Current Anaesthesia & Critical Care 21 (2010) 65–68

Contents lists available at ScienceDirect

Current Anaesthesia & Critical Care

journal homepage: www.elsevier.com/locate/cacc

FOCUS ON: RENAL

Prevention of acute kidney injury in the intensive care unit

Stuart Murdoch*

St James's University Hospital, Beckett Street, Critical Care, Leeds, West Yorkshire LS9 7TF, United Kingdom

Keywords:
Acute kidney injury (AKI)
Diuretics
Drug prevention
N-acetyl cysteine
Dopamine

SUMMARY

Acute Kidney injury (AKI) is a relatively common condition in the intensive care unit and is associated with an increase in mortality. Whilst it can be treated by the use of renal replacement therapies an independent increase in mortality still exists. It is therefore seems intuitive that the prevention of AKI should be associated with a reduction in both mortality and morbidity and an improvement in patient care for this reason there has been many attempts to develop strategies to reduce the incidence of AKI. These strategies involve the use of therapeutic agents to prevent renal failure, the avoidance of nephrotoxic agents and the maintenance of normal hydration and renal perfusion. More recently there has been focus on the early recognition of patients at risk of developing AKI and focussing care to avoid exacerbation of risk factors.

1. Introduction

Acute Kidney Injury (AKI) is a relatively common condition in the intensive care unit (ICU) and is associated with an increased risk of mortality despite the ability to support the functions of the kidneys by means of renal replacement therapy (RRT). Studies looking at mortality in patients in intensive care have demonstrated 60% mortality.[1] The recent National Confidential Enquiry into Patient Outcomes and Deaths (NCEPOD) has highlighted the problem of AKI in the UK associated with acute hospital admissions and reported that only 50% of patients received what could be classed as good care. The report claims that a fifth of patients could have been prevented from developing AKI.[2] Acute kidney injury is more likely to occur in certain groups which include the elderly and those with pre-existing medical conditions such as hypertension and diabetes. However many of these patients have risks which can be modified to prevent injury to the kidney.

Within the ICU it has been demonstrated that AKI is an independent risk factor for mortality, which contrasts with the previously held view that patients die with rather than because of AKI. This view may be due to the relative ease with which RRT can now be provided, although the NCEPOD report demonstrated that some patients with AKI never received RRT. A clear correlation between the degree of AKI and worse patient outcomes (length of stay and mortality) in ICU has been demonstrated (Table 1).[3] It is therefore intuitive that the prevention of AKI should be associated with a reduction in both mortality and morbidity and an improvement in patient care.

Until recently there was no standard definition of what constituted acute kidney injury (AKI), which has limited the general applicability of clinical trials aimed at looking at prevention and treatment of the disease. Recently two very similar definitions and staging systems for AKI have been proposed by the Acute Dialysis Quality Initiative group (ADQI) and the Acute Kidney Injury Network (AKIN).[4] The application of these staging systems should provide a better basis for studies which aim to investigate the prevention of AKI in patients. It is important to recognize that the prevention of any insult to the kidney is important particularly in vulnerable patients on the ICU.

Acute kidney injury can be due to pre-renal, intrinsic renal and post-renal causes and methods to minimise kidney damage can be aimed at these three areas. The cause of kidney injury in critical care is often multi-factorial secondary to ischaemia and sepsis causing hypo-perfusion of the kidneys and acute tubular necrosis (ATN). However patients with sepsis can develop AKI without any other obvious cause and animal studies of AKI secondary to sepsis alone have suggested that hypo-perfusion of the kidney does not always occur.[5] It is well recognised that histopathological examination of the kidney in patients with AKI does not always demonstrate frank proximal tubule cell necrosis.[6] It has been suggested that sublethal cell injury occurs and contributes to proximal tubule cell dysfunction in the absence of obvious cell necrosis.

2. Prevention of acute kidney injury

The cornerstones of preventing AKI are the maintenance of an adequate circulating volume, an adequate perfusion pressure and the avoidance of further insults to the kidney. It has long been

* Tel.: +44 113 206 5789.
E-mail address: stuart.murdoch@leedsth.nhs.uk

0953-7112/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.cacc.2009.10.011

Table 1
The incidence of acute kidney injury on the intensive care unit and its effect on length of stay and mortality.

	No AKI	Risk	Injury	Failure
Incidence %	65.6	19.1	3.8	12.5
Age	60.5	62.1	60.4	61.1
ICU mortality	10.7	20.1	25.9	49.6
Hospital mortality	16.9	29.9	35.8	57.9
ICU length of stay	2	5	8	9

known that if renal blood flow falls below a given level glomerular filtration rate will fall and this can clearly be linked to the development of AKI from the RIFLE criteria. This should be achieved by adequate fluid resuscitation and then the use of inotropes or vasopressors.

