CONTRAST INDUCED NEPHROPATHY AND ITS PREVENTION

Narayan Prasad and Amit Gupta

Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow,U.P.-226014, India

Abstract: Contrast medium-induced nephropathy (CIN) is an impairment of renal function occurring within 3 days following the intravascular administration of contrast media (CM), in the absence of an alternative etiology. A widely used marker for the occurrence of CIN is an increase in serum creatinine by >25% or 0.5 mg/100 ml (44 *m*mol/l) within 48–72 h of contrast administration .The serum creatinine concentration typically peaks on the second or third day after exposure to CM and usually returns to the baseline value within 2 weeks. The assessment of risk factors including dehydration, heart failure, age greater than 70 years, and concurrent use of nephrotoxic drugs, along with measurement of serum creatinine levels in those at risk for impaired kidney function is mandatory. In the presence of risk factors, consideration of alternative imaging techniques, discontinuation of nephrotoxic drugs, and use of low-osmolar or iso-osmolar contrast mediums in reduced doses are recommended. Maintaining adequate hydration and administration of acetylcysteine or other potential prophylactic therapies may be of help in some of these patients.

INCIDENCE AND PREVALENCE

The nephrotoxicity of the radio contrast agent was first described in the 1960s [1]. Since then the incidence of contrast medium induced nephropathy (CIN) has increased with increasing use of contrast agent in patients who are sicker, older, and have other co morbidities like diabetes, renal failure, cardiac failure, and volume depletion [2]. CIN is the third most important cause of hospital acquired ARF and accounts for approximately 11% cases [3]. The prevalence of CIN ranges from 1 to 45% and depends largely upon the comorbidities of the study population and the parameters used to define CIN [4]. CIN occurs in approximately 13% of non-diabetics and 20 % of diabetics who undergo contrast procedure [5]. Only 0.5 to 2 % of patients who develop CIN will receive dialysis. The need of dialysis heralds a poor prognosis, 36% in hospital mortality and a 2 year survival of only 19 % [5].

DEFINITON

Contrast medium-induced nephropathy (CIN) is defined as an impairment of renal function occurring within 3 days following the intravascular administration of contrast media (CM), in the absence of an alternative etiology [2,6]. A widely used marker for the occurrence of CIN is an increase in serum creatinine by >25% or 0.5 mg/dl within 48–72 hours of contrast administration [7–10]. The serum creatinine concentration typically peaks on the second or third day after exposure to CM and usually returns to the baseline value within 2 weeks [11, 12]. Generally, CIN follows a benign course and only rarely necessitates dialysis. Nevertheless, use of CM has been associated with increased in-hospital morbidity, mortality, cost of medical care and long admissions, especially in patients requiring dialysis.

RISK FACTORS

The risk factors for CIN are listed in table 1. However, it is uncertain to what extent these factors independently worsen renal function, as opposed to serving as markers for coexisting conditions. Diabetes is an important risk factor for deterioration in renal function after angiography [5,13,14] Other factors variably associated with increased rates of acute renal failure after the administration of contrast medium include age over 75 years, periprocedural volume depletion, heart failure, cirrhosis, renal disease (or dysfunction), hypertension, proteinuria, concomitant use of nonsteroidal anti-inflammatory drugs, and intra-arterial injection. In the setting of acute myocardial infarction or percutaneous coronary intervention, hypotension or use of an aortic balloon pump has been associated with a higher rate of acute renal failure after exposure to a contrast medium [13, 14]. High doses of contrast medium also increases the likelihood of renal dysfunction. The tolerable dose of contrast medium depends on the kidney function [5, 15, 16].

Correspondence: **Prof. Amit Gupta**

Table 1 : *Risk factors (5, 13-18) for contrast induced nephropathy*

Non-modifiable risk factors

1. Older age
2. Diabetes mellitus
3. Pre existing renal failure (Estimated GFR of up to 60 ml /min/1.73 m2)
4. Advance congestive heart failure
5. Low left ventricular ejection fraction
6. Acute myocardial infarction
7. Cardiogenic shock
8. Renal transplant

