26	100	2194.45 ±3030.59	3389.80 ±4456.03	100	293.47 ±184.17	2379.80 ±4654.70

the left kidney (Fig 7) whereas the striking elevation in group IV was apparrent in the left kidney only.

Effects of Russell's viper venom on renal function (Table 3-6, Fig 8-25)

Group I : control animals.

Right kidney

Data summarized in Fig 8 show that urine volume (V) was gradually decreased by the effect of Russell's viper venom injection. The lowest urine out put was approximately 51% of pre-envenomation period in 30 min then gradually increased to approach the control level by 50 min. At the end of experiment the urine volume increased by approximately 19% from control level. The response of osmolar clearance (C_{Osm}) to the venom was similar to urine volume, the lowering value was significantly found in 30 and 50 min from 61.15 $\pm$ 10.32 to 38.69 $\pm$ 18.84 and 41.22 $\pm$ 14.65 ul/min/kg repectively ($p<0.05$) (Fig 11). Whereas plasma osmolality (P_{Osm}) (Fig 12) slightly increase throughout the experiment. Free water clearance (C_{H_2O}) moderately elevated at the end of the experiment (Fig 9). A mild decrease of urine osmolality was seen. Urinary osmolar excretion ($U_{Osm}V$) significantly decreased by 50 min of envenomation from 16.95 $\pm$ 2.82 to 11.49 $\pm$ 4.14 uOsm/min/kg bw. ($p< 0.05$) (Fig 15). Urinary sodium excretion ($U_{Na}.V$) also decreased throughout the experiment, the significance was seen in 30 and 50 min after envenomation from 6.58 $\pm$ 3.67 to 2.68 $\pm$ 1.52 and 2.44 $\pm$ 1.43 uEq/min/kg bw. respectively ($p<0.05$) (Fig 16). While plasma sodium (P_{Na}) (Fig 13) slightly

increased, a significant difference was noted only at the end of experiment. Fractional excretion of sodium (FE_{Na}) slightly decreased (Fig 21).

There were no significant alterations of plasma potassium (P_K), urinary potassium excretion ($U_K.V$) and fractional excretion of potassium (FE_K). Plasma chloride (P_{Cl}) was rather stable, while urinary chloride excretion ($U_{Cl}V$) also depressed, the significance was noted in 50 min from 4.02 $\pm$ 1.62 to 2.17 $\pm$ 0.98 µEq/min/kgbw. ($p<0.05$). Plasma calcium (P_{Ca}) (Fig 14) significantly decreased in 50 and 70 min ($p<0.05$), whereas urinary calcium excretion ($U_{Ca}.V$) (Fig 19) significantly increased ($p<0.05$) within 10 min of envenomation then gradually decreased throughout the experiment. Fractional calcium excretion (FE_{Ca}) also decreased, a significant level was reached in 70 min ($p<0.05$) (Fig 24). Plasma inorganic phosphorus (P_{Pi}) reduced to a significant level in 30 min ($p<0.01$) and persisted till 70 min ($p <0.05$). Urinary excretion of inorganic phosphorus ($U_{Pi}V$) significantly decreased within 10 min ($p<0.05$) and maintained over 50 min after envenomation. Whereas fractional excretion of inorganic phosphorus (FE_{Pi}) was not significantly alterated (Fig 25).

Left kidney

Russell's viper venom induced a marked reduction of urine volume (V) by approximately 61% of control peroid ($p < 0.01$) in 10 min and it gradually increased to 144% of control level at the end of experiment. Free water clearance (C_{H_2O}) increased continously whereas osmolar clearance (C_{Osm}) and urinary osmolar excretion ($U_{Osm}.V$) showed

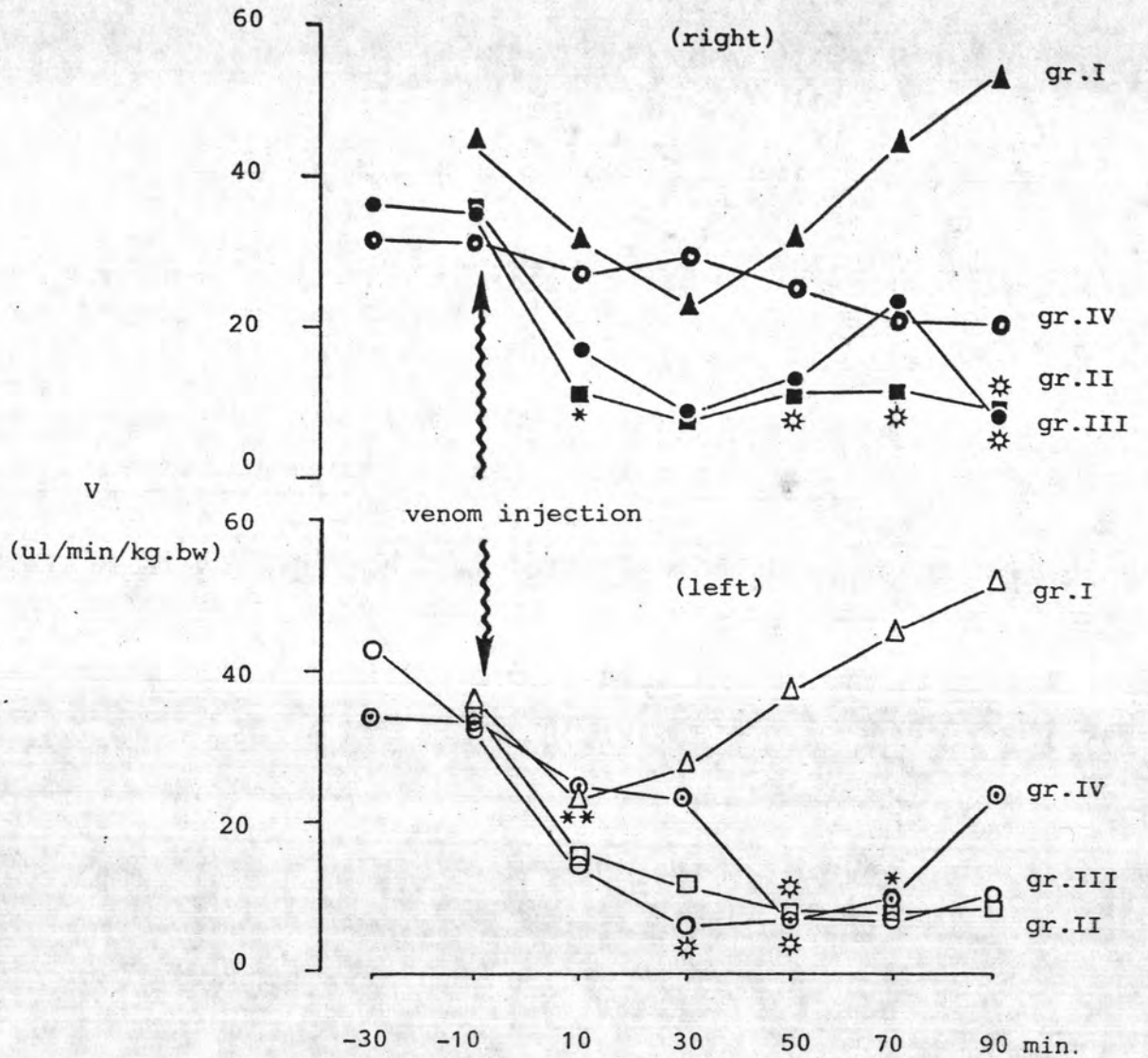

Fig.8: Effects of intravenous injection of Russell's viper venom on urine volume (V) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.

Values are statistically significantly different from group I at the same period, ☼ $p < 0.05$.

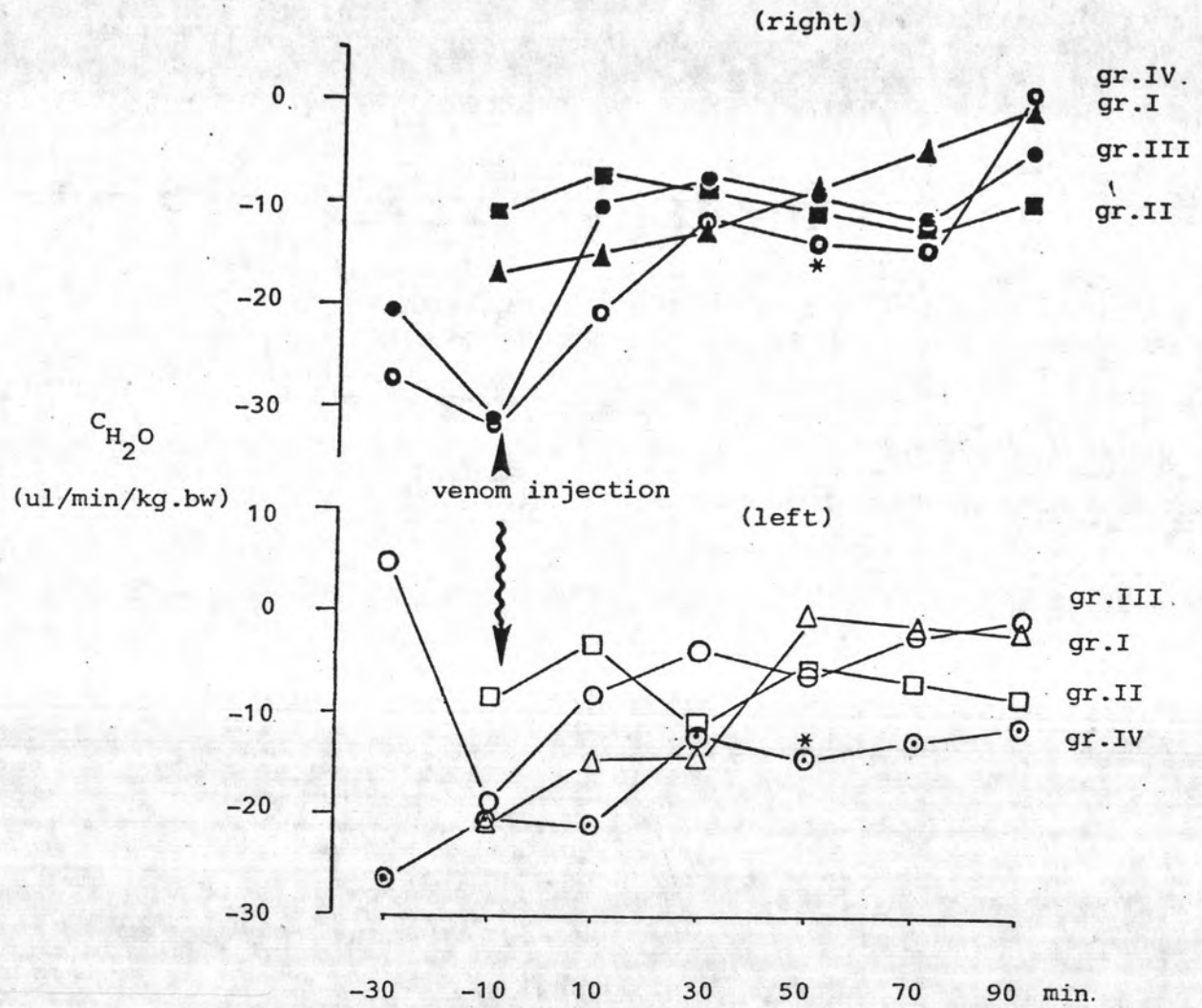

Fig.9: Effects of intravenous injection of Russell's viper venom on free water clearance (C_{H_2O}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different control period cf each group, $p < 0.05$.

