Chapter IV

Results

Group 1

A. Effects of omeprazole on general circulation in the acute hypokalemic dogs induced by furosemide infusion

The results of changes in general circulation in dogs given intravenous omeprazole injection and pretreated with furosemide and PEG are shown in table 1. During given furosemide alone, mean arterial blood pressure (MAP), heart rate (HR), and hematocrit (Hct) (Table 1) did not significantly change from the control value. There were also no differences in these parameters between furosemide infusion alone compared to furosemide infusion plus PEG and furosemide infusion plus omeprazole.

B. Effects of omeprazole on plasma electrolytes in the acute hypokalemic dogs induced by furosemide infusion

The results are shown in table 2. Plasma sodium (P_{Na}) and chloride (P_{Cl}) concentrations did not indicate the significant changes throughout the experimental period. Plasma potassium (P_K) concentration slightly decreased during furosemide infusion.

C. Effects of omeprazole on renal hemodynamics in the acute hypokalemic dogs induced by furosemide infusion

The data in table 3 showed that no significantly changes in glomerular filtration rate (GFR), effective renal plasma flow (ERPF), effective renal blood flow (ERBF), and filtration fraction (FF) were recorded in any period of the experiments.

During given furosemide infusion alone, urine flow rate (V) increased significantly from the control value ($P<.01$). During PEG injection, urine flow rate showed no significant change, when compared with furosemide infusion alone. During given omeprazole injection, urine flow rate decreased significantly from given furosemide alone ($P<.05$).

D. Effects of omeprazole on urinary electrolyte excretions in the acute hypokalemic dogs induced by furosemide infusion

The results of changes in urinary electrolyte excretions in dogs given intravenous omeprazole injection and pretreated with furosemide and PEG are shown in table 4 and figure 4.4. During given furosemide infusion, Urinary titratable acid excretion ($U_{TA}V$) did not significantly change from the control value. During PEG injection with furosemide, $U_{TA}V$ increased significantly to 8.87 $\pm$ 7.85% (fig. 4.1) from the value which given furosemide infusion ($P<.05$). During given omeprazole injection, $U_{TA}V$ showed no significantly difference from furosemide infusion period.

A progressive increase in urinary ammonium excretion ($U_{NH_3}V$) was recorded during given furosemide alone compared with control period

($P<.05$). There was no significantly different in $U_{NH_3}V$ during given furosemide alone compared to PEG injection period. $U_{NH_3}V$ showed no significant change during given omeprazole in comparision to the period of given furosemide infusion.

During given furosemide alone, urinary sodium ($U_{Na}V$) and chloride excretion ($U_{Cl}V$) increased significantly from the control period ($P<.05$, $P < .01$, respectively). Urinary potassium excretion ($U_{K}V$) increase but not significant. No significantly different in $U_{Na}V$, $U_{Cl}V$, and $U_{K}V$ were observed either PEG or omeprazole when compared to given furosemide infusion period.

Fractional excretion for sodium (FE_{Na}), potassium (FE_{K}), and chloride (FE_{Cl}) increased significantly in the period of infusion furosemide alone ($P<.01$). There were no significantly different in FE_{Na}, FE_{K}, and FE_{Cl} during either PEG or omeprazole injection when compared to the period of given furosemide infusion.

Group 2

A. Effects of omeprazole on general circulation in the chronic hypokalemic dogs induced by prolonged furosemide administration

The results in table 5 showed that there were no significantly different in MAP, HR, and Hct throughout the study.

B. Effects of omeprazole on plasma electrolytes in the chronic hypokalemic dogs induced by prolonged furosemide administration

The data in table 6 showed that P_{Na} slightly decreased after chronic oral furosemide. However on the day of experiment, there was no significantly change in P_{Na} after furosemide infusion.

P_K decreased significantly ($P<.01$) after chronic oral furosemide, and it kept a lower level throughout the experiment.

A progressive decrease in P_{Cl} was recorded after chronic oral furosemide ($P<.01$). On the day of experiment, there was no significantly change in P_{Cl} after furosemide infusion.

C. Effects of omeprazole on renal hemodynamics in the chronic hypokalemic dogs induced by prolonged furosemide administration

The results in table 7 showed that there were no significantly changes in GFR, ERPF, ERBF and FF throughout the study. The rate of urine flow markedly increased when given furosemide infusion in comparision with the control period ($P<.01$).

D. Effects of omeprazole on urinary electrolyte excretions in the chronic hypokalemic dogs induced by prolonged furosemide administration

The data in table 8 and figure 4.5 showed that there were no significantly different in $U_{NH_3}V$, N_KV, and FE_K throughout the study.

$U_{TA}V$ decreased significantly ($P<.001$) after furosemide infusion alone, then it increased significantly ($P<.01$) to 96.08 ± 45.41% (fig 4.1) during omeprazole injection compared with furosemide alone.

$U_{Na}V$, $U_{Cl}V$, FE_{Na} and FE_{Cl} increased significantly ($P<.05$, $P<.05$, $P<.01$, $P<.05$, respectively) when furosemide infusion period compared to control period, but during PEG and omeprazole injection they did not show any alterations when compared with furosemide alone.