Modifiable risk factors

1. Volume of contrast media
2. Hypotension
3. Anemia and blood loss
4. Pre or post procedural volume depletion
5. Low serum albumin level(<35g/dl)
6. ACE inhibitors
7. Diuretics
8. Non steroidal anti inflammatory drugs
9. Nephrotoxic antibiotics
10. History of structural kidney disease or damage
11. Intra – aortic balloon pump
12. Cholesterol emboli syndrome

PATHOPHYSIOLOGY

The Pathophysiology of CIN is still controversial despite the advances and research related to nephrotoxicity of contrast agents. The mechanisms are probably multifactorial. The important factors in the pathophysiology of CIN are the reduction in renal perfusion by contrast media (CM) combined with the toxic effects on the tubular cells. In vitro studies and studies in animals suggest a combination of toxic injury to the renal tubules and ischemic injury partly mediated by reactive oxygen species [19, 20]. Low blood flow in the medulla, which has a high demand for oxygen, might result from increased perivascular hydrostatic pressure, high viscosity, or changes in vasoactive substances such as endothelin, nitric oxide, and adenosine [21,22]. Factors impairing medullary vasodilation, such as nonsteroidal anti-inflammatory drugs, may worsen contrast-medium–induced nephropathy. The pathophysiological mechanism of CIN depends on the following factors.

ANATOMICAL FACTORS

The most vulnerable region is the deeper portion of the outer medulla. The relatively high oxygen requirements due to ATP dependent activity of NaK ATPase pump and saltreabsorption, offer an explanation for the vulnerability. Kidney perfusion is very high for the cortex, but the medullary portions are maintained on the verge of hypoxia where pO2 levels can be as low as 20mmHg [23]. This is a deleterious result for upholding the countercurrent mechanism for controlling urine concentration. Contrast media by increasing vascular resistance intensifies hypoxic injury in this region [24]. The thick ascending limbs of the loop of Henle exhibit further hypoxic damage, when the kidney is perfused with erythrocyte-free medium [25].

ADVERSE EFFECTS OF DIFFERENT CM CLASSES

The physiochemical properties of contrast agents are different. They are classified according to their osmolality and ionicity. High osmolar CM have osmolalities approximately six times higher than plasma, low osmolar CM have osmolality twice as high as plasma and iso osmolar has osmolality almost similar to plasma. It has become clear that many of the side effects were caused by the electric charge. Today it seems that this physicochemical subdivision may actually require reconsideration: iso-osmolar CMs are dimers, and consequently have greater viscosities than the monomeric low osmolar CMs. This can have important implications for renal medullary perfusion and oxygenation [26]. Iothalamate, a high osmolar agent, strikingly reduces medullary pO2 to about a third of control levels [27]. Remarkably, the iso-osmolar CM *iotrolan* impairs local pO2 to a greater extent than the low osmolar CM *iopromide* [27]. The decrease in pO2 by the CM iopromide failed to reach statistical significance. It has also been shown that the iso-osmolar CM, *iodixanol*, reduces blood flow to all regions of the kidney to a greater extent than low osmolar and even high osmolar CM [26]. Although this decrease in perfusion was more likely to be due to the profound systemic effects of iodixanol considerable fall in blood pressure**.** Studies have shown that iso-osmolar CM has adverse effects in terms of renal tissue oxygenation, when compared with low osmolar CM [27,28]. Thus, experimental and animal studies suggest greater nephrotoxicity of iso osmolar contrast compared to low osmolar contrast. The lower nephrotoxicity of low osmolar contrast may be due to lesser viscosity than iso osmolar contrast [28].However, a few clinical trials have shown beneficial effect of low osmolar contrast over high osmolar contrast agents [29] and iso osmolar contrast agents over low osmolar contrast agents [6,30]. In contradistinction, other trials have revealed no significant differences between iso and low-osmolar agents in the rates of renal failure requiring intervention or prolonging hospitalization [31] and mean change in serum creatinine [32]. More data are needed to confirm the superiority of one contrast agents over others.