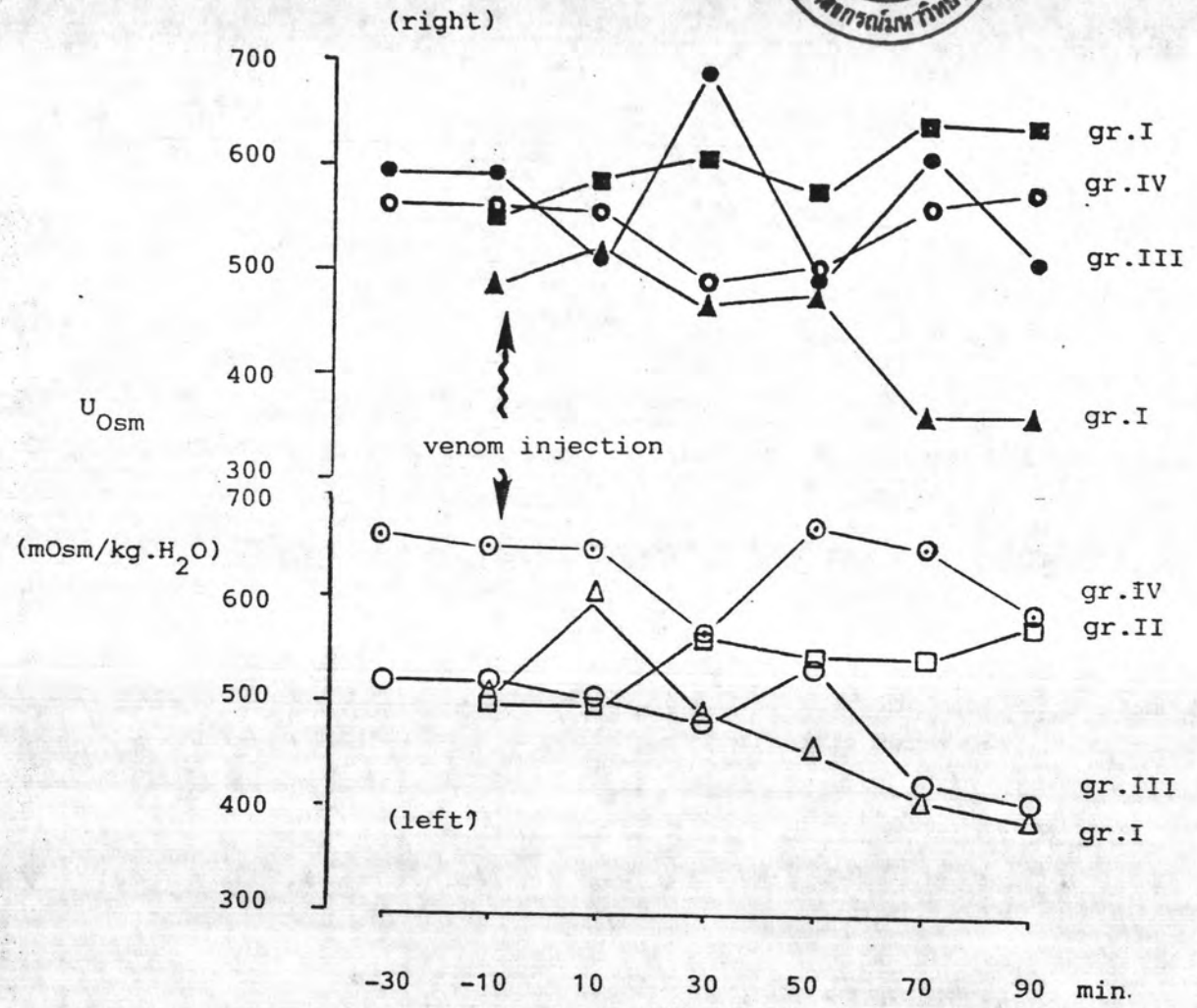

Fig.10: Effects of intravenous injection of Russell's viper venom on urinary osmolality (U_{Osm}) in right kidney (upper panel) and left kidney (lower panel) ingroup I (control animals), group II (animals treated with 2mg/kg/min ofimidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5 mg/kg/min of imidazole).

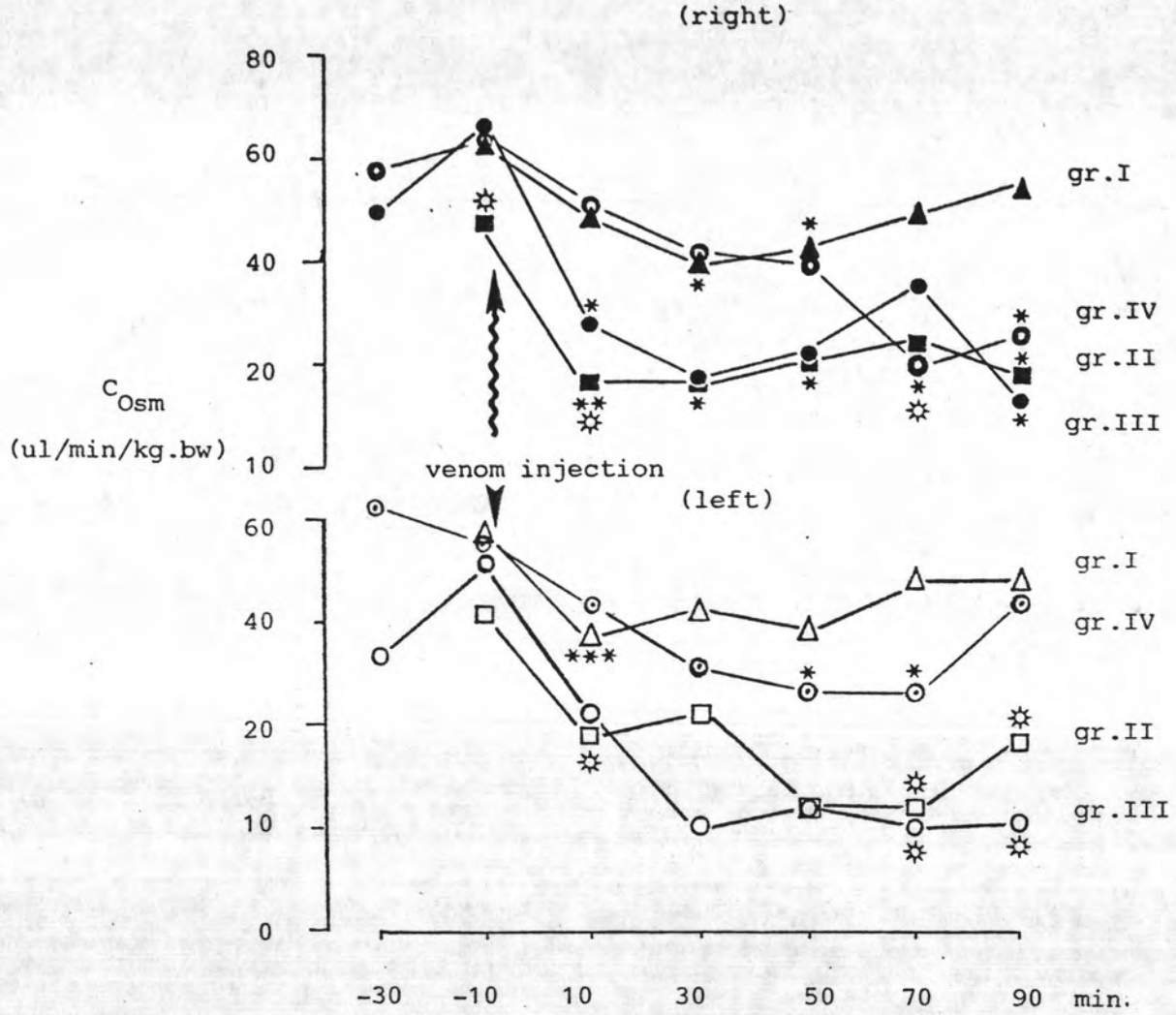

Fig.11: Effects of intravenous injection of Russell's viper venom on osmolar clearance (C_{Osm}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$.

Table 3 Effect of Russell's viper venom on renal function of the right(Rt) and the left (Lt) kidney in dogs.

Parameter		Group I			Group II			Group III			Group IV		
								Pre-treated with IMID(2mg)			Pre-treated with IMID(0.5mg)		
		Control	Post-envenomation		Control	Post-envenomation (+IMID)		Control	Post-envenomation		Control	Post-envenomation	
			30 min	90 min		30 min	90 min		30 min	90 min		30 min	90 min
V (u/min/kg bw)	Rt	44.00 ±29.60	22.65 ±14.52	52.48 ±37.35	35.74 ±23.11	7.19 ±1.84	8.51# ±3.15	36.36 ±32.54	9.75 ±12.47	8.59# ±8.73	31.04 ±17.70	29.69 ±27.54	19.91 ±18.81
	Lt	35.61 ±20.23	27.17 ±16.50	51.41 ±46.59	33.31 ±29.39	11.79 ±4.05	8.60 ±2.38	40.31# ±42.37	6.17 ±3.36	10.10 ±5.82	33.30 ±24.92	22.30 ±26.96	23.75 ±31.45
C_{Osm} (ul/min/Kg bw)	Rt	61.15 ±10.32	38.69* ±18.84	53.39 ±39.52	47.09 ±7.61	16.16* ±10.03	18.71* ±11.07	54.91 ±25.99	17.80 ±23.00	13.75* ±12.13	58.79 ±29.80	42.26 ±34.66	24.35* ±11.93
	Lt	57.19 ±8.16	42.64 ±27.89	48.88 ±28.09	41.58 ±24.32	22.22 ±8.56	17.39# ±9.05	33.93 ±22.84	10.22 ±6.10	11.29# ±10.07	61.76 ±25.93	39.54 ±23.30	42.10 ±19.90
C_{H_2O} (ul/ min/ kg bw)	Rt	-17.01 ±32.81	-13.04 ±11.49	-0.86 ±46.71	-11.35 ±17.10	-8.97 ±8.30	-10.19 ±8.68	-20.52 ±20.69	-8.05 ±10.66	-5.16 ±4.78	-27.75 ±18.33	-12.37 ±24.98	-0.12 ±27.96
	Lt	-21.57 ±14.08	-15.46 ±19.59	2.53 ±52.79	-8.26 ±17.50	-10.43 ±7.53	-8.79 ±6.69	4.63 ±58.61	-4.05 ±2.94	-1.20 ±6.05	-28.43 ±24.31	-12.34 ±24.52	-11.47 ±16.97
U_{Osm} ($mOsm/kg$ H_2O)	Rt	488.40 ±222.86	465.80 ±123.47	353.60 ±186.16	552.00 ±340.47	605.75 ±246.75	644.50 ±164.99	599.60 ±425.95	693.30 ±420.46	517.20 ±126.74	568.50 ±205.57	487.00 ±168.92	571.62 ±167.45
	Lt	516.30 ±178.06	485.50 ±188.90	397.00 ±250.78	505.50 ±366.64	565.40 ±216.40	577.00 ±139.35	523.20 ±355.65	485.00 ±77.33	411.80 ±95.37	669.60 ±328.80	570.12 ±279.86	587.00 ±292.60

a highly significant decrease ($p< 0.001$ and $p<0.01$ respectively) within 10 min. No significant change in urine osmolalily (U_{Osm}) was observed. Urinary excretion and fractional excretion of sodium ($U_{Na}V$ and FE_{Na}) were suppressed significantly in 10 min from 4.47 $\pm$ 1.86 to 2.79 $\pm$ 1.75 µEq/min/kgbw and from 2.21 $\pm$ 0.92 to 1.4 $\pm$ 0.88% repectively ($p<0.001$). Urinary potassium excretion (U_KV) decreased significantly in 10 min ($p<0.05$). There was a mild change in fractional excretion of potassium (FE_K). Fraction excretion and urinary excretion of chloride (FE_{Cl} and $U_{Cl.}V$) were suppressed in 10 min ($p<0.05$ and $p<0.01$ respectively). There were no significant differences in urinary concentration, excretion and fractional excretion of both calcium and inorganic phosphorus.

Group II : animals treated with 2 mg/kg/min of imidazole after envenomation

Right kidney.

Data in Fig 8 indicate that urine volume (V) was markedly depressed approximately to 29% of pre-venom injection level ($p<0.05$) in 10 min and remained at low level till the experiment was over. Free water clearance (C_{H_2O}) slightly increased after envenomation and during imidazole infusion. Whereas plasma osmolalily (P_{Osm}) was gradually increased which a significance ($p<0.05$) was seen at the end of experiment. Both osmolar clearance (C_{Osm}) and urinary osmolar excretion ($U_{Osm}V$) concomitantly decreased significantly throughout the experiment except for 70 min. Whereas urinary osmalality (U_{Osm}) showed no significant alteration. Urinary sodium excretion ($U_{Na.}V$)

significantly reduced throughout the experiment ($p<0.01$ to $p<0.05$). Fractional excretion of sodium (FE_{Na}) also decreased to a significant level in 70 and 90 min from 1.61 $\pm$ 0.64 to 0.51 $\pm$ 0.38 and 0.44 $\pm$ 0.49% respectively ($p<0.05$). Urinary potassium excreion ($U_K.V$) decreased suddenly after envenomation but no significance was seen in 10 min then it returned to approach the control level. Fractional excretion of potassium (FE_K) showed a little change throughout the experiment. Excretion and fractional excretion of chloride ($U_{Cl}.V$ and FE_{Cl}) were changed in similar manner. Urinary calcium excretion ($U_{Ca}V$) decreased significantly, in 50 min after envenomation till the end of experiment ($p<0.05$ and $p<0.001$ respectively). Plasma sodium, potassium, chloride and calcium showed no significant difference from each control period. Except for plasma inorganic phosphorus which increased significantly from 4.48 $\pm$ 0.32 to 5.2 $\pm$ 0.81 mg% ($p<0.05$) in 10 min and persisted in the high level throughout the experiment. In contrast, fractional excretion of inorganic phosphorus decreased continuously over the experiment but no significance was seen. Urinary inorganic phosphorus excretion ($U_{Pi}V$) showed a little change .

