CHAPTER IV

RESULTS

Effects of ethylene glycol on general conditions .

All dogs in group 2 (EG 1.5 ml) and group 3 (EG 3.0 ml) were alert and responsive by the time EG was fed. By 3 hours after EG ingestion, they became slightly depressed with no remarkable change in clinical signs. Until 6 hours after EG ingestion, they became obviously depressed, ataxic, and showed the symptoms of polyuria and polydypsia. By 24 hours after ingestion, 4 out of 9 EG ingested dogs still had polyuria, the others were oliguria. All of them were dehydrated with sunken eyes and skin turgor.

After general anesthesia, EG ingested dogs showed significant hypothermia ($P<0.05$). The average body temperatures were 37.3±0.65 °C in group 1(control), 36.44±0.25 °C in group 2 , and 36.88±0.43 °C in group 3 respectively. In contrast to the clinical sign of dehydration, the hematocrit of EG ingested dogs did not significantly change from the control group as shown in table 1.

Table 1 Effects of ethylene glycol on general conditions.

	Group 1 (Control)	Group 2 (EG 1.5 ml)	Group 3 (EG 3.0 ml)
Body weight (kg)	14.48 ± 2.02	14.5 ± 2.44	14.6 ± 3.89
Body temperature (^{0}C)	37.36 ± 0.65	36.44 ± 0.25 *	36.88 ± 0.43 *
Relative right kidney weight (% bw.)	0.24 ± 0.04	0.27 ± 0.04	0.32 ± 0.05
Haemoglobin (gm/dl)	11.22 ± 1.82	13.35 ± 2.65	11.44 ± 1.83
Haematocrit (%)	36.2 ± 5.94	38.53 ± 6.67	32.76 ± 8.04

Values are mean±SD. Abbreviation: EG, ethylene glycol.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$) which is differed from control values.

Before euthanasia, the right kidney was isolated and weighed. The kidney of EG ingested dogs were swollen and relatively increased in weight. Other changes were not visible.

Effects of ethylene glycol on general circulation.

There was no remarkable cardiovascular change among group 1 , group 2, and group 3 , but the trends of change were observed. In group 2, EG ingested dogs showed insignificant decreases of heart rate, total peripheral resistance, and blood pressure. Cardiac output and cardiac index were slightly increased in group 2 (table 2).

Table 2 Effects of ethylene glycol on general circulation.

	Group 1 (Control)	Group 2 (EG 1.5 ml)	Group 3 (EG 3.0 ml)
Heart rate (beats/minute)	141 ± 23	133 ± 30	133 ± 23
Systolic P. (mmHg)	147.6 ± 17.9	137.3 ± 27.7	153.8 ± 17.3
Diastolic P. (mmHg)	96.2 ± 18.2	99.5 ± 23.6	110.8 ± 13.1
Mean P. (mmHg)	113.6 ± 17.8	112.3 ± 24.7	125.2 ± 14.8
Pulmonary systolic P. (mmHg)	27.2 ± 5.3	25.5 ± 4.9	30.8 ± 6.8
Pulmonary diastolic P. (mmHg)	12.4 ± 5.9	11.5 ± 4.5	16.7 ± 7.8
Pulmonary mean P. (mmHg)	17.4 ± 5.5	16.0 ± 4.3	21.2 ± 7.4
Pulmonary wedge P. (mmHg)	4.0 ± 3.3	5.6 ± 3.8	5.2 ± 1.7
Stroke volume (ml)	23.85 ± 12.93	28.18 ± 11.25	26.60 ± 8.42
Cardiac output (L/min)	3.16 ± 1.78	3.56 ± 1.08	3.42 ± 0.70
Cardiac index (ml/min/Kg)	224.20 ± 9.60	252.50 ± 8.60	225.20 ± 4.00
Stroke-work index (gm-m/m^2)	68.43 ± 47.29	66.48 ± 23.68	69.68 ± 19.56
TPR (x10^3 dyn-sec/m^5)	3.04 ± 0.74	2.81 ± 1.43	3.00 ± 0.52
PVR (x10^3 dyn-sec/m^5)	0.48 ± 0.21	0.39 ± 0.20	0.49 ± 0.10

Values are mean±SD. Abbreviation: EG, ethylene glycol; P, pressure; PVR, pulmonary vascular resistance; TPR; total peripheral resistance.

Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$), ** ($P<0.01$) which are differed from control values.

Effects of ethylene glycol on the acid-base status.

As shown in table 3, the averages of arterial blood pH of dogs in group 2 and 3 were significantly decreased ($P<0.05$). The averages of arterial blood pH in group 1, 2 and 3 were 7.33±0.18, 7.14±0.06 and 7.1±0.05 respectively. No significant changes in arterial pCO_2, pO_2 and O_2 saturation were observed. Meanwhile concentrations of arterial HCO_3 and arterial tCO_2 in group 2 and 3 were significantly lowered than that in group 1 ($P<0.05$). Moreover, the concentration of arterial HCO_3 in group 3 was significantly lowered than that in group 1 ($P<0.01$).

Not only the acid-base status of arterial blood significantly changed but also the acid-base status of central venous blood and renal venous blood. The averages of central venous blood pH, HCO_3 and tCO_2 in group 2 and 3 were markedly decreased from those of the control group ($P<0.01$). On the other hand, central venous pO_2 in group 2 and 3 were increased significantly ($P<0.05$). Although central venous pCO_2 in group 2 and 3 were lower than that in group 1, there was no significant change of central venous pCO_2 among groups.

Renal venous blood pH in group 2 and 3 significantly decreased ($P<0.01$). In addition, the decreases of renal venous HCO_3 ($P<0.01$)and tCO_2 ($P<0.05$) were observed . The averages of renal venous pO_2 showed no significant increases in group 2 and 3.

In contrast to the O_2 consumption, the renal O_2 uptake in group 2 and 3 were significantly decreased($P<0.05$) as shown in table 3.

Table 3 Effects of ethylene glycol on the acid-base status.

	Group 1 (Control)	Group 2 (EG 1.5 ml)		Group 3 (EG 3.0 ml)	
Arterial blood pH	7.33 ± 0.18	7.14 ± 0.06	*	7.1 ± 0.05	*
Arterial pCO2 (mmHg)	32.8 ± 17.6	30.1 ± 5.0		28.8 ± 9.4	
Arterial pO2 (mmHg)	96.9 ± 31.9	108.1 ± 8.1		114.9 ± 15.3	
Arterial HCO3 (mmol/L)	15.25 ± 3.89	10.21 ± 0.39	*	9.00 ± 3.04	**
Arterial tCO2 (mmol/L)	16.28 ± 4.40	11.13 ± 0.56	*	9.93 ± 3.33	*
Arterial O2 saturation (%)	93.74 ± 4.98	96.30 ± 0.90		97.29 ± 0.8	
Central venous blood pH	7.25 ± 0.09	7.12 ± 0.05	**	7.08 ± 0.04	**
Central venous pCO2 (mmHg)	41.8 ± 12.1	33.9 ± 11.0		33.1 ± 11.0	
Central venous pO2 (mmHg)	46.1 ± 3.0	61.0 ± 5.8	*	61.6 ± 13.0	*
Central venous HCO3 (mmol/L)	17.95 ± 2.59	10.98 ± 0.83	**	10.02 ± 3.36	**
Central venous tCO2 (mmol/L)	19.23 ± 2.89	11.99 ± 0.96	**	11.07 ± 3.69	**
Central venous O2 saturation (%)	75.70 ± 3.15	82.54 ± 4.84		80.41 ± 5.40	
O2 consumption (ml/min/Kg)	5.58 ± 1.13	5.89 ± 2.02		5.70 ± 1.56	
Renal venous blood pH	7.28 ± 0.09	7.14 ± 0.05	**	7.09 ± 0.03	**
Renal venous pCO2 (mmHg)	38.4 ± 14.9	34.3 ± 6.4		34.8 ± 12.6	
Renal venous pO2 (mmHg)	59.1 ± 13.2	76.9 ± 10.7		76.9 ± 14.4	
Renal venous HCO3 (mmol/L)	17.18 ± 3.50	11.40 ± 0.96	*	10.57 ± 3.63	**
Renal venous tCO2 (mmol/L)	18.42 ± 3.83	12.45 ± 1.12	*	11.65 ± 4.03	*
Renal venous O2 saturation (%)	82.94 ± 3.99	88.24 ± 3.73		88.97 ± 6.50	
Renal O2 uptake (10^{-1} ml/min/Kg)	2.70 ± 1.81	0.53 ± 0.69	*	0.55 ± 0.97	*

Values are mean±SD. Abbreviation: EG, ethylene glycol; HCO3, bicarbonate; pCO2,partial pressure of carbon dioxide; pO2, partial pressure of oxygen; O2, oxygen; tCO2, total carbon dioxide.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$), ** ($P<0.01$) which are differed from control values.