Group 3

A. Effects of omeprazole on general circulation in the acute hypokalemic dogs induced by insulin infusion

The data in table 9 showed that there were no significantly different in MAP, HR, and Hct between any period of the experiments.

B. Effects of omeprazole on plasma electrolytes in the acute hypokalemic dogs induced by insulin infusion

The results in table 10 showed that P_K decreased significantly from 3.96 ± 0.49 to 3.5 ± 0.52 mEq/L ($P<.01$) after infusion of insulin and from to 3.5 ± 0.52 to 3.19 ± 0.44 mEq/L ($P<.05$) during insulin alone compared to omeprazole injection.

There were no significantly different in P_{Na} and P_{Cl} between any period of the experiments.

C. Effects of omeprazole on renal hemodynamics in the acute hypokalemic dogs induced by insulin infusion

The results showed in table 11, there was no significantly difference in V during given insulin infusion alone. The rate of urine flow increased significantly during given either PEG or omeprazole when compared to infuse insulin alone ($P<.01$, $P<.01$, respectively).

There were no significantly different in GFR, ERPF, ERBF and FF throughout the study.

D. Effects of omeprazole on urinary electrolyte excretions in the acute hypokalemic dogs induced by insulin infusion

The data in table 12 and figure 4.6 showed that $U_{TA}V$ decreased but no significant after insulin infusion alone, while it showed no change during either PEG or omeprazole injection when compared to insulin alone.

$U_{NH_3}V$ slightly decreased after insulin infusion except for during given omeprazole injection it increased significantly by approximately $67.78 \pm 53.37\%$ (fig 4.2) when compared to given insulin alone ($P<.05$).

$U_{Na}V$ increased but no significant after insulin infusion. $U_{Cl}V$ increased significantly ($P<.05$) during either insulin alone or omeprazole injection, while FE_{Cl} increased throughout the study and significant during either PEG or omeprazole injection when compared to insulin alone.

No significantly changes in U_KV and FE_K were recorded in any period of the experiments.

Table 1 Effects of omeprazole on general circulation in the acute hypokalemic dogs induced by furosemide infusion (Mean ± S.D.)

Variables	control	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
MAP (mm. Hg)	102.39 ±20.19	108.14 ±22.04	110.24 ±20.36	108.44 ±20.45
HR (beats/min)	167 ±29	175 ±38	183 ±38	184 ±37
Hct (%)	29.10 ±9.40	31.22 ±8.79	29.90 ±8.61	31.30 ±9.01

Table 2 Effects of omeprazole on plasma electrolytes in the acute hypokalemic dogs induced by furosemide infusion (Mean ± S.D.)

Variables	control	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
P_{Na} (mEq/L)	144.60 ±7.44	142.63 ±5.56	139.20 ±1.60	140.33 ±4.12
P_{K} (mEq/L)	3.26 ±0.19	3.14 ±0.31	2.86 ±0.17	3.01 ±0.15
P_{Cl} (mEq/L)	113.20 ±6.14	105.87 ±3.52	106.60 ±2.73	106.60 ±5.12

Table 3 Effects of omeprazole on renal hemodynamics in the acute hypokalemic dogs induced by furosemide infusion (Mean ± S.D.)

Variables	control	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
V (ml/min/kg)	0.01 ±0.004	0.23**,a ±0.05	0.19 ±0.04	0.15*, C ±0.03
GFR (ml/min/kg)	1.36 ±0.43	1.30 ±0.25	1.39 ±0.22	1.25 ±0.24
ERPF (ml/min/kg)	5.82 ±2.76	4.79 ±1.74	5.08 ±2.00	4.62 ±1.91
ERBF (ml/min/kg)	8.35 ±3.46	7.51 ±2.60	7.67 ±2.84	7.18 ±2.73
FF (%)	26.95 ±7.13	30.95 ±10.59	31.78 ±11.61	31.82 ±11.72

a = furosemide alone compared to control period

C = omeprazole injection compared to furosemide alone

* P<.05, ** P<.01

The data calculated as one kidney

Table 4 Effects of omeprazole on urinary electrolyte excretions in the acute hypokalemic dogs induced by furosemide infusion (Mean ± S.D.)