Left kidney

Envenomation produced a prompt reduction of urine volume (V) within 10 min and the progressive reduction occurred when imidazole was infused, however no significant difference from pre-venom injection peroid was seen. Free water clearance (C_{H_2O}) slightly increased in 10 min then it decreased to approach the control level at the end of experiment. Osmolar clearance (C_{Osm}) were depressed

throughout the experiment without significant difference from the control period. Urinary osmolar excretion ($U_{Osm}V$) also depressed in similar manner whereas urinary osmolality (U_{Osm}) was slightly increased. Urinary sodium excretion ($U_{Na}V$) gradually decreased by approximately 19% of the control value while fractional excretion of sodium (FE_{Na}) increased in 10 min then it decreased to a significant level in 70 and 90 mins ($p<0.05$). Urinary potassium excretion ($U_{K}V$) was depressed throughout the experiment. Fractional excretion of potassium (FE_{K}) slightly increased in 10 min then returned to the control level and incresaed again at the end of experiment. Urinary chloride excretion ($U_{Cl.}V$) showed no significant reduction throughout the experiment. While fractional excretion of chloride (FE_{Cl}) increased significantly from 2.1 $\pm$ 1.29 to 3.05 $\pm$ 2.62% ($p<0.05$) then it decreased in a non significant manner. Urinary excretion of calcium ($U_{Ca}V$) was decreased gradually throughout the experiment while fractional excretion of calcium (FE_{Ca}) increased the first 30 min after envenomation then it decreased throughout the experiment without any significance. Urinary inorganic phosphorus excretion ($U_{Pi}V$) was markedly reduced, the significance was seen in 50 min from 14.68 $\pm$ 9.56 to 6.47 $\pm$ 6.02 µg/min/kg ($p<0.05$). Fractional excretion of inorganic phosphorus (FE_{Pi}) increased to a high level within 30 min then it declined to a significant level in 50 and 70 min from 26.68 $\pm$ 16.96 to 18.31 $\pm$ 14.48 and 14.27 $\pm$ 9.67% respectively ($p<0.05$).

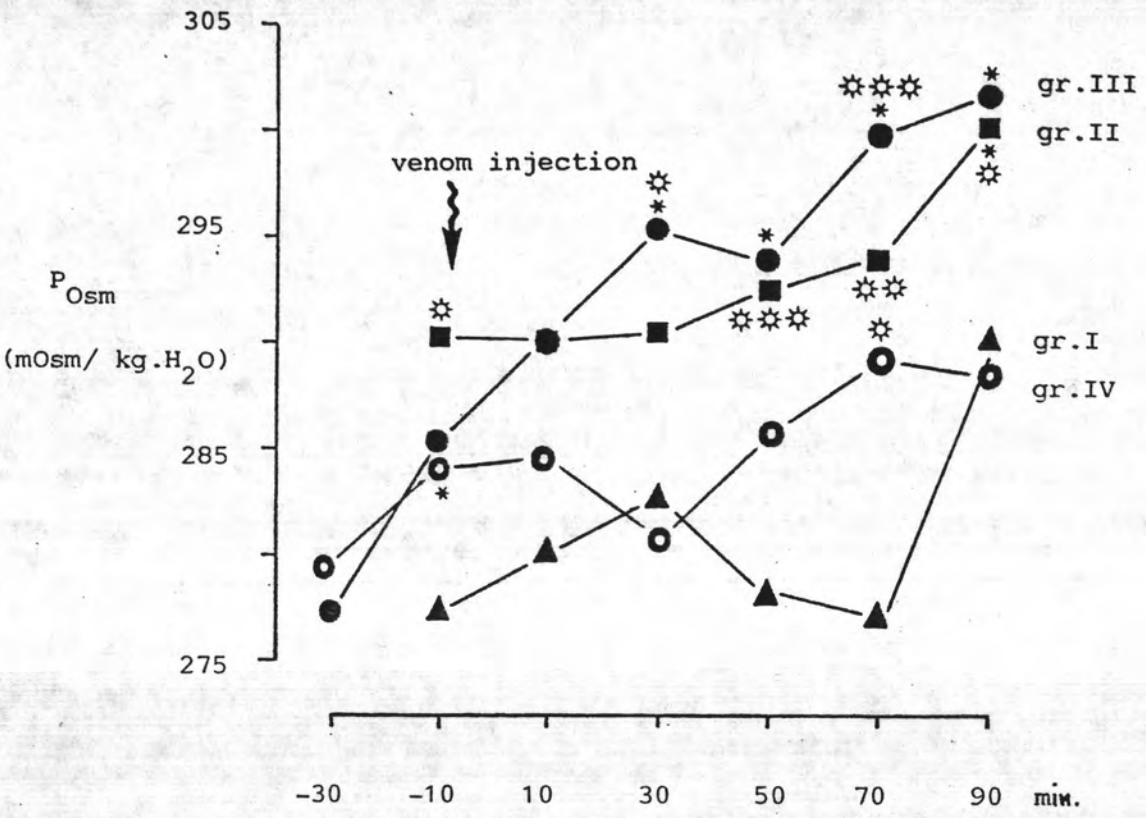

Fig. 12: Effects of intravenous injection of Russell's viper venom on plasma osmolality ($P_{)sm}$) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$.

Values are statistically significantly different from group I at the same period , ✡ $p < 0.05$, ✡✡ $p < 0.01$, ✡✡✡ $p < 0.001$.

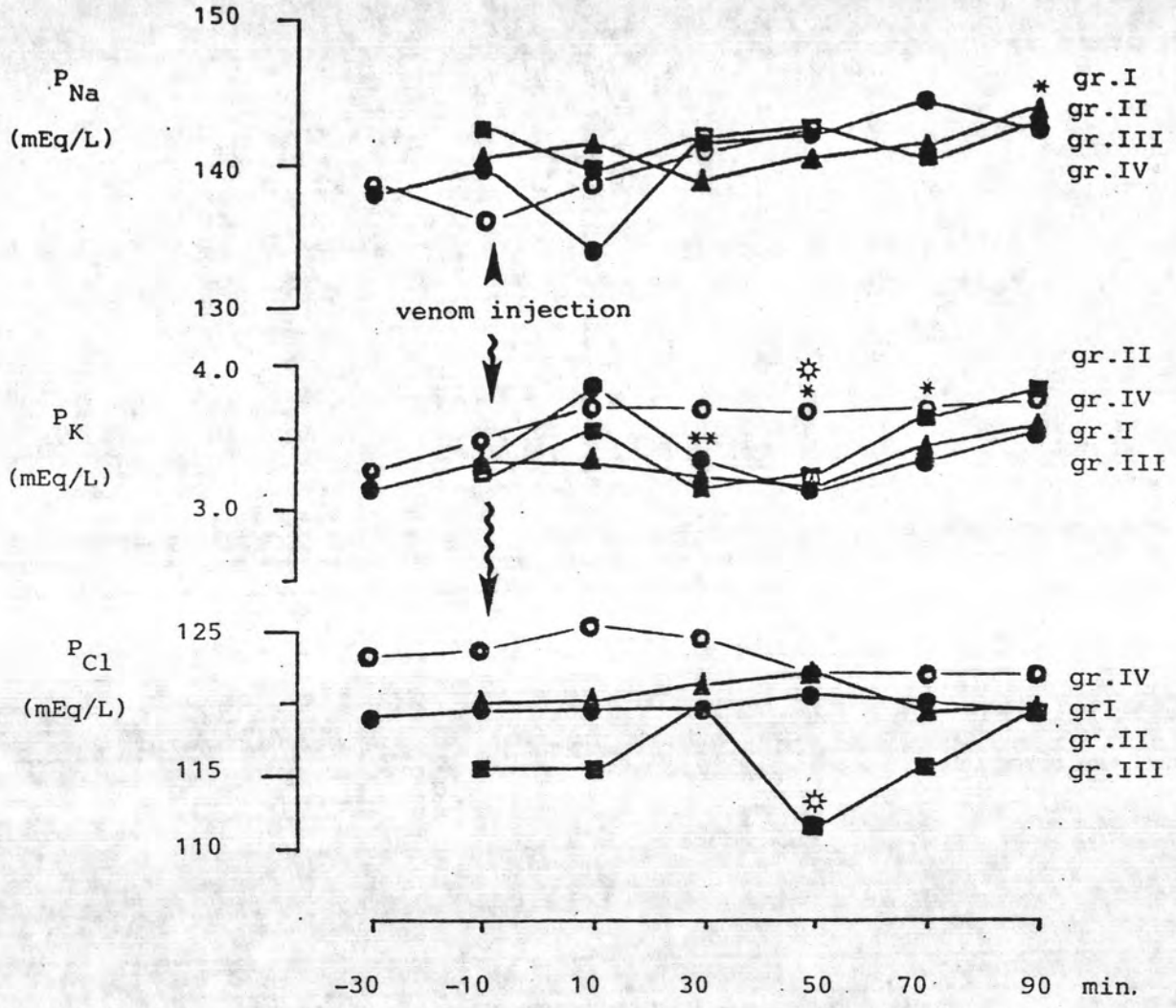

Fig.13: Effects of intravenous injection of Russell's viper venom on plasma sodium (P_{Na}) (upper panel), plasma potassium (P_K) (mid panel) and plasma chloride (P_{Cl})(bottom panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

values are statistically significantly different from control period of each group, $*p < 0.05$, $**p < 0.01$.

values are statistically significantly different from group I at the same period, ☼ $p < 0.05$.

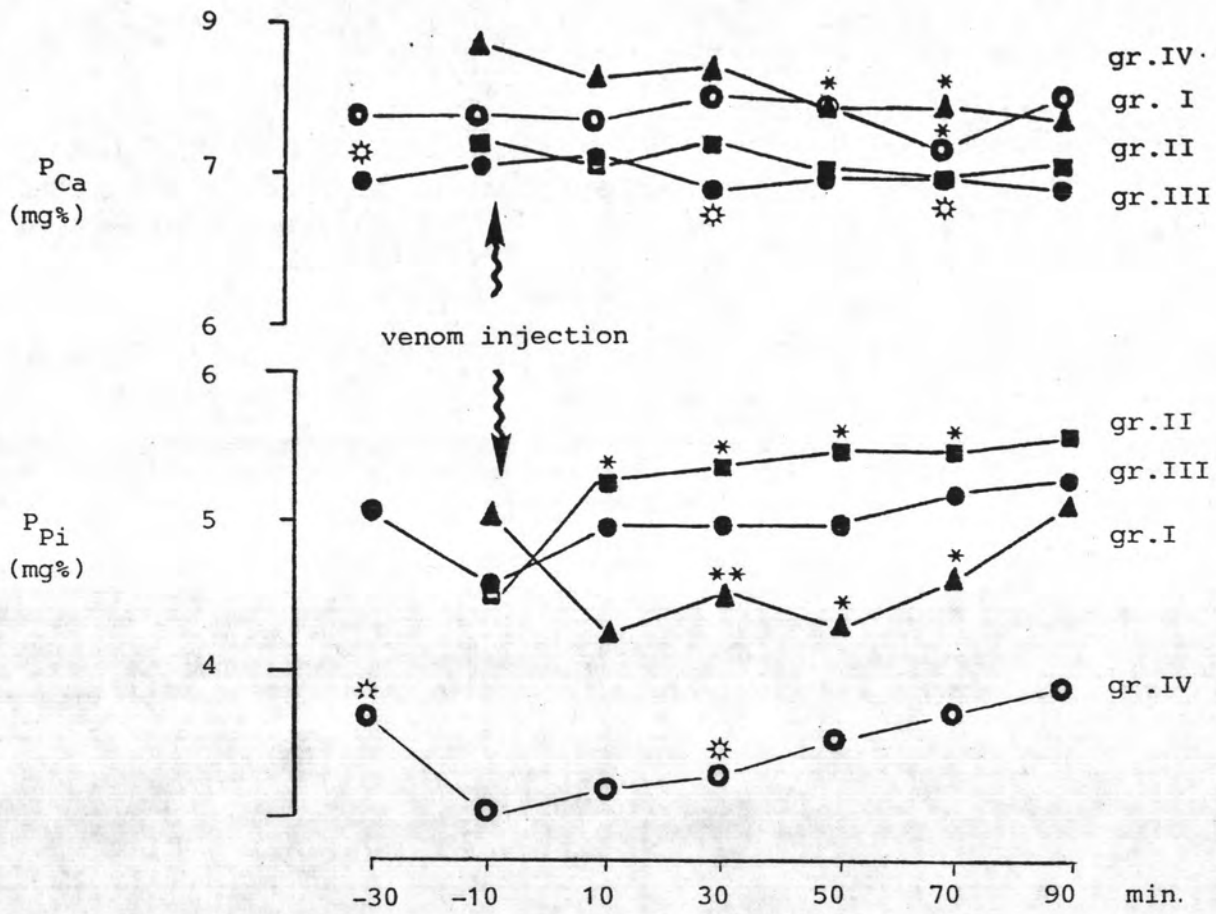

Fig.14: Effects of intravenous injection of Russell's viper venom on plasma calcium (P_{Ca}) (upper panel) and plasma inorganic phosphorus (P_{Pi}) (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.

Values are sratistically significantly different from group I at thw same period, $p < 0.05$.

Table 4 Effect of Russell's viper venom on plasma osmolarity and electrolytes in dogs.

