CHAPTER V

DISCUSSION

Ethylene glycol (EG) and its metabolites have many effects on bodily function in ingested dogs. The present study showed that the body temperatures of EG ingested dogs decreased. The depression, coma and sedative effects of EG were also observed. It may be related to the lost of body fluid and electrolytes during polyuric period at the first 24 hours after EG ingestion . In addition, EG and its metabolites can inhibit energy formation, especially the glyoxylic acid which has been shown to be a very potent in vitro inhibitor of mitochondrial electron transfer activities (Bachmann and Golberg, 1971) which may cause the reduction of energy and heat production.

The clinical sign of dehydration was apparent in EG ingested dogs. However it did not affect cardiovascular functions. Although cardiac index in group 2 animals(EG 1.5.ml/kg) was slightly increased while total peripheral resistance and pulmonary vascular resistance were decreased. It has been known that EG is an osmotically active substance which its half life is more than 10 hours in dogs (Dial et al., 1994a) and more than 7 hours in human (Jacobsen et al., 1988). The serum half life of EG can be increased if ingested animals are treated by ethyl alcohol or 4-methylpyrazole. Therefore, EG could partially hold the fluid in plasma before it was excreted via the kidney. The present results had shown the unchanged values of cardiac index, vascular resistance, and heart rate.

Gross appearance of the right swollen kidney was observed in EG ingested dogs which was coincided with an increase in the relative right kidney weight. It would affect renal hemodynamics particularly the effective renal blood flow and glomerular filtration rate decreased significantly, whereas the renal vascular resistance markedly increased. These changes have been similarly reported in the case of renal

ischemia (Burke et al., 1984). The filtration fraction of EG ingested animals tended to be increased. An alteration in renal hemodynamics may be resulted from the constriction of both afferent and efferent arterioles, but the degree of constriction of the efferent arterioles might be more than that of the afferent arterioles resulting in an increase in filtration fraction(Rose,1994).

In the present study, most of the EG ingested dogs showed the decreases in blood pH and bicarbonate, and metabolic acidosis. However, the blood pCO_2 was in normal limit. The changes of capillary wedge pressure and pulmonary vascular resistance were apparent which indicated that there was no pulmonary edema formation. Therefore respiratory acidosis would not be suspected in this study. Urine pH of the EG ingested dogs decreased when compared to the control group. Titratable acids of the EG ingested dogs and the net acid excretions were also decreased. Therefore the occurrence of acidemia would be due to the impairment of either the acid excretion or the bicarbonate reabsorption by the kidney including an acidity of the EG metabolites. The EG metabolite acidity especially the glycolic acid has been shown to be the major cause of metabolic acidosis in human (Jacobsen et al., 1988) and dogs (Dial et al., 1994a). Blood samples collected from both the pulmonary and the femoral arteries showed similar patterns of blood pH, concentration of plasma bicarbonate, and plasma total carbon dioxide which also reflected the metabolic acidotic status of the animals as described by Ilkiw, Rose, and Martin (1991).

Urinary excretion of electrolytes were decreased especially urinary excretion of potassium ion in EG ingested dogs. These changes were due to the decrease of glomerular filtration rate. The decrease in urinary excretion of ammonium of EG ingested animals was also noted which indicated that the decrease in glutamine catabolism in the renal tubular cell was affected (Rose, 1994). However, the decreases in osmolar clearance and water reabsorption in the EG ingested animals would be another explanation for the decrease in the capacity of renal tubular cells.

On the contrary to the other study in cats that the glucosuria was developed with the hyperglycemia (Dial et al., 1994b), in this study, the glucosuria was apparent with the normoglycemia. The evidences from this study would support the present result that the glucosuria of EG ingested dogs would come from the decrease in the capacity of renal tubular cell rather than from the overloading of the transport maximun of glucose.

The present results showed decreases of the concentrations of urine urea nitrogen , urine electrolytes, and urine osmolality. These changes would also reflected the loss of renal tubular capacity to concentrate urine. The lack of energy produced from the mitocnondria including the decrease of glomerular filtration rate would be involved.

In the present study, after 24 hours of EG ingestion, reperfusion injury was not developed. Since the effective renal blood flows did not returned to the normal level. The renal oxygen uptake was lowered in EG ingested dogs. These results implied that the burst of superoxide formation during reperfusion would not be developed.

Xanthine oxidase activity in the kidney tissue of EG ingested dogs was decreased in the present study. This change may be caused by the decrease in cellular pH which has been reported by Porras, Olsen, and Palmer (1981) that when the pH has been decreased from 9.9 to 6.2, the reaction constants of xanthine oxidase for oxygen bining and the rapid rate of electron transfer have been decreased 20-folds.

The lipid peroxide levels in the kidney tissue of EG ingested dogs were increased in group 2 and 3. The increases of lipid peroxide level would reflect the increase of free radical formation in the kidney. However, the increase of lipid peroxide may come from other sources. Since an evidence of leukocytosis in EG intoxications was reported by Trall et al. (1984), and the phagocytic cells especially neutrophils can produce free radicals via oxidase and myeloperoxidase enzyme systems during having the phagocytic activity in injured kidney tissues (Weiss, 1986).

In addition, the increased adhesiveness of neutrophils, the cellular swelling from neutrophil injury, and the large number of involving neutrophils may contribute to the mechanical obstruction of some capillary beds. These sequence of the events were called the no-reflow phenomenon (Lantz, 1995). Ischemia also continues in these tissue beds and results in necrosis due to the inability to reestablish blood flow which would be another explanation.

In conclusion, this study showed that the EG affected mainly the acid-base status and renal functions. Metabolic acidosis may be developed from either the impair renal tubular function or the acidity of the EG metabolites. The changes of renal functions may be due to the decrease of blood perfusion to the kidneys and the renal tubular cell degeneration resulting from the toxic effects of the EG metabolites. The mechanism of renal tubular necrosis was appeared to be due to the free radical formations, proposed from the increase of lipid peroxide levels, although the xanthine oxidase activities were not increased. However, the reperfusion injury was not developed in this study.