Variables	control	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
$U_{TA}V$	0.53	0.70	1.25*, b	1.23
(μEq/min/kg)	±0.38	±0.19	±0.44	±0.51
$U_{NH_3}V$	0.3	1.17*, a	1.25	0.98
(μEq/min/kg)	±0.22	±0.27	±0.21	±0.17
$U_{Na}V$	2.49	26.09*, a	26.19	23.77
(μEq/min/kg)	±1.62	±5.9	±6.59	±6.37
$U_{K}V$	0.86	3.12	1.90	1.93
(μEq/min/kg)	±0.39	±1.81	±0.12	±0.32
$U_{Cl}V$	1.97	27.45**, a	29.58	26.57
(μEq/min/kg)	±1.39	±5.13	±6.62	±6.95
FE_{Na}	1.17	15.28**, a	14.06	15.71
(%)	±0.57	±4.14	±4.88	±4.42
FE_{K}	21.32	53.23**, a	49.00	51.74
(%)	±8.0	±9.15	±9.10	±8.67
FE_{Cl}	1.34	21.4**, a	20.51	20.37
(%)	±0.58	±4.53	±6.23	±6.44

a = furosemide alone compared to control period

b = PEG injection compared to furosemide alone

* P<.05, ** P<.01

The data calculated as one kidney

Table 5 Effects of omeprazole on general circulation in the chronic hypokalemic dogs induced by prolonged furosemide administration (Mean ± S.D.)

Variables	before given oral furosemide	after oral furosemide	furosemide	furosemide+PEG	furosemide +PEG+omeprazole
MAP (mm. Hg)	-	125.36 ±16.96	131.79 ±19.39	136.45 ±19.16	136.00 ±20.06
HR (beats/min)	-	166 ±19	162 ±11	158 ±12	160 ±21
Hct (%)	36.80 ±4.93	38.90 ±5.65	43.01 ±3.90	42.70 ±4.73	43.10 ±4.36

Table 6 Effects of omeprazole on plasma electrolyte in the chronic hypokalemic dogs induced by prolonged furosemide administration (Mean ± S.D.)

Variables	before given oral furosemide	after oral furosemide	furosemide	furosemide+PEG	furosemide +PEG+omeprazole
P_{Na} (mEq/L)	146.20 ±12.27	133.00 ±3.16	133.40 ±4.49	134.40 ±2.73	134.10 ±4.71
P_{K} (mEq/L)	4.00 ±0.56	2.14**,0 ±0.19	2.28*,a ±0.17	2.62**,b ±0.12	2.54**,c ±0.14
P_{Cl} (mEq/L)	113.40 ±5.68	91.40**,0 ±5.08	92.20 ±7.50	88.20 ±4.62	94.40 ±6.73

0 Control period compared to before given oral furosemide

a furosemide alone compared to control period

b PEG injection compared to furosemide alone

c omeprazole injection compared to furosemide alone

* P<.05, ** P<.01

Table 7 Effects of omeprazole on renal hemodynamics in the chronic hypokalemic dogs induced by prolonged furosemide administration (Mean ± S.D)

Variables	after oral furosemide	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
V (ml/min/kg)	0.03 ±0.02	0.12**,a ±0.04	0.13 ±0.07	0.14 ±0.09
GFR (ml/min/kg)	0.94 ±0.16	0.98 ±0.18	0.98 ±0.14	0.97 ±0.19
ERPF (ml/min/kg)	7.39 ±1.64	8.30 ±2.15	8.61 ±2.78	7.85 ±2.12
ERBF (ml/min/kg)	12.25 ±3.13	14.82 ±4.59	15.15 ±5.09	13.85 ±3.68
FF (%)	13.22 ±2.56	13.11 ±4.79	13.89 ±8.04	13.83 ±7.09

a = furosemide alone compared to control period

** P<.01

The data calculated as one kidney.

Table 8 Effects of omeprazole on urinary electrolyte excretions in the chronic hypokalemic dogs induced by prolonged furosemide administration (Mean ± S.D.)

Variables	after oral furosemide	furosemide	furosemide + PEG	furosemide + PEG + omeprazole
$U_{TA}V$	0.77	0.46***,a	0.59	0.73**,c
(μEq/min/kg)	±0.30	±0.29	±0.36	±0.38
$U_{NH_3}V$	0.48	0.47	0.51	0.48
(μEq/min/kg)	±0.20	±0.19	±0.20	±0.21
$U_{Na}V$	3.57	12.09*,a	11.72	12.42
(μEq/min/kg)	±3.01	±6.27	±6.69	±8.76
$U_{K}V$	0.88	1.12	1.11	1.28
(μEq/min/kg)	±0.21	±0.22	±0.15	±0.20
$U_{Cl}V$	2.88	12.58*,a	12.26	12.35
(μEq/min/kg)	±2.66	±7.01	±6.59	±8.26
FE_{Na}	2.66	9.07**,a	8.69	9.96
(μEq/min/kg)	±1.97	±3.94	±4.37	±5.65
FE_{K}	44.53	50.40	44.35	57.23
(μEq/min/kg)	±12.03	±8.48	±6.19	±16.91
FE_{Cl}	3.04	13.56*,a	13.64	13.51
(μEq/min/kg)	±2.35	±6.16	±5.80	±6.85

a = furosemide alone compared to control period

c = omeprazole injection compared to furosemide alone

* P<.05, ** P<.01, *** P<.001

The data calculated as one kidney.

Table 9 Effects of omeprazole on general circulation in the acute hypokalemic dogs induced by insulin infusion (Mean ± S.D.)