Parameter	Group I			Group II			Group III				Group IV	
	Control	Post-envenomation		Control	Post-envenomation (+IMID)		Control	Pre-treated with IMID(2mg) Post-envenomation		Control	Pre-treated with IMID(0.5mg) Post-envenomation	
		30 min	90 min		30 min	90 min		30 min	90 min		30 min	90 min
P_{Osm} (mOsm/kg H_2O)	277.60 ±6.87	282.80 ±3.70	290.40 ±7.19	290.20 ±8.05	290.80 ±10.08	300.60 ±4.82 #,*	277.40 ±18.11	295.40 ±8.29 #,*	301.60 ±9.60 *	279.20 ±4.32	281.20 ±6.37	286.80 ±6.14
P_{Na} (mEq/L)	140.60 ±3.28	138.80 ±1.48	143.80 ±1.92 *	142.00 ±6.40	141.60 ±4.27	142.60 ±6.42	137.60 ±4.92	141.20 ±1.48	142.00 ±4.89	138.60 ±6.65	141.60 ±7.40	142.20 ±5.11
P_K (mEq/L)	3.36 ±0.27	3.28 ±0.37	3.54 ±0.43	3.24 ±0.51	3.10 ±0.60	3.82 ±0.93	3.10 ±0.33	3.34 ±0.28 **	3.50 ±0.64	3.42 ±0.35	3.68 ±0.49	3.78 ±0.34
P_{Cl} (mEq/L)	119.40 ±61.88	121.00 ±6.89	118.80 ±4.76	115.80 ±6.14	118.20 ±7.19	118.40 ±9.36	117.60 ±5.91	118.20 ±6.54	118.20 ±7.15	123.80 ±12.75	124.00 ±9.13	123.80 ±7.59
P_{Ca} (mg%)	8.65 ±1.03	8.38 ±1.04	7.76 ±0.98	7.48 ±0.76	7.45 ±0.61	7.09 ±0.60	6.91 ±0.29 #	6.84 ±0.96 #	6.82 ±0.72	7.73 ±0.96	7.92 ±0.79	8.00 ±1.01
P_{Pi} (mg %)	5.02 ±0.84	4.41 ±0.88 **	5.05 ±0.54	4.48 ±0.32	5.33 ±0.70 *	5.50 ±1.29	5.02 ±1.47	4.94 ±1.64	5.25 ±1.16	3.62 ±0.99 #	3.32 ±0.49 #	3.99 ±0.93

Group III : animals pretreated with 2 mg/kg/min of imidazole

Right kidney

Intrarenal infusion of imidazole did not cause a significant change in any parameters. When Russell's viper venom was injected, it produced a marked but not significant reduction of urine volume (V). After envenomation free water clearance (C_{H_2O}) was increased throughout the experiment. Osmolar clearance (C_{Osm}) was slightly increased by imidazole but decreased significantly by the effect of envenomaiton in 10 and 90 min from 54.91 $\pm$ 25.99 to 28.26 $\pm$ 12.38 and 13.75 $\pm$ 12.13 µl/min/kg bw. respectively ($p<0.05$) while urinary osmolality (U_{Osm}) did not significantly change throughout experiment. Urinary osmolar excretion (U_{Osm} V) sharply reduced to a significant level in 10 and 90 min after envenomation from 15.05 $\pm$ 6.69 to 8.14 $\pm$ 3.59 and 4.06 $\pm$ 3.51 µOsm/min/kg bw. respectively ($p<0.05$). While plasma osmolalily (P_{Osm}) was increased gradually sustained a significant level ($p<0.05$) till the end of experiment. Urinary sodium excretion ($U_{Na}V$) descreased significantly in 10, 70 and 90 min ($p<0.05$). Fractional excretion of sodium (FE_{Na}) was variable. Urinary potassium excretion (U_KV) was suppressed significantly in 10 and 90 min from 0.81 $\pm$ 0.33 to 0.44 $\pm$ 0.44 and 0.17 $\pm$ 0.18 µEq/min/kg bw. ($p<0.05$). Plasma potassium (P_K) and fractional excretion of potassium (FE_K) slightly changed. Urinary chloride excretion ($U_{Cl}V$) declined significantly in 70 and 90 min ($p<0.05$ and $p<0.01$ respectively). Fractional excretion of chloride (FE_{Cl}) was variable in response to venom injection. Urinary calcium excretion ($U_{Ca}.V$) slightly increased by imidazole infusion and it was depressed by venom

injection throughout the experiment, significance was found at the end of experiment ($p<0.05$). While plasma calcium (P_{Ca}) was well maintained. Plasma inorganic phosphorus (P_{Pi}) was also stable. Fractional excretion of inorganic phosphorus (FE_{Pi}) was variable but no significance was noted whereas urinary inorganic phosphorus excretion ($U_{Pi}V$) was significantly depressed by venom injection in 10 and 90 min from 16.43 $\pm$ 9.3 to 7.31 $\pm$ 6.78 and 4.02 $\pm$ 5.23 µg/min/kg bw respectively ($p<0.05$).

Left kidney.

No significant difference of any parameter during was apparent pretreated with imidazole intrarenally. When Russell's viper venom was given, urine volume (V) reduced markedly throughout the experiment. The lowest value, 25% of control level was occurred in 30 min however no significance was noted. Free water clearance (C_{H_2O}) was obviously decreased by imidazole. But gradually elevated to approach the control level when the venom was injected. Osmolar clearance (C_{Osm}) increased in response to imidazole and depressed by envenomation throughout the experiment. There was a mild change of urinary osmolality (U_{Osm}) while urinary osmolar excretion (U_{Osm} V) was decreased significantly from 13.43 $\pm$ 6.3 to 3 $\pm$ 1.84 uOsm/min/kg bw ($p<0.01$) in 30 min after envenomation and persisted throughout the experiment. Urinary excretion of sodium ($U_{Na}.V$) progressively decreased to a significant level in 30 min from 4.32 $\pm$ 3.02 to 0.61 $\pm$ 0.35 µEq/min/kg bw ($p<0.05$) and sustained over the experiment. Urinary potassium excretion ($U_K V$) decreased significantly ($p<0.01$) in 30 min and sustained till the experiment was over. Urinary chloride

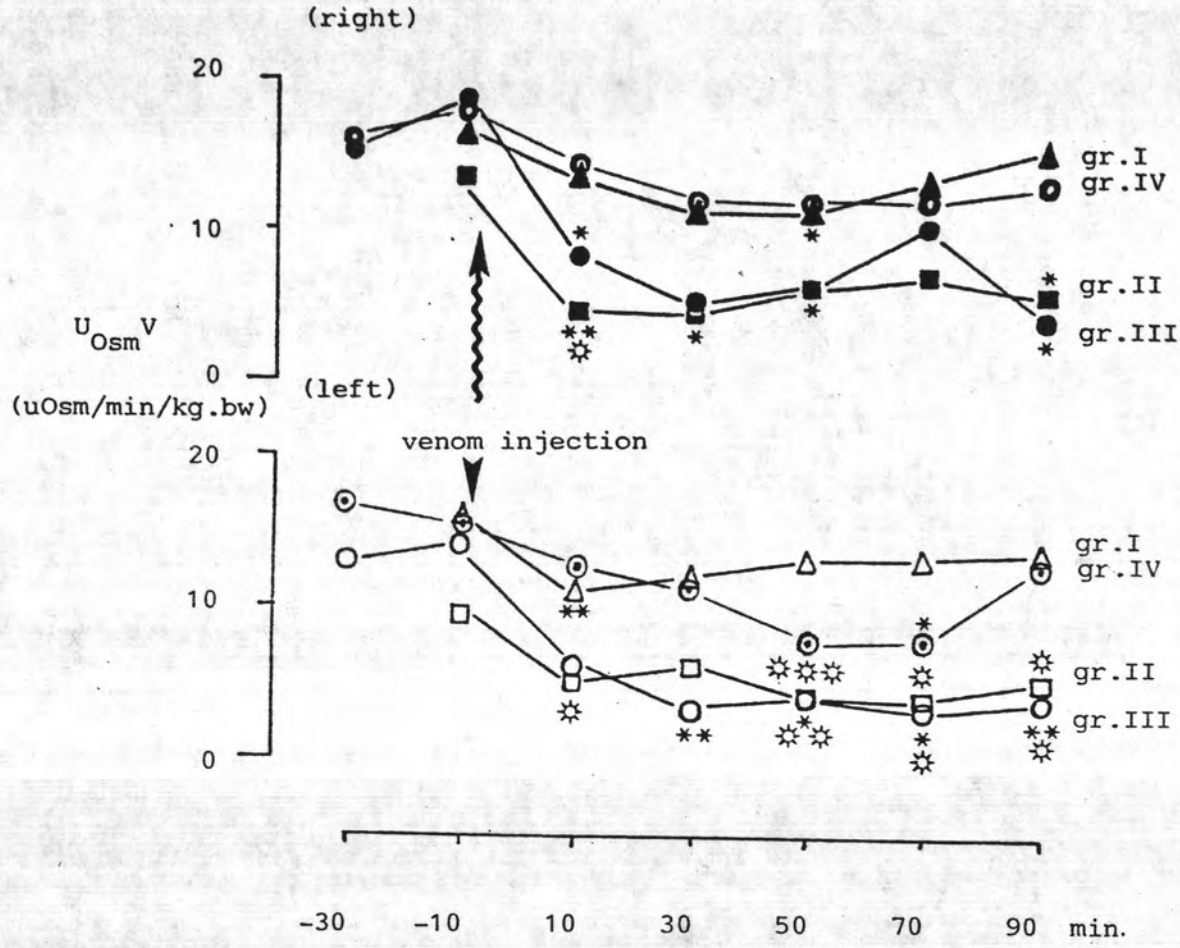

Fig. 15: Effects of intravenous injection of Russell's viper venom on urinary osmolar excretion ($U_{Osm}V$) in right kidney (upper panel) and left kidney (lower panel) in group I(control), group II (imidazole-treated after envenomation) and group III(pretreated with imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

The values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.

Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$, ✡✡ $p < 0.01$, ✡✡✡ $p < 0.001$.

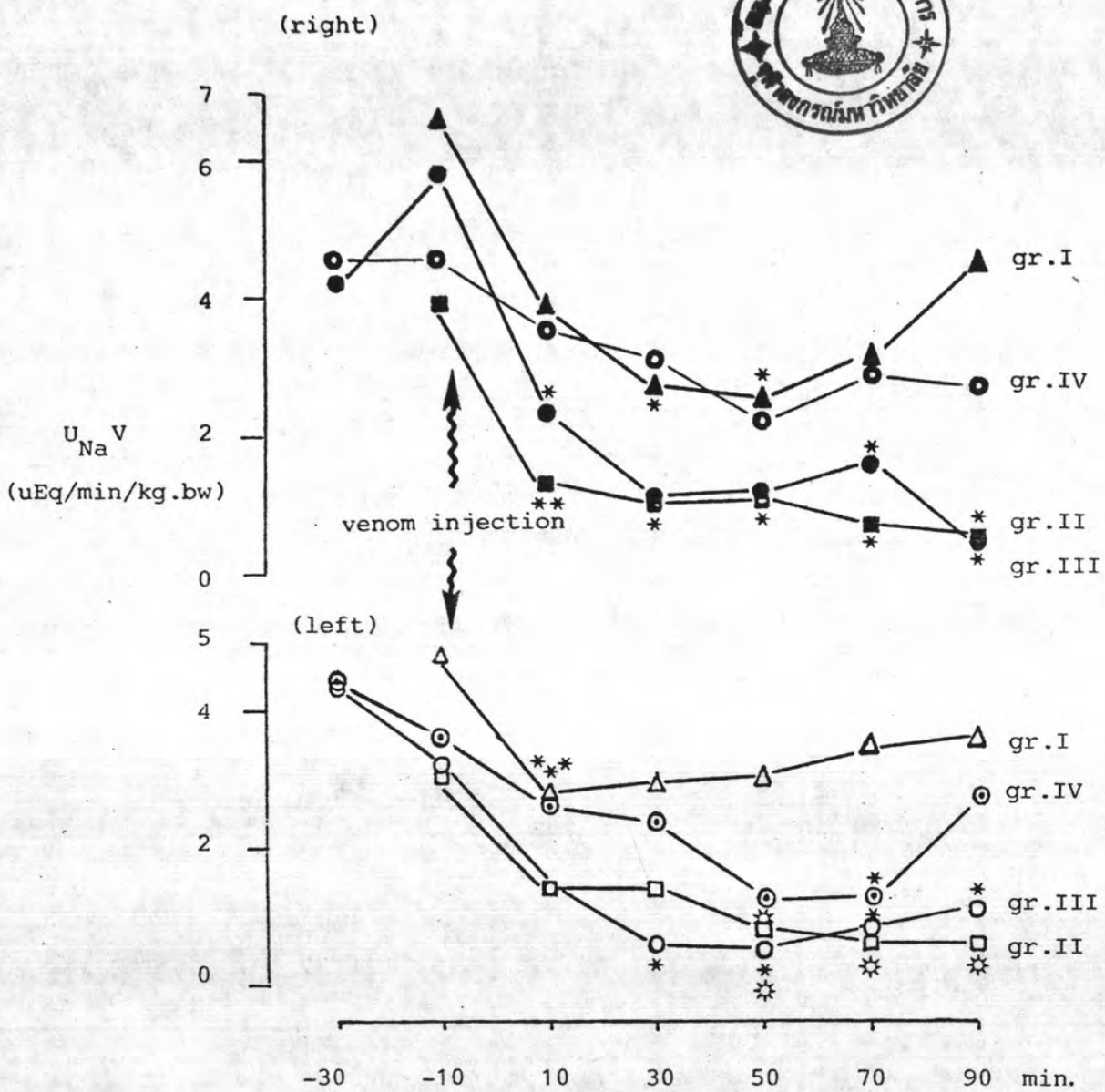

Fig.16: Effects of intravenous injection of Russell's viper venom on urinary sodium excretion ($U_{Na}V$) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole), and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.
Values are statistically significantly different from group I at the same period, ☼ $p < 0.05$.