Effects of ethylene glycol on renal hemodynamics.

By 24 hours after treated with ethylene glycol, dogs in group 2 and 3 showed significant decreases in glomerular filtration rate (GFR), effective renal plasma flow (ERPF), and effective renal blood flow (ERBF) as compared to those in group 1 ($P<0.01$). There was significant increase of filtration fraction in group 3 as compared to that of the control group($P<0.05$). The rate of urine flow (V) decreased while renal vascular resistance (RVR) increased in group 2 and 3 with no statistical differences (table 4).

Table 4 Effects of ethylene glycol on renal hemodynamics.

	Group 1 (Control)	Group 2 (EG 1.5 ml)		Group 3 (EG 3.0 ml)	
V (μl/min/Kg)	80.29 ± 35.97	47.69 ± 48.62		58.92 ± 79.82	
ERPF (ml/min/Kg)	11.53 ± 5.21	2.09 ± 2.30	**	2.55 ± 3.75	**
ERBF (ml/min/Kg)	17.81 ± 6.71	3.35 ± 3.74	**	3.59 ± 5.32	**
GFR (ml/min/Kg)	3.14 ± 0.84	0.67 ± 0.70	**	0.95 ± 1.36	**
FF (%)	28.85 ± 5.10	49.43 ± 34.92		68.38 ± 31.24	*
RVR (10^3 dyn-sec/cm^5)	38.72 ± 11.7	10552.50 ± 20493.9		69442.83 ± $1.3x10^4$	

Values are mean±SD. Abbreviation: EG, ethylene glycol; ERBF, effective renal blood flow; ERPF, effective renal plasma flow; FF, filtration fraction; GFR, glomerular filtration rate; RVR, renal vascular resistance; V, urine volume.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$), ** ($P<0.01$) which are differed from control values.

Effects of ethylene glycol on renal tubular functions.

Data in table 5 showed that urine pH of animals in group 2 and 3 was significantly decreased ($P<0.01$). There were decreases of urinary excretion of electrolytes, but significant differences were noted on urinary excretion of potassium and bicarbonate. On the contrary, most of the fractional excretions of electrolytes were increased, but the significant increase was noted on the fractional excretion of potassium in group 3 animals only. The averages of fractional water excretion and free water clearance showed no significant increases in group 2 and 3 animals. On the other hand, the average of osmolar clearance showed no significant decreases in group 2 and 3 animals.

Table 5 Effects of ethylene glycol on renal tubular functions.

	Group 1 (Control)	Group 2 (EG 1.5 ml)		Group 3 (EG 3.0 ml)	
Urine pH	7.10 ± 0.28	6.34 ± 0.34	**	6.35 ± 0.37	**
$U_{Na}V$ (µmol/min/Kg)	10.93 ± 6.36	3.41 ± 3.06		5.08 ± 6.40	
$U_{K}V$ (µmol/min/Kg)	2.86 ± 0.86	0.58 ± 0.62	**	0.92 ± 1.21	**
$U_{Cl}V$ (µmol/min/Kg)	9.23 ± 5.78	1.79 ± 1.73		3.36 ± 4.29	
$U_{HCO3}V$ (µmol/min/Kg)	1.19 ± 0.15	0.03 ± 0.02	**	0.03 ± 0.03	**
$U_{NH4}V$ (µmol/min/Kg)	0.18 ± 0.12	0.05 ± 0.06		0.15 ± 0.25	
TA (µmol/min/Kg)	0.62 ± 0.27	0.51 ± 0.47		0.43 ± 0.78	
NAE (µmol/min/Kg)	1.41 ± 0.82	1.03 ± 1.00		1.56 ± 2.20	
FE_{Na} (%)	2.43 ± 0.98	9.13 ± 8.92		18.57 ± 17.77	
FE_{K} (%)	27.28 ± 5.58	35.80 ± 17.08		92.24 ± 64.05	*
FE_{Cl}(%)	2.41 ± 1.11	6.70 ± 8.78		15.35 ± 17.51	
FE_{HCO3}(%)	2.88 ± 1.31	1.76 ± 2.36		4.44 ± 4.87	
$FE_{H2O}(10^3\%)$	2.64 ± 1.44	11.15 ± 7.01		20.88 ± 19.97	
Osmolar clearance (µl/min/Kg)	114.51 ± 54.62	34.69 ± 32.90		59.43 ± 76.45	
Free water clearance (µl/min/Kg)	-39.06 ± 70.12	-1.875 ± 69.11		-13.43 ± 95.29	