Variables	control	insulin	insulin + PEG	insulin + PEG + omeprozole
MAP (mm. Hg)	117.69 ±18.08	119.98 ±13.60	119.48 ±10.37	114.92 ±9.37
HR (beats/min)	147 ±20	150 ±22	149 ±30	150 ±27
Hct (%)	29.9 ±7.96	29.6 ±7.35	28.7 ±6.84	28.15 ±6.59

Table 10 Effects of omeprazole on plasma electrolytes in the acute hypokalemic dogs induced by insulin infusion (Mean ± S.D.)

variables	control	insulin	insulin + PEG	insulin + PEG + omeprazole
P_{Na} (mEq/L)	143.40 ±2.24	143.40 ±2.82	142.80 ±2.14	140.90 ±5.19
P_{K} (mEq/L)	3.96 ±0.49	3.50**,a ±0.52	3.32 ±0.49	3.19*,c ±0.44
P_{Cl} (mEq/L)	115.8 ±6.99	114.80 ±4.15	115.00 ±4.65	115.00 ±7.33

a = insulin alone compared to control period

c = omeprazole injection compared to insulin alone

* P<.05, ** P<.01

Table 11 Effects of omeprazole on renal hemodynamics in the acute hypokalemic dogs induced by insulin infusion (Mean ± S.D.)

Variables	control	insulin	insulin + PEG	insulin + PEG + omeprazole
V (ml/min/kg)	0.01 ±0.0078	0.02 ±0.02	0.03 **,b ±0.02	0.03**,c ±0.02
GFR (ml/min/kg)	1.34 ±0.26	1.42 ±0.49	1.18 ±0.42	1.41 ±0.43
ERPF (ml/min/kg)	6.39 ±1.07	6.29 ±0.81	5.87 ±0.38	8.17 ±3.68
ERBF (ml/min/kg)	9.15 ±1.43	9.43 ±1.63	8.13 ±1.03	11.85 ±6.52
FF (%)	21.34 ±4.91	21.98 ±7.12	21.49 ±6.61	20.54 ±4.87

b = PEG injection compared to insulin alone

c = omeprazole injection compared to insulin alone

** P<.01

The data calculated as one kidney

Table 12 Effects of omeprazole on urinary electrolyte excretions in the acute hypokalemic dogs induced by insulin infusion (Mean ± S.D.)

Variables	control	insulin	insulin + PEG	insulin + PEG + omeprozole
$U_{TA}V$	0.47	0.17	0.17	0.18
(μEq/min/kg)	±0.29	±0.05	±0.07	±0.06
$U_{NH_3}V$	0.37	0.29	0.27	0.40*,c
(μEq/min/kg)	±0.22	±0.11	±0.12	±0.09
$U_{Na}V$	2.04	3.66	4.11	4.30
(μEq/min/kg)	±1.52	±2.36	±1.72	±1.81
$U_{K}V$	1.04	1.13	0.76	0.79
(μEq/min/kg)	±0.31	±0.49	±0.40	±0.19
$U_{Cl}V$	1.79	3.47*,a	4.45	4.73*,c
(μEq/min/kg)	±1.64	±2.39	±2.11	±1.81
FE_{Na}	1.05	1.96	2.55	2.53*,c
(μEq/min/kg)	±0.74	±1.52	±1.72	±1.49
FE_{K}	18.54	20.02	17.46	19.26
(μEq/min/kg)	±8.28	±5.84	±8.32	±6.9
$FE_{Cl}V$	1.16	2.24	3.36*,b	3.42**,c
(μEq/mik/kg)	±0.97	±1.64	±2.16	±1.95