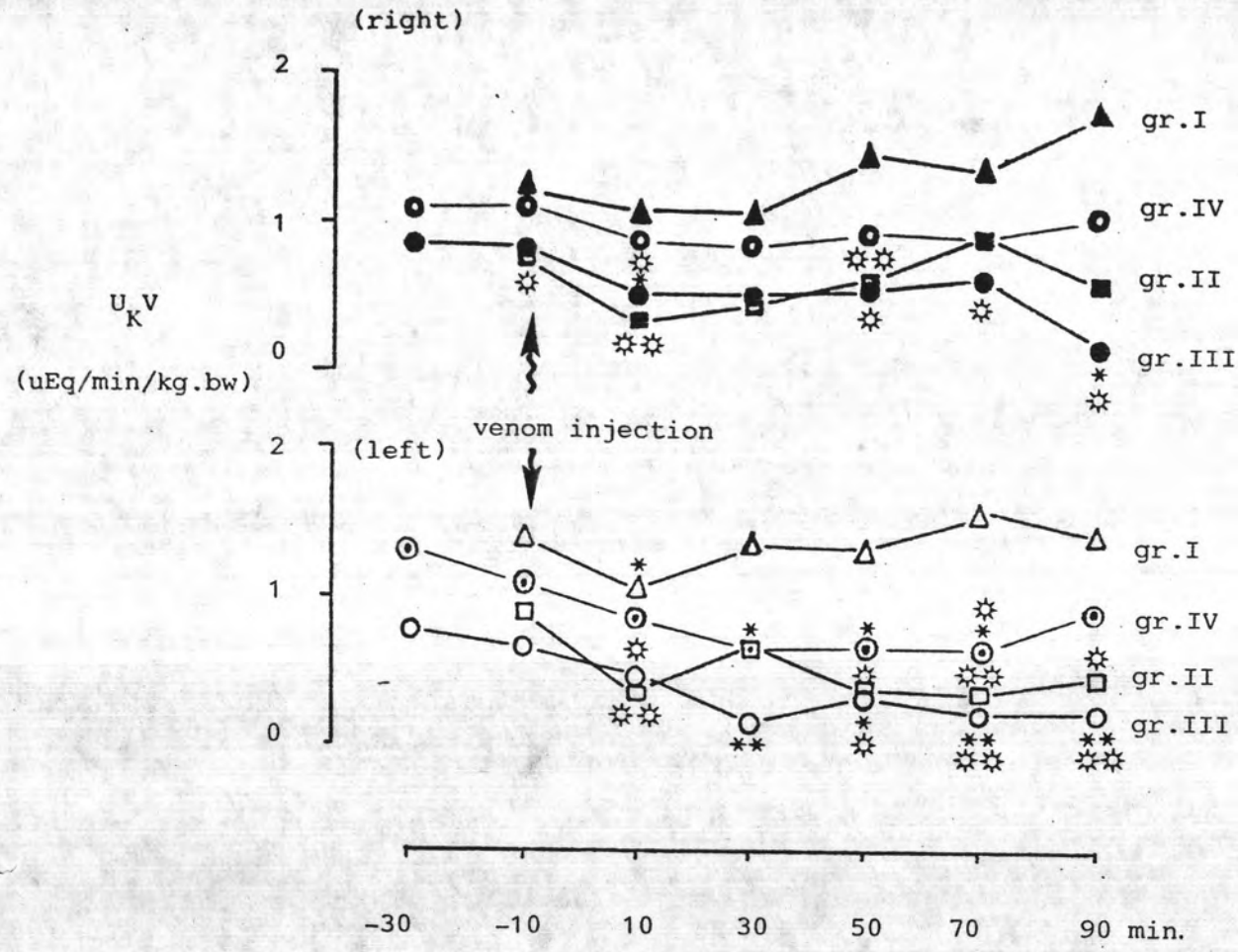

Fig.17: Effects of intravenous injection of Russell's viper venom on urinary excretion of potassium ($U_K V$) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.

Values are statistically significantly different from group I atthe same period , ✡ $p < 0.05$, ✡✡ $p < 0.01$.

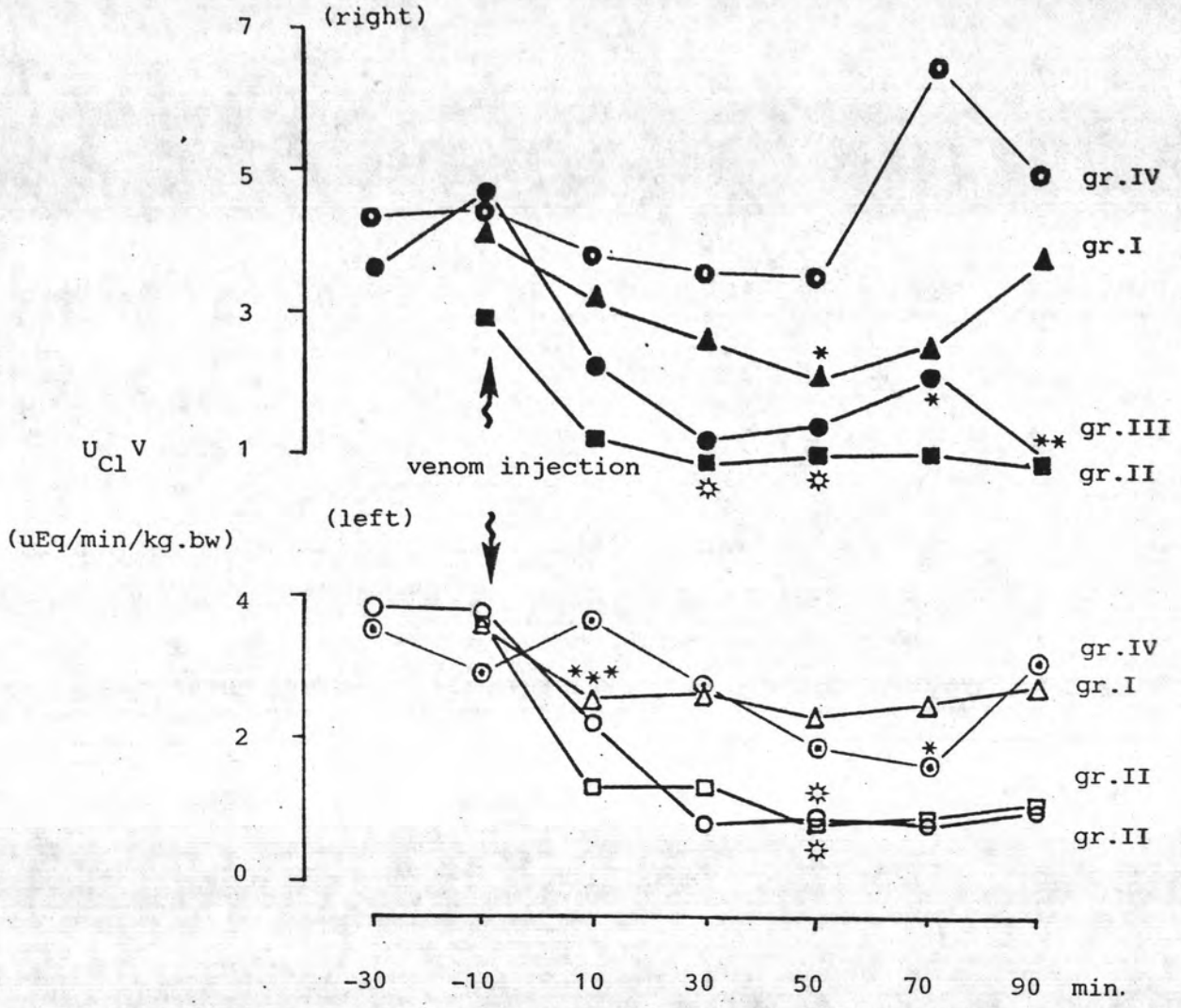

Fig.18: Effects of intravenous injection of Russell's viper venom on urinary chloride excretion ($U_{Cl}V$) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (ani (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.
Values are statistically significantly different from group I at the same period, ✡ $p < 0.05$.

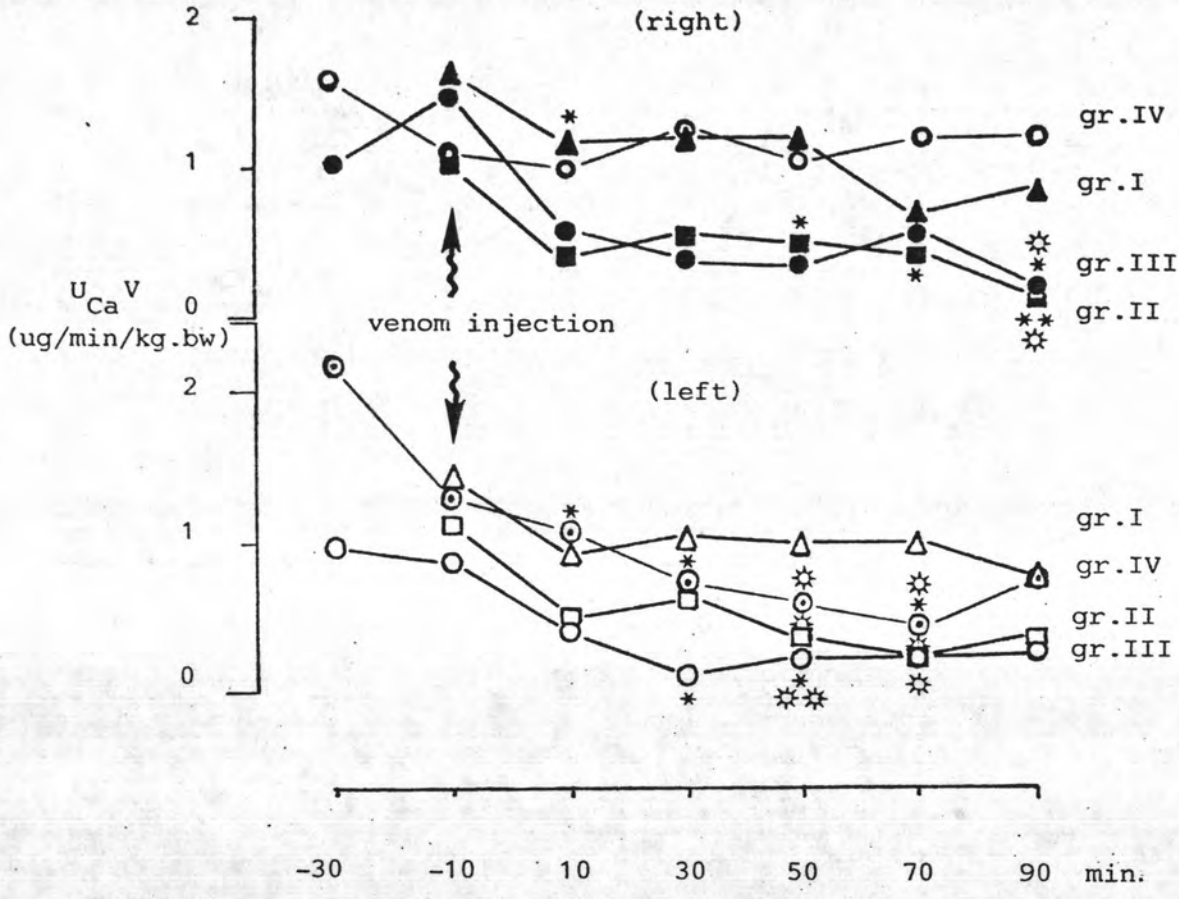

Fig.19: Effects of intravenous injection of Russell's viper venom on urinary calcium excretion ($U_{Ca}V$) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (aniamls treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).
Values are statistically significantly different from control period of each group, * $p < 0.05$, ** $p < 0.01$.
Values are statistically significantly different from group I at the same period, ✲ $p < 0.05$, ✲✲ < 0.01.