Values are mean±SD. Abbreviation: Cl, chloride; EG, ethylene glycol; FE, fractional excretion of electrolyte; HCO3, bicarbonate; K, potassium; Na, sodium; NAE, net acid excretion; NH4, ammonium; TA , titratable acid; UV, urinary excretion of electrolyte.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$), ** ($P<0.01$) which are differed from control values.

Effects of ethylene glycol on concentrations of urea nitrogen, glucose, electrolytes, and osmolality in plasma.

The increases of plasma urea nitrogen, sodium, and potassium were observed in group 2 and3 dogs but significant difference did not appear when compared to those of dogs in group 1. In addition, anion gaps of dogs in group 2 and 3 (20.75±12.63 and19.62±7.51 mmol/L) were higher than the result in group 1 (9.49± 5.09 mmol/L). The measured osmolalities of dogs were increased in group 2 ($P<0.05$) and 3 ($P<0.01$). Osmolal gaps of dogs in group 2 and 3 (20.81±8.34 and 38.46±13.05 mOsm/Kg) were higher than that of group 1 (9.32±5.50 mOsm/Kg) because the increase of the measured osmolality was higher than the increase of the calculated

osmolality. Therefore, the increase of the osmolal gap was seen , especially in group 3 ($P<0.01$).

Table 6 Effects of ethylene glycol on concentrations of urea nitrogen, glucose , electrolytes, and osmolality in plasma.

	Group 1 (Control)	Group 2 (EG 1.5 ml)	Group 3 (EG 3.0 ml)
Plasma urea nitrogen (mg/dl)	15.96 ± 4.60	29.63 ± 18.76	31.21 ± 21.20
Plasma glucose (mg/dl)	75.33 ± 17.71	66.42 ± 15.54	67.61 ± 20.08
Plasma Na (mmol/L)	134.50 ± 2.78	137.50 ± 3.67	137.60 ± 2.79
Plasma K (mmol/L)	3.34 ± 0.28	3.59 ± 0.65	3.62 ± 0.89
Plasma Cl (mmol/L)	114.25 ± 5.14	110.13 ± 8.90	112.60 ± 4.52
Anion gap (mmol/L)	9.49 ± 5.09	20.75 ± 12.63	19.62 ± 7.51
Calculated osmolality (mOsm/Kg)	285.60 ± 5.98	296.75 ± 13.50	297.40 ± 12.12
Measured osmolality (mOsm/Kg)	292.50 ± 10.44	317.25 ± 10.99 *	335.80 ± 23.35 **
Osmolal gap (mOsm/Kg)	9.32 ± 5.50	20.81 ± 8.34	38.46 ± 13.05 **

Values are mean±SD. Abbreviation: Cl, chloride; EG, ethylene glycol; K, potassium; Na, sodium.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * ($P<0.05$), ** ($P<0.01$) which are differed from control values.

Effects of ethylene glycol on concentrations of urea nitrogen, glucose, electrolytes and osmolality in urine.