a = insulin alone compared to control period

b = PEG injection compared to insulin alone

c = omeprazole injection compared to insulin alone

* $P<.05$, ** $P<.01$

The data calculated as one kidney

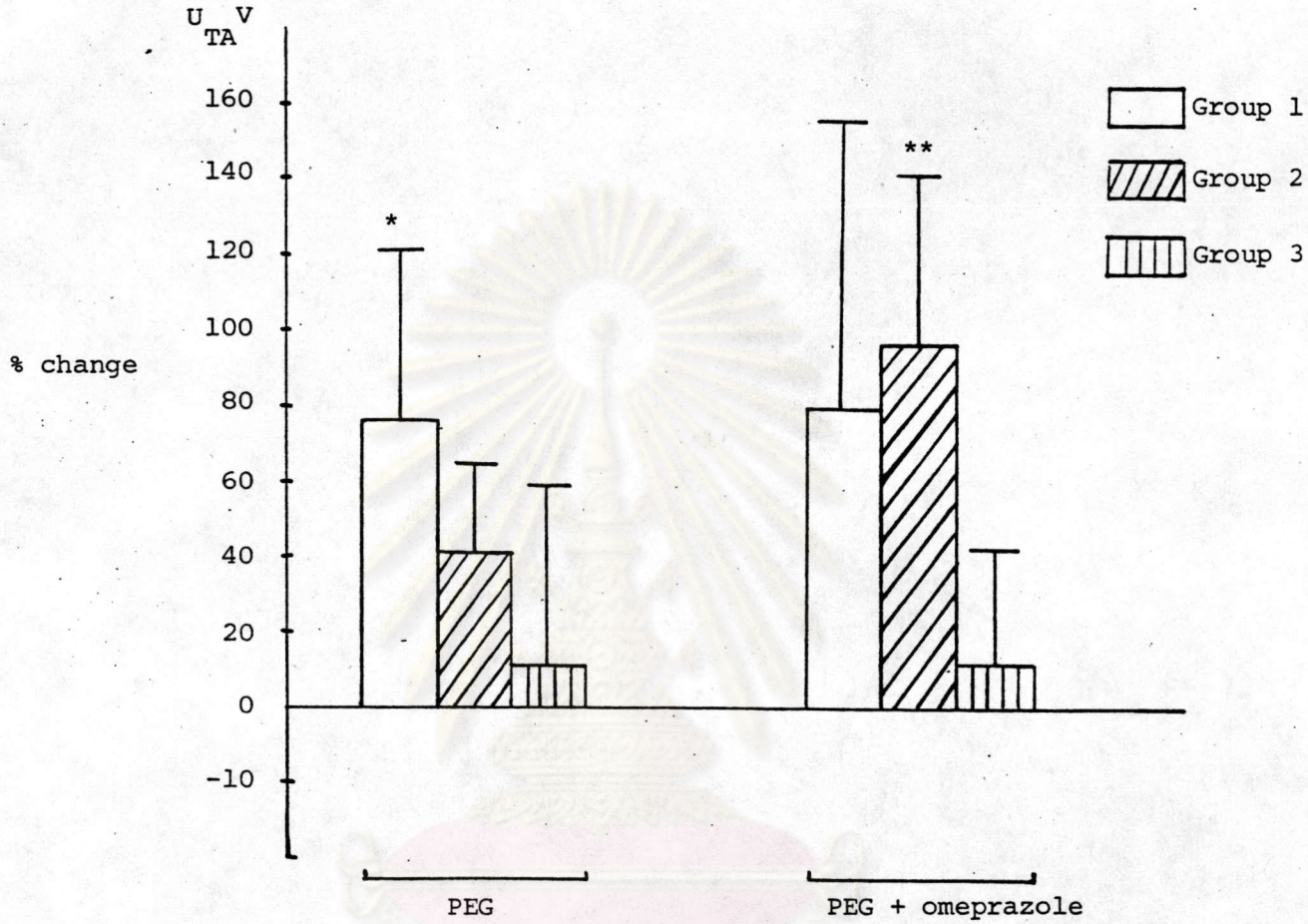

Fig. 4.1 : Percentage changes of urinary titratable acid excretion ($U_{TA}V$) in hypokalemic dogs injection with PEG or PEG + omeprazole and pretreated with furosemide (Gr. 1 and 2) and insulin (Gr. 3) infusion

The values are mean $\pm$ S.D.

P-values with respect to furosemide (Gr. 1 and 2) or insulin (Gr. 3) infusion .

* $P < .05$ ** $P < .01$

Fig. 4.2 : Percentage change of urinary ammonium excretion ($U_{NH_3}V$) in hypokalemic dogs injection with PEG or PEG + omeprazole and pretreated with furosemide (Gr. 1 and 2) and insulin (Gr. 3) infusion

The values are mean $\pm$ S.D.