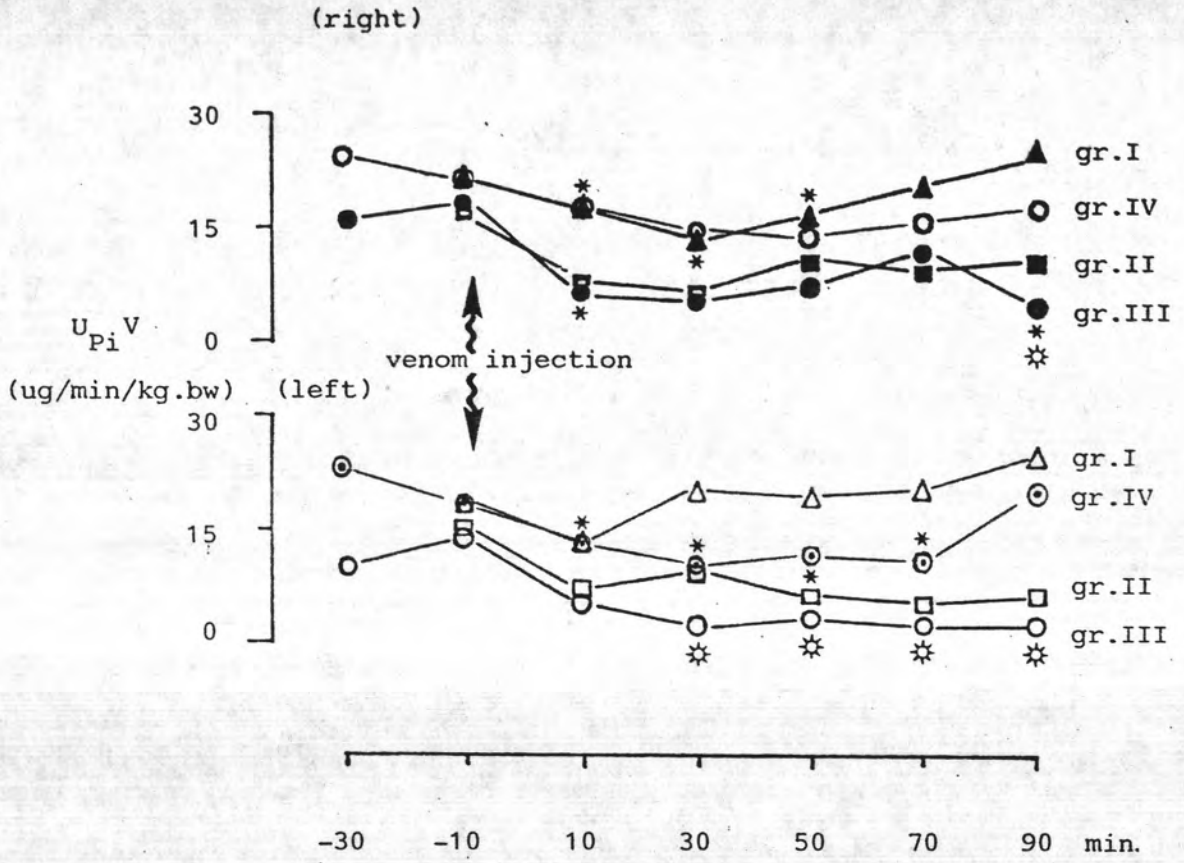

Fig.20: Effects of intravenous injection of Russell's viper venom on urinary inorganic phosphorus excretion ($U_{Pi}V$) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/kmin of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).
Values are statistically significantly different from control period of each group, * $p < 0.05$.
Values are statistically significantly different from group I at the same period, ☼ $p < 0.05$.

Table 5 Effect of Russell's viper venom on urinary osmolar and electrolytes excretion of the right (Rt) and the left (Lt) kidney in dogs.

Parameter	Group I			Group II			Group III			Group IV		
							Pre-treated with IMID(2mg)			Pre-treated with IMID(0.5mg)		
	Control	Post-envenomation		Control	Post-envenomation (+IMID)		Control	Post-envenomation		Control	Post-envenomation	
		30 min	90 min		30 min	90 min		30 min	90 min		30 min	90 min
$U_{Osm}V$ Rt	16.95	10.97	15.29	13.66	4.66 *	5.58 *	15.05	5.27	4.06 *	16.50	11.92	14.17
(mOsm/min /Kg bw)	±2.82	±5.33	±10.95	±2.16	±2.87	±3.20 #	±6.69	±6.89 **	±3.51 #,**	±8.60	±9.81	±12.06
Lt	15.83	12.03	14.04	9.99	6.41	5.20	13.43	3.00	3.93	17.30	11.22	12.00
	±2.10	±7.85	±7.76	±7.62	±2.39	±2.66	±6.31	±1.84	±2.38	±7.42	±6.61	±5.46
$U_{Na}V$ Rt	6.85	2.68 *	4.42	3.80	0.95 *	0.46 *	4.18	1.09	0.41 *	4.59	2.92	2.58
(μEq/min /Kg bw)	±3.67	±1.52	±5.20	±1.61	±0.22	±0.65 #	±2.48	±1.42 *	±0.43 *	±4.01	±3.47	±3.90
Lt	4.47	2.85	3.52	2.94	1.35	0.57	4.32	0.61	1.06	4.32	2.25	2.74
	±1.86	±2.04	±2.64	±1.94	±0.72	±0.35	±3.02	±0.35	±0.85	±3.72	±1.81	±2.02
$U_{K}V$ Rt	1.26	1.12	1.70	0.73	0.47	0.55	0.81	0.44	0.17 #,*	1.13	0.80	1.09
(μEq/min /kg bw)	±0.31	±0.64	±1.07	±0.20	±0.41	±0.85 #	±0.33	±0.69 **	±0.18 ##,**	±0.27	±0.25 *	±0.53
Lt	1.36	1.33	1.38	0.83	0.61	0.43	0.75	0.18	0.22	1.32	0.62	0.96
	±0.55	±1.08	±0.66	±0.47	±0.28	±0.41	±0.53	±0.23	±0.25	±0.27	±0.17	±0.15

Table 5 Effect of Russell's viper venom on urinary osmolar and electrolytes excretion of the right (Rt) and the left (Lt) kidney in dogs.

Parameter	Group I			Group II			Group III			Group IV		
	Control	Post-envenomation		Control	Post-envenomation		Control	Pre-treated with IMID(2mg) Post-envenomation		Control	Pre-treated with IMID(0.5mg) Post-envenomation	
		30 min	90 min		30 min	(+IMID) 90 min		30 min	90 min		30 min	90 min
$U_{Cl}.V$ Rt (μEq/min /Kg bw)	4.02 ±1.62	2.62 ±1.51	3.78 ±4.89	2.77 ±1.81	0.85 ±0.26 #	0.85 ±0.84	3.64 ±1.83	1.24 ±1.62	0.95 ±0.91 **	4.36 ±3.89	3.49 ±4.34	5.00 ±6.02
Lt	3.56 ±2.10	2.47 ±1.43	2.59 ±2.42	3.57 ±3.16	1.27 ±0.86	1.02 ±0.43	3.88 ±3.20	0.85 ±0.42	1.03 ±0.63	3.47 ±2.74	2.68 ±2.11	2.95 ±2.21
$U_{Ca}.V$ Rt (μg/min /Kg bw)	1.59 ±0.92	1.13 ±0.72	0.77 ±0.38	1.05 ±0.41	0.54 ±0.22	0.17 #,** ±0.13	1.00 ±0.61	0.39 ±0.28 *	0.21 #,* ±0.18	1.54 ±1.23	1.31 ±1.60	1.21 ±1.83
Lt	1.39 ±1.14	1.00 ±0.96	0.75 ±0.48	1.13 ±0.87	0.66 ±0.41	0.35 ±0.14	0.99 ±0.66	0.18 ±0.08	0.29 ±0.16	2.32 ±1.21	0.77 ±0.59	0.73 ±0.48
$U_{Pi}.V$ Rt (μg/min /kg bw)	21926 ±10.63	13.48 * ±8.81	25.44 ±17.31	17.42 ±9.65	6.35 ±6.49	11.43 ±10.08	16.43 ±9.30	5.58 ±8.70 #	4.02 #,* ±5.23 #	24.60 ±9.42	14.37 ±7.48 *	16.18 ±10.46
Lt	18.33 ±10.87	20.03 ±19.25	23.98 ±16.64	14.68 ±9.56	9.12 ±9.96	5.90 ±8.08	10.19 ±10.73	2.48 ±3.36	2.46 ±3.55	23.03 ±8.42	10.51 ±4.67	21.39 ±8.68

Abbreviation are defined in Table 1.

excretion ($U_{Cl}V$) was decreased by envenomation throughout the experiment. Urinary calcium excretion ($U_{Ca}.V$) promptly reduced after envenomation, the significance was seen in 50 and 70 min from 0.99 $\pm$ 0.66 to 0.18 $\pm$ 0.08 and 0.22 $\pm$ 0.16 µg/min/kg bw respectively ($p<0.05$) and maintained at the low level througout the experiment. Urinary inorganic phosphorus excretion ($U_{Pi}V$) continuously declined throughout the experiment without any significance. All fractional excretion of electrolytes (FE_{Na}, FE_{K}, FE_{Ce}, FE_{Ca} and FE_{Pi}) were sharply increased in 50 min and maintained at high level till the experiment was over. No significance was seen.

Group IV : animals pretreated with 0.5 mg/kg/min of imidazole

Right kidney

Intrarenal arterial infusion of 0.5 mg/kg/min of imidazole caused no change in urine flow rate (V). When the venom was given, it slightly decreased throughout the experiment. Free water clearance (C_{H2O}) was slightly decreased by imidazole but sharply increased after envenomation and maintained at high level throughout the experiment. The change was significantly higher than preenvenomation period was noted within 50 min whereas osmolar clearance (C_{Osm}) was increased by imidazole and gradually decreased after envenomation which was significantly different from preenvenomation at 70 and 90 min ($p<0.05$). Urinary osmolar was maintained quite well while plasma osmolarity was significantly increased by imidazole ($p<0.05$) and returned to approach the control level in 30 min after envenomation then increased continuously throughout the experiment. Urinary sodium excretion ($U_{Na}V$) gradually decreased throughout the experiment. In

contrast with plasma sodium which slightly increased whereas fractional excretion of sodium was maintained. Plasma potassium significantly increased 50 and 70 min ($p<0.05$) after envenomation. While urinary and fractional excretion of potassium altered slightly. Urinary excretion of chloride was slightly decreased by envenomation but suddenly increased in 70 and 90 min period as same as fractional excretion of chloride. In contrast, plasma chloride slightly increased during first envenomation period but slightly decreased after 50 min and persisted till the experiment was over. Plasma calcium, urinary excretion and fractional excretion of calcium slightly changed by the effect venom injection. While plasma inorganic phosphorus suddenly decreased by imidazole infusion then gradually increased by envenomation to approach the control level at the end of experiment, urinary inorganic phosphorus excretion was depressed throughout the experiment whereas fractional excretion of inorganic phosphorus was promptly increased within 10 min of envenomation then decreased to maintain near the control level throughout the experiment.

Left kidney

Intrarenal arterial infusion of 0.5 mg/kg/min of imidazole did not affect urine flow rate (V) but after envenomation it progressively declined to a significant level in 70 min ($p<0.05$). In contrasted, free water clearance (C_{H_2O}) continuously increased to a significant level in 50 min after envenomation. Osmolar clearance (C_{Osm}) responded to venom injection in the same pattern as urine flow rate, significant decrease did not occurred in 50 and 70 min ($p<0.05$). Urinary osmolar excretion and sodium excretion was also altered in the

same manner as urine flow rate, significant decrease was noted at 70 min period ($p<0.05$). Urinary excretion of potassium was gradually decreased throughthout the experiment, significantly diffrent from control period ($p<0.05$) was seen in 30,50 and 70 min after envenomation. Urinary excretion of chloride was decreased by imidazole. When the venom was given, it suddenly increased then gradually decreased to a significant level in 70 min ($p<0.05$). Both urinary excretion of calcium and inorganic phosphorus gradually decreased in the same pattern throughout the experiment. The significant difference from each control period ($p<0.05$) was noted in 30,50 and 70 min after envenomation. All of fractional excretions of electrolyte excepted for inorganic phosphorus were all well maintained whereas fractional excretion of inorganic phosphorus was fluctuated and sharply increased at the end of experiment, however no significant difference was apparent.

Comparison the effects of Russell's viper venom on renal function of three groups are shown in Fig 9 which indicated that free water clearance (C_{H_2O}) of these animals changed in the same manner after envenomation in spite of the lowering level was seen in group III by the effect of imidazole prior to envenomation. Urine volume (V) of group II, III and IV were suppressed throughout the experiment during imidazole infusion . In contrast with group I which recieved the venom alone, it's urine volume was improved. These differences among groups were significantly found ($p<0.05$) in both kidneys excepted for the right kidney of group IV (Fig 8). Urinary osmolality (U_{Osm}) was not significantly different from other groups (Fig 10).