The surviving sepsis guidelines[7] suggest that fluid therapy should be to a central venous pressure (CVP) greater than or equal to 8 mmHg in non-ventilated patients or 12 mmHg in ventilated patients and the administration of fluid boluses until no further hemodynamic response is seen. It is beyond the scope of this article to discuss the end target of fluid resuscitation, but fluid should be administered to ensure adequate volume expansion of the patient without causing harm. There is considerable debate about the benefits and harm of various fluids, but there is no good evidence comparing fluid types for the prevention of AKI. Fluid therapy can however be pre-emptive, studies have shown that the administration of fluid to patients prior to exposure to contrast media results in a reduced rise in serum creatinine.[8]

The ideal blood pressure to aim for in the prevention of AKI is unclear; the surviving sepsis guidelines suggest a mean arterial pressure (MAP) of 65 mmHg. This may seem low for patients who are normally hypertensive who may expect to need a higher drive pressure, in this situation it may be prudent to aim for a higher pressure and see its effect on kidney function. The evidence to support the use of vasopressors to prevent kidney injury is relatively sparse and generally consists of single centre studies in small numbers of patients. The evidence suggests that norepinephrine is safe to use and is more effective than high dose dopamine in restoring blood pressure and improving urine output.[9,10]

The aim of vasopressor therapy is to improve the perfusion pressure to the kidney, in general the resistance to flow from the venous pressure can be ignored. However in situations of raised intra-abdominal pressure the resistance to flow can be such that renal perfusion is impeded and AKI occurs.[11] Early recognition and subsequent treatment of raised intra-abdominal pressure is essential to restore kidney function.

The release of myoglobin from damaged muscle can result in rhabdomyolysis, which in turn can result in AKI. Rhabdomyolysis was first described in patients who had suffered crush injuries but is now recognised to have other aetiologies including drugs, exercise, infections and ingestion of toxins. The mechanism of AKI in rhabdomyolysis is unclear but may be due to the crystallisation of myoglobin crystals in the renal tubule causing obstruction. It has been demonstrated that early fluid therapy in patients who have suffered a crush injury improves outcome.[12] Prevention of AKI in the high-risk patient consists of volume expansion and the maintenance of a urine output, alkalinisation of the urine is often advocated as a way to prevent the myoglobin crystallising.

3. Nephrotoxic drugs

Acute kidney injury can be caused by a wide range of drugs, the avoidance of these drugs, where clinically appropriate or the alteration of their dosage can reduce the incidence of AKI. Some drugs which are nephrotoxic should be avoided in patients with or at risk of AKI. This is most important for non-steroidal anti-inflammatory drugs which in an unwell hypovoleamic patient play a significant role in causing hypo-perfusion of the kidney. Angiotensin converting enzyme (ACE) inhibitors should also be used with caution in patients at risk of AKI.

3.1. Aminoglycosides

These drugs are excreted by glomerular filtration and it appears that peak levels of the drugs correlate with toxicity. Studies have suggested that aminoglycosides are a common cause of AKI, this toxicity can be avoided by the choice of another appropriate antibiotic. Indeed the need for these drugs for certain infections has been questioned, but with emerging antibiotic resistance and concerns about vulnerability to other infections as a result of antibiotic treatment aminoglycosides may be used more widely than previously. It has been suggested that alteration in the dosing regimen of these drugs from divided doses throughout the day to once daily dosing is as efficacious and possibly less nephrotoxic.[13] Once daily regimens tend to rely on nomo-grams which take into account body weight, renal function and existing aminoglycoside level.

3.2. Amphotericin B

Conventional treatment with Amphotericin B results in AKI in over a quarter of patients, with the risk increasing with cumulative dose given. Kidney injury results from constriction of the afferent arterioles leading to a drop in renal blood flow and glomerular filtration rate, which can occur after a single dose of amphotericin. Strategies exist that administer fluid to the patient both prior to and after administration of amphotericin, which may act to increase GFR but have not been tested in a randomised controlled trial (RCT). Despite the significant renal toxicity of amphotericin, its effective nature against fungi have made it, until recently, the main stay of treatment. This toxicity led to the development of lipid carriers for the drug which are effective in preventing toxicity as they result in lower renal concentrations and are concentrated in reticuloendothelial tissues such as the liver and spleen. It has been demonstrated that these preparations of amphotericin are less nephrotoxic than conventional amphotericin.[14,15] The introduction of newer antifungal agents and reductions in the cost of liposomal amphotericin B, has opened up new strategies to treat fungal infections and at the same time prevent AKI.

4. Radio-contrast induced nephropathy

This is a common cause of AKI in hospital,[16] its mechanism is unclear but appears to due to a combination of direct renal tubular epithelial cell toxicity and renal medullary ischaemia. A transient decrease in glomerular filtration rate occurs in almost all patients after exposure to contrast media. The degree of injury depends upon the presence of patient risk factors which include; diabetes mellitus, pre-existing renal disease, other drugs being taken, hypovolaemia and factors related solely to the radiographic contrast. In patients with normal renal function and no other risk factors the injury is rarely significant. In many patients the degree of AKI is relatively minor. However the studies that have been reported are predominantly before the introduction of the RIFLE criteria. One of the unique factors about radio-contrast induced nephropathy is that the timing of the insult is usually known and pre-emptive action can be taken to reduce the nephrotoxicity. It is also possible to recruit relatively large numbers of patients to studies making the results potentially more powerful.