P-values with respect to furosemide (Gr. 1 and 2) or insulin (Gr. 3) infusion

* $P < .05$

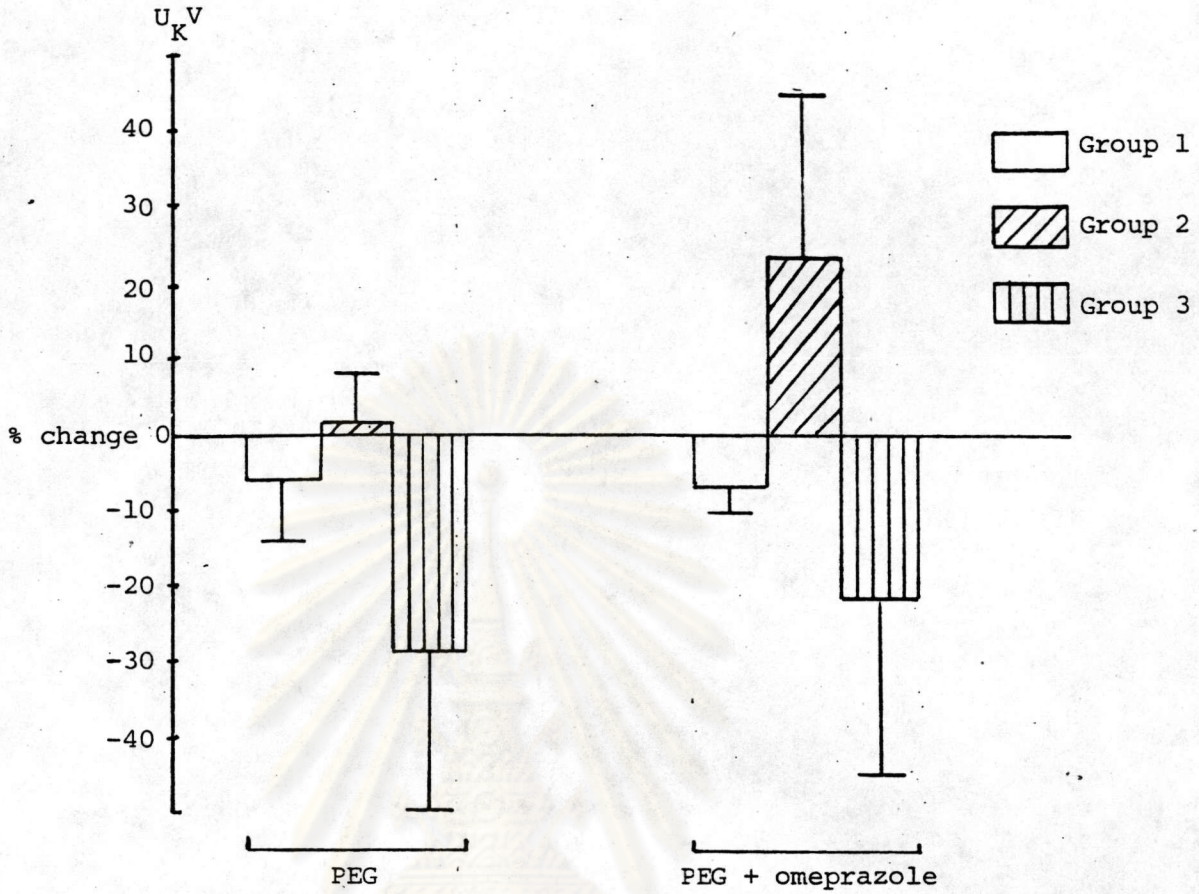

Fig 4.3 : Percentage change of urinary potassium excretion (U_KV) in hypokalemic dogs injection with PEG or PEG + omeprazole and pretreated with furosemide (Gr. 1 and 2) and insulin (Gr. 3) infusion compared with furosemide (Gr. 1 and 2) or insulin (Gr. 3) infusion

The values are mean $\pm$ S.D.