Osmolar clearance (C_{Osm}) of the left kidney of group II and III were significantly lower than group I ($p<0.05$) (Fig 11). The right kidney also revealed the same difference but the significance was seen in group II at 10 min and group IV at 70 min of envenomation ($p<0.05$). Plasma osmolality (P_{Osm}) of all groups were elevated but the higher degree of elevation was found significantly in group II and III which differed from group I ($p<0.05$ to 0.001) at the same period of time (Fig 12). It should be noted that the significant difference between group I and II ($p<0.05$) was seen in the control period but the difference was more significant when imidazole had been infused in group II ($p<0.001$). Plasma potassium increased by envenomation in group IV was significantly different from group I at 50 min period ($p<0.05$). Plasma inorganic phosphorus of group IV was lower than other groups. The significant difference from group I was seen in the control peroid and in 30 min after envenomation. However this pattern of response was same as group III. Plasma calcium (P_{Ca}) of group II and III were lower than group I (Fig 14), however the significant difference between group was noted only in group III ($p<0.05$) which this difference was seen prior to both imidazole infusion and venom injection.

Urinary osmolar excretion ($U_{Osm}V$) depressed in all groups (Fig 15) but the more decreased was found in both kidneys of group II in 10 min ($p<0.05$) and of the left kidney in 50 min ($p<0.001$), 70 and 90 min ($p<0.05$) compared to group I. This significant lowering was also found in the left kidney of group III when compared to group I in 50 min ($p<0.01$) and the others peroid of experiment ($p<0.05$). The

depressed response of urinary sodium excretion ($U_{Na}V$) to the venom injection of group I and IV tended to approach the control level but not found in group II and III which persisted at low level throughout the experiment (Fig 16). These difference among groups were significant in left kidney of the two groups ($p<0.05$). Envenomation produced a mild decrease in urinary potassium excretion (U_KV) then increased above the control level in group I (Fig 17). This decline also seen in group II, III and IV in a greater extent, the significant difference among groups were appeared in both kidneys in 10 min ($p<0.01$ and $p<0.05$ respectively). After 50 min of envenomation, urinary potassium excretion of group I slightly increased above the control level and the other groups were still depressed significantly different from group I. More significances were presented in left kidney (Fig 17). The reduction of urinary chloride excretion ($U_{Cl}.V$) was similar to urinary potassium excretion, significant difference was seen in 30 and 50 min ($p<0.05$) in right kidney of group II and in 50 min ($p<0.05$) in left kidney of both group II and III compared to group I (Fig 18). Urinary calcium excretion ($U_{Ca}V$) showed a more decrease in both group II and III compared to group I (Fig 19). This difference was significantly noted in the right kidney of both groups at the end of experiment ($p<0.05$) and also showed in the left kidney of all imidazole-treated groups in 50 and 70 min ($p<0.01$ and $p<0.05$). The response of urinary inorganic phosphorus excretion ($U_{Pi}V$) (Fig 20) was similar to urinary calcium excretion but the significant difference occurred only between group III and I at the end of experiment in right kidney and in 30 min till the end of experiment in the left kidney ($p<0.05$). Fractional excretion of sodium, potassium, chloride

and calcium (Fig 21-24) showed a similar pattern in both right and left kidneys of all groups. In the left kidney, fractional excretion of these electrolytes were sharply elevated in group III in 50 min and maintained the high level over the experiment. However no significant difference among groups were seen. Fractional excretion of inorganic phosphorus (Fig 25) in response to envenomation was sharply swung in the left kidney of all groups, no significant difference among groups were noted. In the right kidney, the swinging was found in a less extent.

In conclusion (see table 1-6), a small dose of Russell's viper venom produced a transient decline in blood pressure which associated with trasient reduction in renal hemodynamic and renal function. Administration of thromboxane synthetase inhibitor, imidazole only at the dose of 2 mg/kg/min prevented profound hypotensive effect of the venom. Prolonged infusion of imidazole caused a marked increase in mean arterial blood pressure and packed cell volume (table 1) but aggravated renal hemodynamic and renal function (table 3-6). In addition, imidazole induced an increase in plasma osmolarity but not plasma electrolytes (table 2). Deterioration of renal hemodynamic and renal function were more pronounced in the left kidney of group III which recieved imidazole infusion longer and directly via intrarenal artery. The most interesting result was fraction excretion of all electrolytes. The striking elevation was apparent only in the kidney of group III.

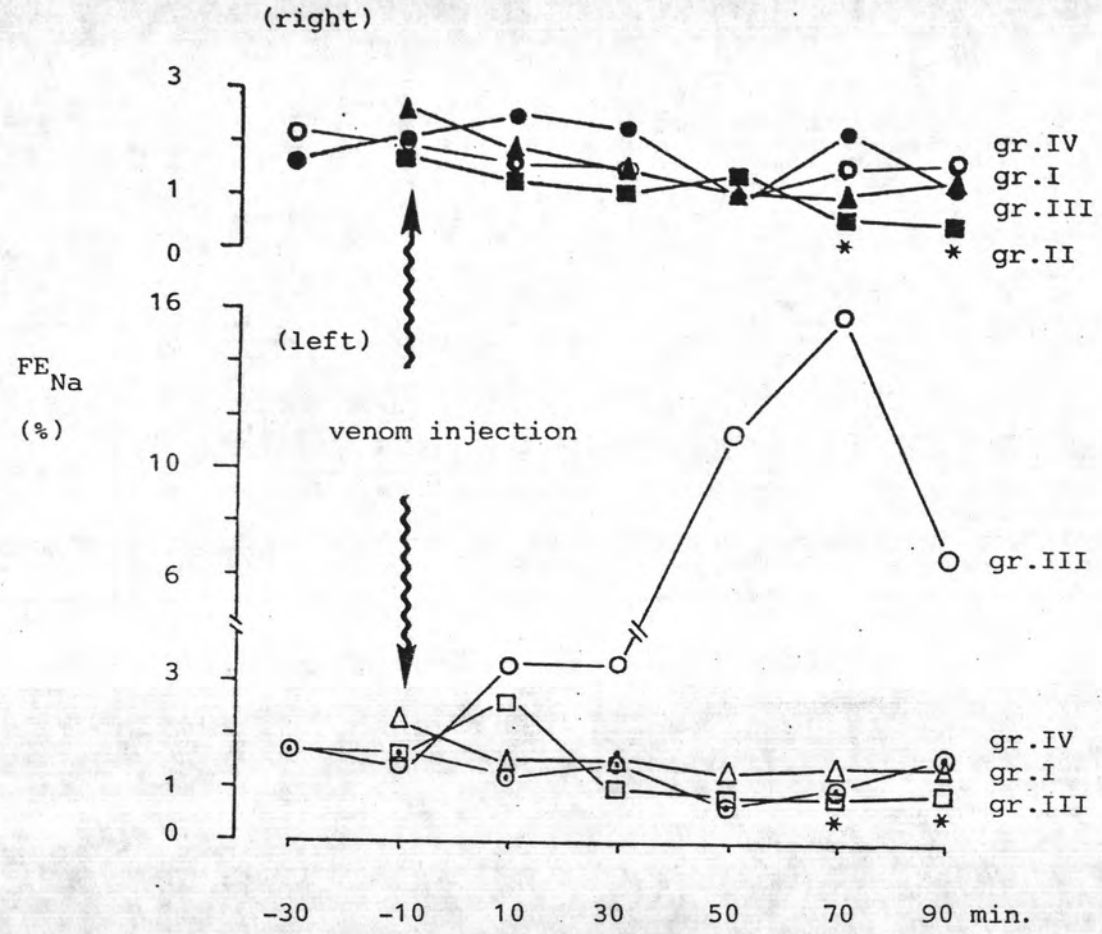

Fig.21: Effects of intravenous injection of Russell's viper venom on fractional excretion of sodium (FE_{Na}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole). Values are statistically significantly different from control period of each group, * $p < 0.05$

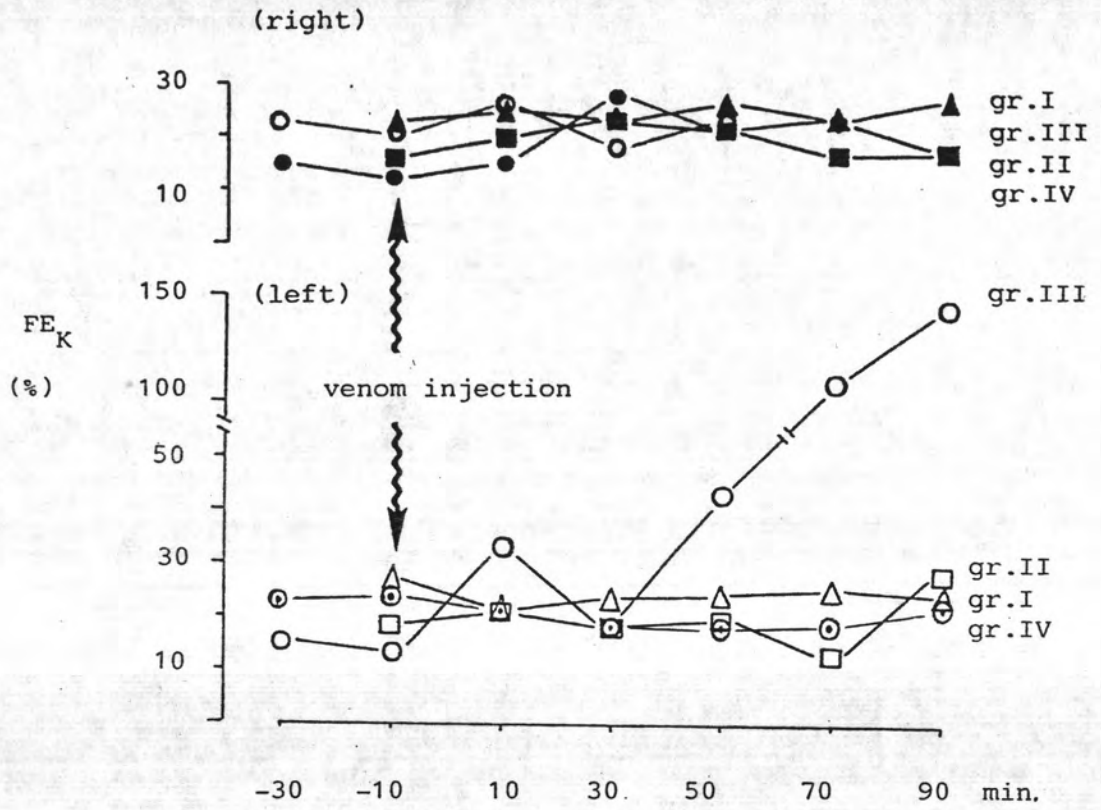

Fig.22: Effects of intravenous injection of Russell's viper venom on fractional excretion of potassium (FE_K) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

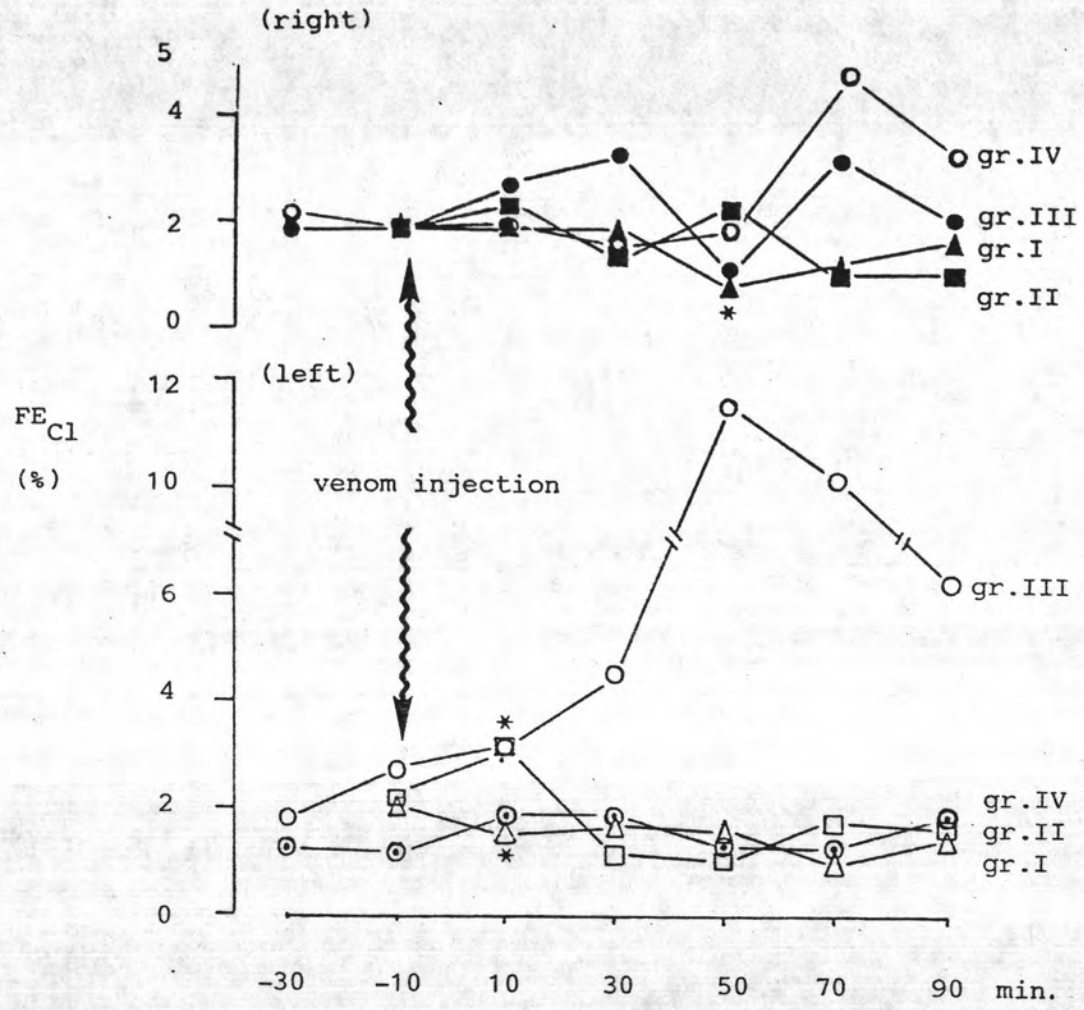

Fig.23: Effects of intravenous injection of Russell's viper venom on fractional excretion of chloride (FE_{Cl}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole). Values are statistically significantly different from control period of each group, $* p < 0.05$.

