Acute kidney injury (aki)

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Acute Kidney Injury (AKI) is a widely prevalent condition characterized by abnormalities in fluid and electrolyte balance is quite a common condition faced by practitioners in modern times. Urine output is lowered (anuria) and fluid imbalance occurs in critically ill patients (Kellum et. al., 2008). AKI complicates the course in 5% to 30% of victims of severe viper poisoning. No consensus exists on the single mechanism causing acute renal failure after viper bite. However it is known that viper venom induces several clinical abnormalities that favor the development of acute kidney injury. These include varying degree of bleeding, hypotension, circulatory collapse, intravascular hemolysis, and disseminated intravascular coagulation with or without microangiopathy. A direct cytotoxic action of snake venom on the kidney is also suspected to occur (Chugh et. al., 1989).

Snake bite induced AKI is considered a neglected tropical disease of 21st century since even after huge mortality and morbidity governments both nationally and internationally pay less attention to build up the infrastructure for its treatment. Currently ASVS (Anti Snake Venom Serum) is the only known treatment available. But ASVS binds only to free venom and not to already bound venom (Bawaskar et. a., l 1999). Thus ASVS administration should be done within an hour of snake bite. Previously many other different snake venom were used for studying renal injury. But in my study I zeroed in on Russell’s Viper venom since it is the most dangerous and predominant snake in Asia as well as India accounting for thousands of death each year. The objective of our study was to find whether the conditions associated with snake venom induced AKI can be prevented.

Little is known about the contributing factors in the pathogenesis of snake bite induced acute kidney injury. In chronic renal disease role of oxidative, carbonyl and nitrosative stress has been studied to some extent and is associated with significantly declined reduced glutathione status (Mukhopadhyay et al., 2008). This indicated a state of oxidative stress associated with carbonyl stress in the said diseases. These findings compelled us to investigate the protein modification as reactive carbonyl species, including MG, nonenzymatically and rapidly glycate proteins and alter its conformation (Miyata et al., 1999). I studied these factors in snake bite patients and in experimental model of SAKI to delineate the pathogenesis of SAKI and to evaluate the established and traditional methods of treatment.

Clinical studies

In the prospective study on SAKI patients we have found about 44. 13% of snake envenomed patients develops AKI and about 33. 7% of total envenomed patients receives hemodyalysis as a renal replacement therapy during the study period. The percentage of patients developing SAKI might be on the higher side than other reports because of the nature of this particular study centre, which is a tertiary care centre specially equipped for dialysis in AKI. Victims are referred to this hospital when renal complication develops. However patients are also referred from in house departments for dialysis. In such cases ASVS administration was recorded.

The male to female ratio among victims was found to be 2. 23: 1, which is again on higher side for female, as found from other reports. Whether male are particularly vulnerable, or gender inequality is a reason behind this

discrepancy – needs to be studied. However age was consistent with other reports and also with the finding – AKI affects younger population of developing countries but older in developed countries. Oliguria and bleeding manifestation were the common presentation of SAKI patients. The most common indication of HD was oliguria and rising creatinine level. Average bite to HD time was 3. 2 days.

An increased OSI associated with elevated TOS in patients with snake envenomation indicating OS mediated pathogenesis of SAKI. In NSAKI and SAKI group the OSI is found to be increased by 1. 5 and 1. 58 times of normal respectively indicating redox imbalance after snake envenomation. Our data is consistent with other studies carried out in this field which indicates an OS mediated tissue damage in Uremia (Zengin et al., 2014; Mukhopadhyay et al., 2008). Furthermore, our report point out that MG concentration is rapidly and significantly elevated in patients with snake envenomation (2. 69 and 4. 07 times of control in NSAKI and SAKI respectively) which was consistent with our previous study (Mukhopadhyay et al., 2008).

These findings are indicative of increased OS mediated and/or associated formation of reactive carbonyl species, including MG, causing a significant CS in SAKI. The elevated MG may be one of the causative factors for renal failure, possibly through rapid modification of protein. It is also suggested from the correlation data that CS rather than OS is more associated with protein modification. Giulivi and Davies (1993) have argued that protein oxidation and proteolysis may actually be more sensitive measures of OS than lipid peroxidation. AOPP is an exquisite marker of phagocyte derived OS

and has an important role in renal failure and dialysis related complications (Witko-Sarsat et al., 2003).

AOPP is generated from HOCl mediated damage of protein which is formed from myeloperoxidase of activated neutrophils, a hallmark of inflammation (Witko-Sarsat et al., 1996). In our present study, we have found that AOPP is significantly elevated (1. 8 times of control in SAKI group compared to 1. 36 times that in NSAKI) in patients with snake envenomation. Similarly increased levels of other protein damage markers viz. AGE, dityrosine and pentosidine were found to increase in SAKI by 1. 5-3. 5 times and in NSAKI by 1. 32-1. 57 times of normal level.

To the best of our knowledge this is the first report of elevated AOPP and other protein damage markers in SAKI. It was clear that the protein damage markers were distributed over a wider range in case of SAKI patients. This wider range of distribution of protein damage markers could be explained on the basis that in case of snake bite, the degree of exposure and the resistance against the toxins may be different in different patients. Protein modification has been implicated in chronic diseases, but studies on its involvement in acute diseases have been limited to AOPP rise in uncategorized AKI (Lentini et al., 2010), as prognostic marker of AKI after coronary artery bypass grafting (Liang et al., 2012) and in animal model of nephrectomy nephrectomy (Šebeková et al., 2001, . Rabbani et al., 2007).

From this study it can be assumed that venom poison may elevate AOPP and other nonenzymatic protein modification via accumulation of MG and elevation of OS. These damaged proteins may interact with receptor for AGE

(RAGE) and lead to renal damage via apoptosis and/or epithelial to mesenchymal transition leading to renal fibrosis (Oldfield et al., 2001; Guo et al., 2008; Chung et al., 2010).