P-values with respect to furosemide (Gr. 1 and 2) or insulin (Gr. 3) infusion

Group 1

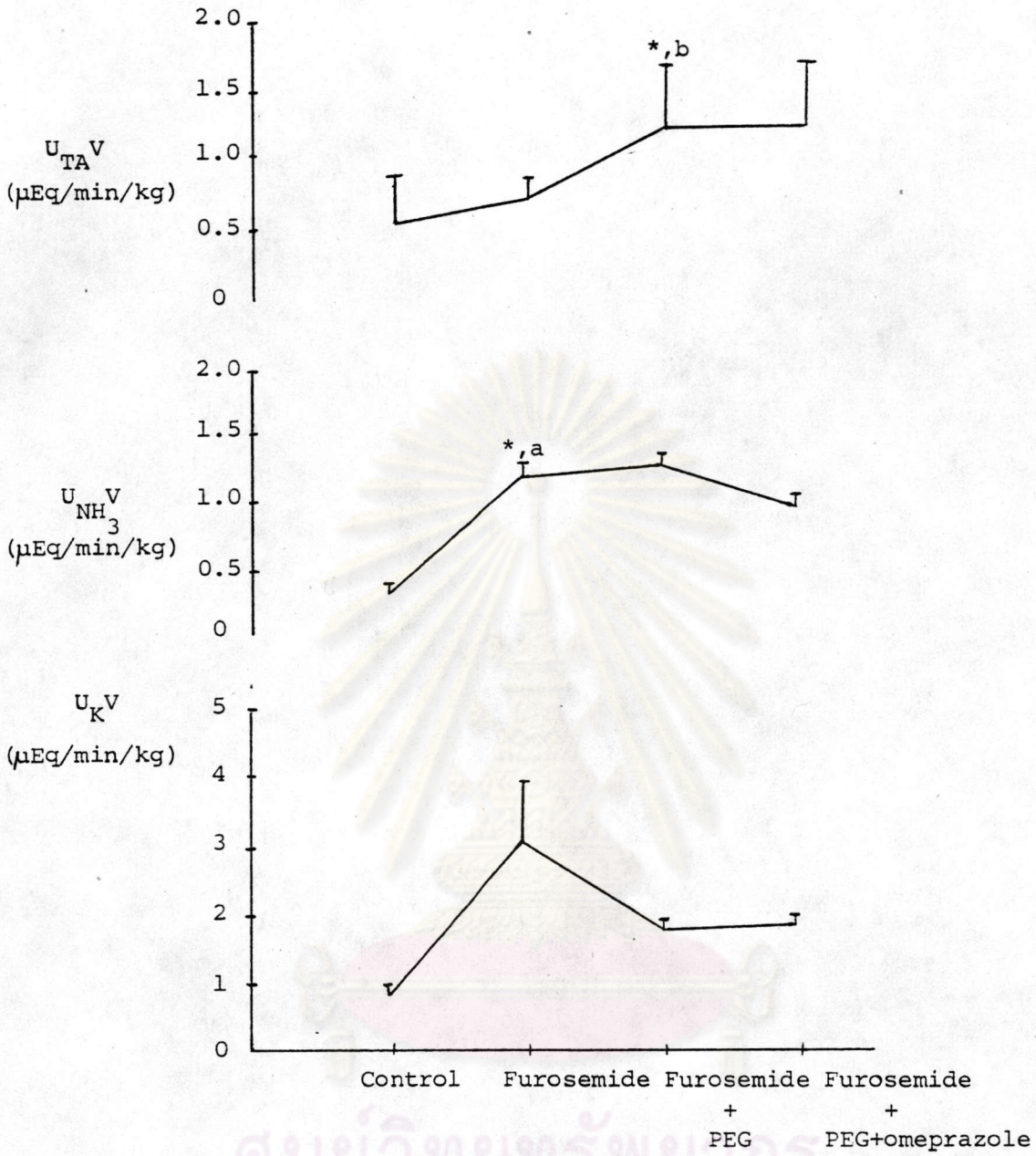

Fig 4.4 : Effects of omeprazole on $U_{TA}V$, $U_{NH_3}V$, and U_KV in the hypokalemic dogs induced by furosemide infusion.
The value is mean ± S.D.
a = furosemide infusion V.S. control period
b = furosemide + PEG V.S. furosemide alone
* $P < .05$
The data calculated as one kidney

Group 2

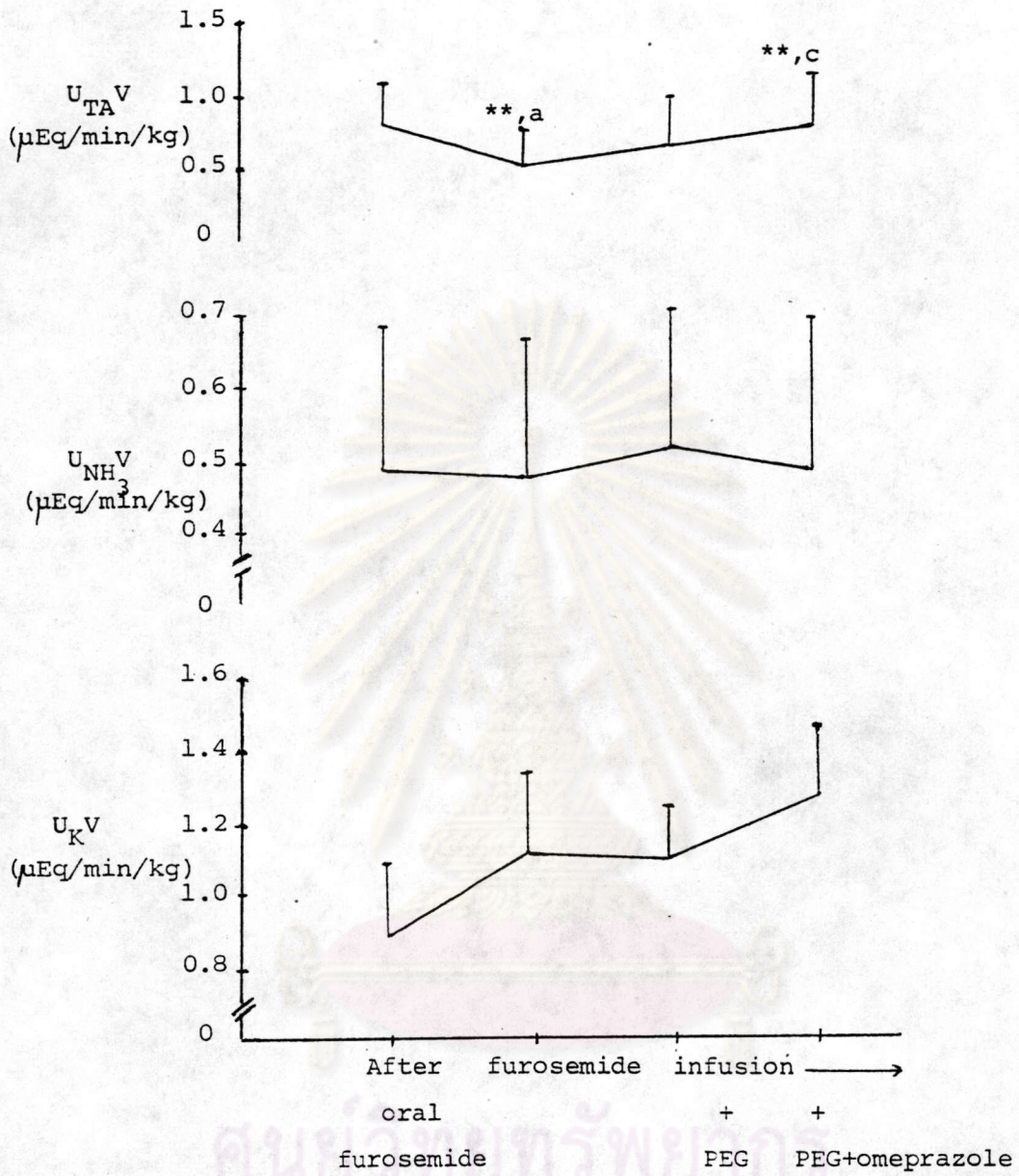

Fig. 4.5 : Effects of omeprazole on $U_{TA}V$, $U_{NH_3}V$, and U_KV in the hypokalemic dogs induced by prolonged oral furosemide.