The significant decrease in the level of urine urea nitrogen was significantly noted in group 1 animals (177.26±75.08 mg/dl) when compared to those in group 2 and 3 animals (65.26±20.66 and 66.449±21.46 mg/dl) ($P<0.01$). On the other hand, urine glucose level was lower in group 1 (4.13±2.02 mg/dl) than those in group 2 (10.93±15.91 mg/dl) and group 3 (31.59±25.76 mg/dl). The significant increase of urine glucose was shown in group 3 ($P<0.01$). The average concentration of urine sodium in EG ingested dogs was lower than that in control dogs without significance. The average concentration of urine potassium was significantly decreased from 38.44±9.64 mmol/L in group 1 to 12.55±4.28 mmol/L in group 2 and 19.42±10.72

mmol/L in group 3 (P<0.01). The concentration of urine chloride was significantly changed only in group 2 (P<0.05), although there were decreases in both of group 2 and 3 animals. Urine anion gap were higher in group 2 (60.58±22.41 mmol/L) and group 3 (61.13±28.26 mmol/L) than that in group 1 animals(46.60±20.36 mmol/L). In contrast to the plasma osmolality, urine osmolality in group 2 and 3 animals appeared to be lower than that in group 1 animals, however, the significant difference appeared in group 2 (P<0.05) in both calculated and measured osmolality when compared to those in group 1 and 3.

Table 7 Effects of ethylene glycol on concentrations of urea nitrogen, glucose, electrolytes, and osmolality in urine.

	Group 1 (Control)	Group 2 (EG 1.5 ml)		Group 3 (EG 3.0 ml)	
Urine urea nitrogen (mg/dl)	177.26 ± 75.08	65.26 ± 20.66	**	66.49 ± 21.46	**
Urine glucose (mg/dl)	4.13 ± 2.02	10.93 ± 15.91		31.59 ± 25.76	**
Urine Na (mmol/L)	145.80 ± 62.06	98.75 ± 38.58		115.00 ± 31.88	
Urine K (mmol/L)	38.44 ± 9.64	12.55 ± 4.28	**	19.42 ± 10.72	**
Urine Cl (mmol/L)	119.35 ± 52.36	49.56 ± 29.83	*	72.35 ± 21.16	
Urine anion gap (mmol/L)	46.60 ± 20.36	60.58 ± 22.41		61.13 ± 28.26	
Urine calculated osmolality (mOsm/Kg)	432.00 ± 158.69	246.50 ± 76.16	*	295.00 ± 77.81	
Urine measured osmolality (mOsm/Kg)	460.80 ± 183.18	270.00 ± 57.17	*	357.20 ± 69.55	
Urine osmolal gap (mOsm/Kg)	36.40 ± 26.68	25.29 ± 17.15		71.90 ± 38.41	

Values are mean+SD. Abbreviation: Cl, chloride; EG, ethylene glycol; K, potassium; Na, sodium.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * (P<0.05), ** (P<0.01) which are differed from control values.

Effects of ethylene glycol on renal lipid peroxide concentration and xanthine oxidase activity.

The changes of lipid peroxide concentration were observed by measuring malondialdehyde as shown in table 8. The increase in the level of malondialdehyde in

kidney tissues were significantly noted (P<0.01) in group 2 and 3 animals (126.47± 18.02 and 137.13±59.07 mmol/gm.kidney protein) as compared to that in group 1 animals (65.64±20.80 mmol/gm.kidney protein). On the contrary, xanthine oxidase activities were lower in group 2 and 3 animals (30.96± 5.25 and 57.12±24.18 munit/gm.kidney protein) than that in group 1 animals (75.00±10.44 munit/gm.kidney protein). The significant difference of xanthine oxidase activity between group 2 and group 3 animals was evident (P<0.05).

Table8 Effects of ethylene glycol on renal lipid peroxide concentration and xanthine oxidase activity.

	Group 1 (Control)	Group 2 (EG 1.5 ml)	Group 3 (EG 3.0 ml)
Malondialdehyde (nmol/gm.kidney protein)	65.64 ± 20.8	126.47 ± 18.02 *	137.13 ± 59.07 *
Xanthine oxidase activity (munit/gm.kidney protein)	75.00 ± 10.44	30.96 ± 5.25 **$	57.12 ± 24.18

Values are mean±SD. Abbreviation: EG, ethylene glycol.
Significant difference values using one-way ANOVA and Duncan's new multiple rank test are indicated by * (P<0.05), ** (P<0.01) which are differed from control values.
$ (P<0.05) is indicated the significant difference between EG 1.5 ml and EG 3.0 ml.