Chapter I

Introduction

Acute renal failure (ARF) is the cause of death in Russell's viper bited patient (Aung-Khin, 1978; Sarangi, Panaik, Das, Tripathy, Misra & Swain, 1980). Oliguria occured in the first day of envenomation (Sitprija & Boonpuknavig, 1985). In experimental dog injected with Russell's viper venom there were marked reductions in renal blood flow and glomerular filtration rate which concomittant with an increase in renal vascular resistance There were marked alterations in general circulation e.g. decrease in blood pressure, heart rate, and cardiac output, increase in total peripheral resistant (Chaiyabutr, 1985; Tongvonchai, 1984; Tungthanathanich, 1983). In spite of the general circulation had returned to normal, ARF still persisted (Tongvonchai, 1984; Tungthanathanich, 1983). The elevation of renal vascular resistance lasted 24 hours while the renal blood flow and glomerular filtration rate were depressed below the control level before envenomation (Chaiyabutr, 1985; Tongvonchai, 1985). The role of Russell's viper venom induced ARF is still unclear in either alteration of systemic circulation (Tungthanathanich, 1983; Varaguman & Panabokke, 1970) or the direct nephrotoxic effect of the venom since it has been noted that renal failure occured in Russell's viper bite without hypotension (Sitprija et al, 1985). The venom may act as metabolic inhibitor to abolish the energy supply for ionic transport mechanism in the proximal tubular cell which has been also reported in the Triturus kidney (Chaiyabutr, Sitprija, Sugino & Hoshi, 1985).

It has been known that arachidonic acid (AA) is the precursor for prostaglandins synthesis. AA is released from phospholipid in the cell membrane by action of phospholipase enzyme. The next step, AA is converted into endoperoxide prostaglandin G_2 and prostaglandin H_2 (PGG_2 and PGH_2) by action of cyclooxygenase enzyme. Then PGH_2 is converted into two vasoactive agent; prostacyclin (PGI_2) and thromboxane A_2 (TXA_2) by action of the enzymes prostacyclin synthetase and thromboxane synthetase respectively. It is of interest that Russell's viper venom contains phospholipase A_2 (PLA_2), the enzyme which causes hypotension (Huang & Lee, 1984). In addition PLA_2 fraction from Russell's viper venom induced TXA_2, PGI_2 and histamine released from guinea-pig lung (Huang, 1984 a), and increased plasma level of PGI_2 and TXA_2 in rat (Huang, 1984 b). In various experimental model of ARF provided evidences that TXA_2 might play an important role. There was a linear relation between production of TXB_2, metabolite of TXA_2 and serum creatinine in glycerol-induced ARF rabbit (Benabe, Klahr, Hoffman & Morrison, 1980). In induced glomerulonephritis rat, the increased production of TXA_2 and PGI_2 were found in glomerulus (Lanos, Andres & Dunn, 1983). So did to the dog (Balint & Lazzlo, 1985; Cadnapaphornchai, Bondar & McDonald, 1982) and rat (Yarger, schocken & Harris, 1980) when their ureters were obstructed, TXA_2 played an important role in altering the kidney function. Administration of thromboxane synthetase inhibitor (TSI) relieved renal vasoconstriction (Balint et al, 1985) and improved the depressed renal function (Cadnapaphornchai, Bondar & Mc.Donald, 1982; Yarger, Schocken & Harris, 1980) in these animals.

The view point of prostaglandin in Russell's viper venom

induced ARF has been shown that the renal function of the dogs pretreatd with indomethacin was better than that of the control group recieved Russell's viper venom alone (Tongvonchai, 1984). This data suggested that prostaglandin might be an important mediator of Russell's viper venom induced ARF but the specific PGs can not be indicated since indomethacin inhibits the conversion of AA into PGs at cyclooxygenase pathway. ARF in envenomated animal may be the result of imbalance of the two prostanoid; PGI_2 and TXA_2 which the primer is a potent vasodilator and the latter is a powerful vasoconstrictor.

According to previous experiment (Chaiyabutr, 1985; Tungthanathanich, 1983) hypotension induced by Russell's viper venom became to approach the pre-envenomated level within 30 minutes. This rising of blood pressure may be the effect of vasopressive mediator such as renin-angiotensin system (Chaiyabutr, 1985) and catecholamine (Chaiyabutr et al, 1984). It is also possible that TXA_2 may take part in alteration leading to the insults of renal function. The study of TXA_2 in dog recieved Russell's viper venom treated with thromboxane synthetase inhibitor has not been reported. To examine this hypothesis imidazole was used as TSI which inhibits conversion of PGH_2 to TXA_2.