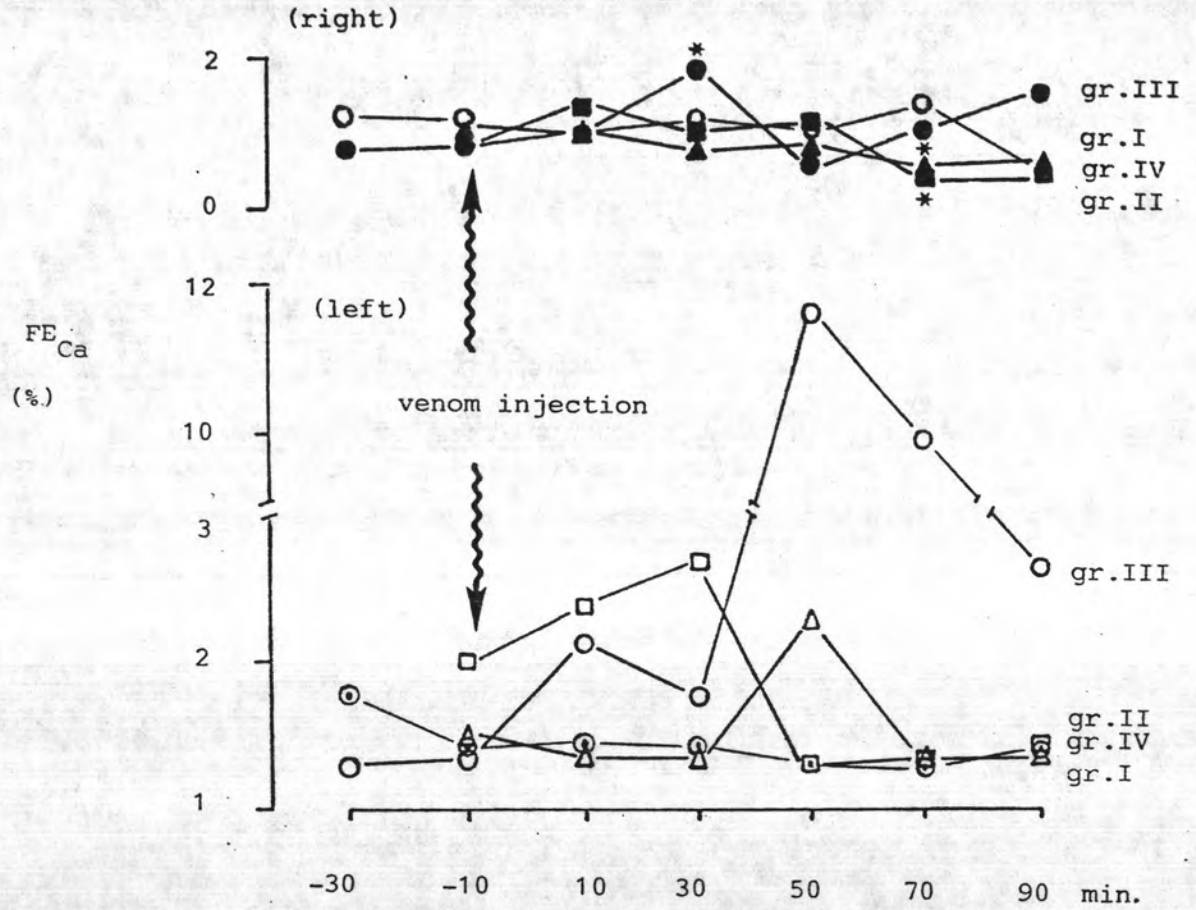

Fig.24: Effects of intravenous injection of Russell's viper venom on fractional excretion of calcium (FE_{Ca}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (animals pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole). Values are statistically significantly different from control period of each group, * $p < 0.05$.

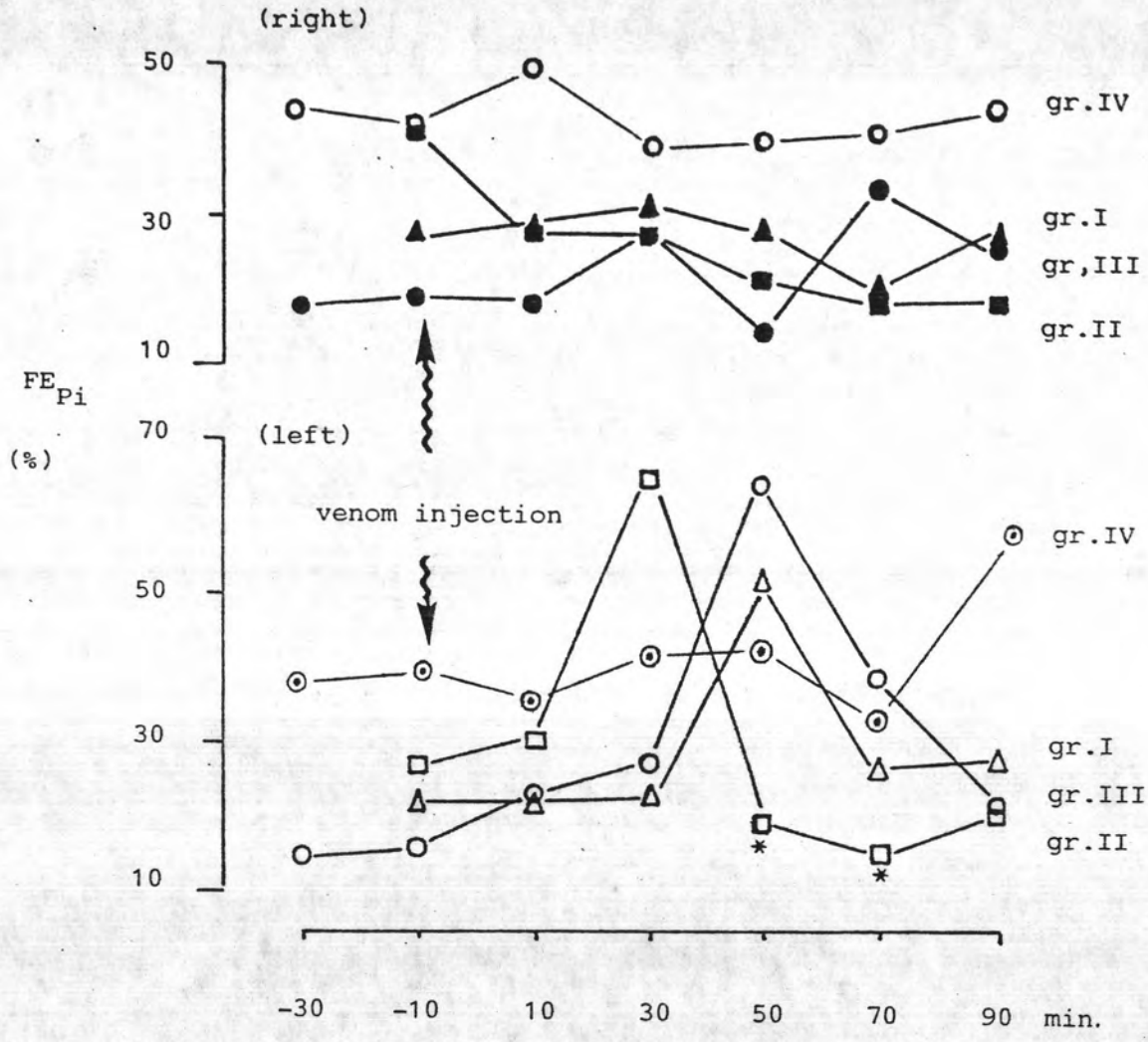

Fig.25: Effects of intravenous injection of Russell's viper venom on fractional excretion of inorganic phosphorus (FE_{Pi}) in right kidney (upper panel) and left kidney (lower panel) in group I (control animals), group II (animals treated with 2mg/kg/min of imidazole after envenomation), group III (aniamls pretreated with 2mg/kg/min of imidazole) and group IV (animals pretreated with 0.5mg/kg/min of imidazole).

Values are statistically significantly different from control period of each group, * $p < 0.05$.

Table 6 Effect of Russell's viper venom on fractional electrolytes excretion of the right (Rt) and the left (Lt) kidney in dogs.

Parameter		Group I			Group II			Group III			Group IV		
								Pre-treated with IMID(2mg)			Pre-treated with IMID(0.5mg)		
		Control	Post-envenomation		Control	Post-envenomation (+IMID)		Control	Post-envenomation		Control	Post-envenomation	
			30 min	90 min		30 min	90 min		30 min	90 min		30 min	90 min
FE_{NA} (%)	Rt	2.58 ±1.39	1.41 ±0.81	1.35 ±1.98	1.61 ±0.64	1.07 ±0.90	0.44 ±0.49 *	1.70 ±1.38	2.21 ±1.59	1.19 ±1.34	2.01 ±1.88	1.47 ±1.23	1.57 ±2.25
	Lt	2.21 ±0.92	1.42 ±0.53	1.34 ±0.89	1.57 ±0.74	0.94 ±0.25	0.87 ±0.52	1.60 ±1.10	3.29 ±4.53	6.83 ±10.95	1.60 ±1.17	1.42 ±1.15	1.63 ±1.22
FE_K (%)	Rt	22.31 ±7.87	23.54 ±7.41	26.18 ±12.78	15.96 ±8.64	23.10 ±1.35	17.25 ±15.42	14.20 ±6.97	28.13 ±23.59	17.05 ±14.50	24.77 ±14.35	19.98 ±5.04	26.06 ±10.49
	Lt	26.04 ±8.34	22.89 ±8.00	23.10 ±10.80	17.79 ±9.56	17.45 ±8.36	27.99 ±29.08	14.87 ±12.17	17.76 ±12.60	145.56 ±228.13	23.02 ±13.03	17.46 ±5.15	22.75 ±3.37
FE_{Cl} (%)	Rt	1.85 ±0.67	1.74 ±1.10	1.57 ±1.85	1.83 ±0.88	1.21 ±1.02	0.96 ±0.86	1.72 ±1.23	3.15 ±2.59	1.19 ±2.03	2.01 ±2.03	1.67 ±1.54	3.11 ±3.65
	Lt	1.98 ±1.25	1.53 ±0.58	1.36 ±0.91	2.10 ±1.29	1.07 ±0.46	1.55 ±1.04	1.73 ±1.33	4.44 ±5.41	6.13 ±6.68	1.29 ±1.14	1.60 ±0.93	2.09 ±1.62
FE_{Ca} (%)	Rt	1.04 ±0.57	0.86 ±0.59	0.56 ±0.22	0.95 ±0.38	1.02 ±0.43	0.46 ±0.20	0.80 ±0.54	1.89 * ±1.14	1.54 ±1.18	1.23 ±1.11	1.13 ±1.01	0.45 ±0.10
	Lt	1.05 ±0.90	0.72 ±0.54	0.63 ±0.44	2.01 ±2.45	3.32 ±2.54	0.98 ±0.78	0.067 ±0.38	1.53 ±1.70	3.82 ±4.32	1.53 ±0.97	0.95 ±0.47	0.75 ±0.48
FE_{Pi} (%)	Rt	27.13 ±12.82	30.73 ±23.42	26.77 ±16.65	40.81 ±19.27	26.19 ±32.78	17.82 ±24.71	18.46 ±12.17	27.58 ±19.78	25.59 ±24.51	44.79 ±15.39	38.38 ±13.85	43.44 ±36.19
	Lt	21.67 ±9.70	22.26 ±11.36	26.22 ±19.35	26.68 ±16.96	64.93 ±111.28	19.13 ±14.83	15.29 ±13.11	27.25 ±26.42	21.41 ±16.18	37.37 ±20.74	40.94 ±15.92	56.20 ±25.51