The value is mean ± S.E.

a = furosemide infusion period V.S. after oral furosemide

c = furosemide infusion + PEG + omeprazole V.S. furosemide infusion period.

** = $P < .01$

The data calculated as one kidney

Group 3

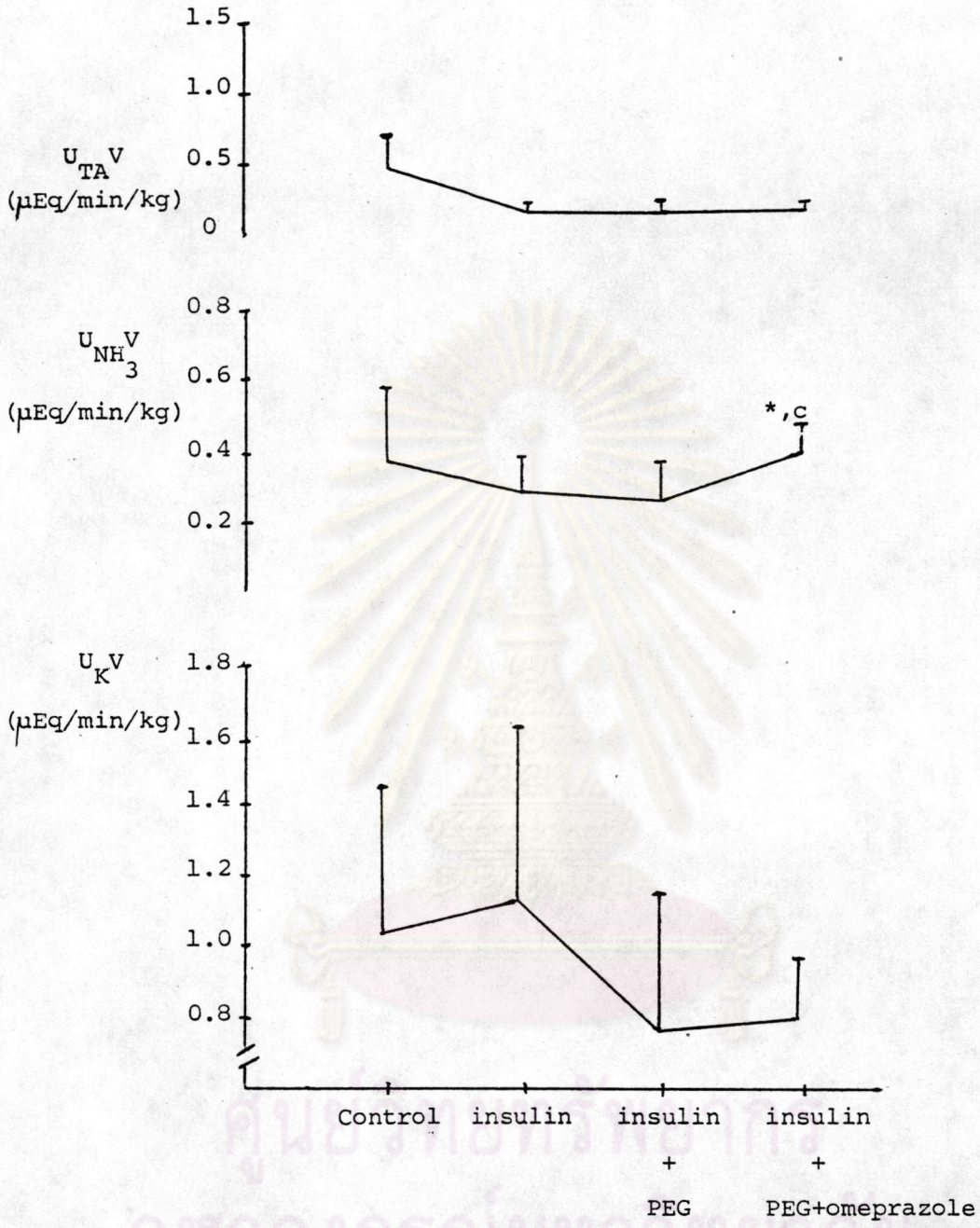

Fig. 4.6 : Effects of omeprazole on $U_{TA}V$, $U_{NH_3}V$, and U_KV in the hypokalemic dogs induced by insulin infusion.

The value is mean ± S.E.

c = insulin + PEG + omeprazole V.S. insulin alone

* $P < .05$

The data calculated as one kidney.