Acute Tubular Necrosis: Can it be Prevented?

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Acute tubular necrosis (ATN), is a misnomer in clinical context because the problem is not localised at renal tubules only. Of all the causes of acute renal failure (ARF), acute pre-renal azotemia and ATh are the most common and with the advent of dialytic therapy and other treatment modalities ATN still carries considerable morbidity and mortality which can be as high as 80% when ATN occurs in patients in Intensive Care Units.

Although, it may be difficult to prevent ATh, as the onset of the ischaemic or toxic insult leading to ATN is generally unpredictable, there are clinical circumstances where renal insults can be foreseen. Examples are elective surgery (especially in cases with compensated renal function), renal transplantation, radiocontrast examination (with special reference in diabetics and renal compromised individuals), aminoglycoside treatments, chemotherapy, extensive burns, muscle trauma and in certain situations of obstetrical setting like excessive peripartum blood loss, PET, septic abortions, intrauterine fetal death etc. Combination of two or more conditions increases the susceptibility.

Prevention may be schematically subdivided into “primary” (to prevent the appearance of disease) and secondary (to reduce the rate of progression and complications of disease).

Renal blood flow declines with a decrease in cardiac output, whatever may be the cause. The clinical estimation of volume depletion is not an easy task, but prompt restitution of normal extracellular fluid volume can prevent progression of ischaemic ATN. Various studies, both retrospective and prospective, controlled and uncontrolled have been done, analysing the use of diuretics, (mannitol and frusemide), vasoactive agents (dopamine, calcium blockers and atrial natriuretic peptide) and nutritional therapy (use of essential amino-acids) in primary and secondary prevention of ATN.

Conger[1] has compiled the data from multiple studies to reach the conclusion that use of mannitol as prophylactic agent showed significant positive effect only in situation of renal transplantation, while in vascular surgery including abdominal aortic surgery, biliaxy tract surgery, in patients for exposure to contrast media treatment with mannitol neither improved GFR nor altered mortality. In contrast, use of mannitol has increased the risk of contrast nephmpathy in diabetics[2]. This particular group of patients can only be benefitted by pre-loading them with normal saline prior to major surgery or contrast studies. Saline infusion at a rate of 1 ml/lkg/hour started 12 hours before and continued during the procedure and for 12 hours after, has been found to be effective and is recommended[3]. Similarly, ensuring adequate extracellular fluid volume prior to major surgery has proved to be an excellent preventive measure.

Nearly identical results have been achieved with the use of fnisemide in primary prevention. When instituted in secondary prevention, it induced increase urine flow rate but did not have the same predictive implications as a spontaneously higher (non oliguric) urine flow rate. Whether continuous infusion of frusemide is more efficacious than bolus injection, is still an unsettled issue.

Low dose dopamine, the so-called renal dose i.e., 0.5-2 mg/kg/min has been used to increase urineoutputinanattempt to prevent ATN inoliguric, critically ill patients. However, the ability of dopamine to achieve these goals is poorly documented and largely anecdotal. Dopamine has a synergistic action with frusemide and may be of benefit in improving azotemia and shortening the duration of ARF when used in early phases, say within 12-24 hours of onset of oliguria[4].

Ischaemic or toxic insults provoke increments in ‘free’ calcium intracellular concentrations and attendant cell injury. The calcium channel blockers have multifactorial effects. They cause vasodilatation of afferent arterioles, their haemodynamic effect causes solute diuresis, in addition, they

exert direct cytoprotective effect on renal cells. A number of studies reviewed by Epstein, have shown that oral administration of a calcium channel blocker protects against the fall in GFR that may occur after administration of hyperosmolar radiocontrast media[5]. Use of calcium blockers in post-transplant patients enhances decline in serum creatinine and prevents the incidence of post transplant ischaemic ATh[1,6].

The use ofatrial natriuretic peptide(ANP) has also been reviewed in context to prevention of ATN. At the glomerular level ANP dilates the afferent arteriole and constricts the efferent, thus causing increase in GFR. ANP when used in combination with dopaniine was found effective in inhibiting a decrease in GFR in animals challenged with renal ischaemia. In addition, this combination was also found effective as a secondary preventive measure[7]. Preliminary results concerning the protective effect of ANP in contrast nephropathy, in humans, have shown a reduced incidence in the treated group. Paradoxically, this toxicity was increased in diabetics[2]. Nutritional therapy with essential and non-essential-amino acids (EAA and NEAA) has been studied and it was observed

•that EAA-glucose supplementation was associated with a significantly better recovery of renal function and survival[8]. But the results of the studies describing nutritional therapy are conflicting as most of them have not examined the nitrogen balance. In summary, itcanbe acceptedthatcorrectionofvolume depletion, oreven where possible, amoderateover-expansion of the extra-cellularvolume, remains one of the most effective measures to prevent clinical ATN. The use of mannitol and frusemide remains controversial because of lack ofcontmlled studies, even morn controversial is the use of low dose dopamine. The clinical results of AN? uptil now are not so promising and at the moment their use cannot be recommended. Calcium channel blockers protect against development of ATN in patients with renal transplantation. The most reasonable appmachto nutritional therapy is to give sufficient calories and protein to minimize negative nitrogen balance. Any measure can only be of value when used pmmptly in an appropriate situation.

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