CM AND TUBULOGLOMERULAR FEEDBACK (TGF)

CM cause diuresis and activates TGF, which is a key regulator of kidney hemodynamics. Activation of TGF causes vasoconstriction of the glomerular afferent arterioles, and results in a decrease in the glomerular filtration rate (GFR) and an increase in renal vascular resistance. TGF may be responsible for almost 50% of the increase in renal vascular resistance induced by high osmolar ionic CMs. High osmolar CMs are thought to have a greater effect on TGF [33].
However, experimental studies [34,35] with retrograde perfusions of the tubule have already shown that osmolality has no effect on TGF. With orthograde perfusion, quite a lot of transport occurs between tubular fluid and interstitium, and even non-ionic fluids occasionally may be able to elicit the TGF response. Further experiments using mannitol, an osmotic diuretic, do not support that the osmotic diuresis theory. Increases in osmolality, such as after mannitol infusion or after CM application, decreases NaCl concentration at the macula densa. However, this increase in osmolality also simultaneously increases tubular flow. Therefore, the resulting net change in the amount of NaCl passing the macula densa is negligible [36]. Finally, blocking the TGF by furosemide does not decrease serum creatinine after administration of CM, which is usually the parameter taken to indicate CIN [2]. Consequently, combining these factors, the theory that the osmolality of a CM causes CIN via the TGF does not appear likely.

ATHEROEMBOLISATION

In addition two other factors involved in the pathophysiology of CIN are micro showers of atheroemboli and atheroemboli induced intrarenal vasoconstriction.

CLINICAL FEATURES

CIN usually manifests as non-oliguric acute renal failure. Patients who have mild renal dysfunction or normal renal function before receiving contrast agents usually have oliguria that lasts for 2-5 days, with recovery to baseline function by day 7. Dialysis requirement is infrequent [7, 8]. Some degree of residual renal impairment has been reported in as many as 30% of those who are affected by CIN [8]. The occurrence of CIN and other co morbid factors like hypotension, sepsis, cardiac disease, atheroembolic disease and use of nephrotoxic medications may contribute to CIN in ICU settings and prolong hospital stay [37] and mortality. Levy et al [38] have shown a significantly high mortality in 34% in hospitalized patients compared to 7% in control group ($p<0.001$,odds ratio 5.5). even when severity of co morbid illness was controlled by matching patients by acute physiological and chronic health evaluation scoring. Contrast agents may precipitate *metformin induced lactic acidosis* when CIN occurs specially in patients with impaired renal function [39].

DIAGNOSIS

CIN usually develops within 24 to 72 hours following a radiocontrast study. Oliguria is a rare manifestation. The oliguric CIN is characterized by low fractional excretion of sodium during the initial stage , despite no clinical evidence of volume depletion [39]. The urine analysis reveals renal tubular epithelial cells casts, coarsely granular brown casts, but occasionally may be negative [41-42]. Radio contrast agents may alter urinary sediments even before the rise in serum creatinine. A persistent nephrogram 24 to 48 hours after the contrast study was reported to be sensitive marker of presence of ARF. The positive nephrogram is seen in 83% of patients who develop renal failure while 93 % of patients who do not develop CIN lack its specificity for diagnosis [43]. Recently, it has been shown that urinary liver type fatty acid binding protein (L-FABP) level can serve clinically as a *predictive marker* for contrast medium-induced nephropathy [44].

PREVENTION

There is no definite treatment of CIN. CIN preventive strategies should be used in patients who have evidence of chronic kidney disease (CKD). The preventive strategies include risk evaluation and preventive steps.
The basic concepts in prevention of CIN are *hydration, choice and quantity of contrast*, pre, para and post procedural *end organ protection* with pharmacotherapy and post procedural monitoring and care.

RISK EVALUATION

The risk of a decline in kidney function after the administration of contrast medium rises exponentially with the number of risk factors present [45-47]. Validated risk-prediction models have been developed for patients undergoing percutaneous coronary intervention (Table 2) [14,17]. Most risk factors can be detected by history taking and physical examination.

It is not necessary to measure the serum creatinine levels of every patient before exposure to a contrast medium, but measurements should be made before intraarterial use of the medium and in patients with a history of kidney disease, proteinuria, kidney surgery, diabetes, hypertension, or gout [48]. The creatinine clearance rate or the glomerular filtration rate should be estimated from the serum creatinine level, according to either the Cockcroft–Gault [49] or the Modification of Diet in Renal Disease [50] formula to identify more accurately patients with values below 50 ml per minute per 1.73 m^2, who are at increased risk for nephropathy [45].

Alternative imaging methods not requiring contrast medium should be considered for use in patients with any risk factors. Serum creatinine levels should be measured 24 to 48 hours after administration of the contrast medium. Because of the risk of lactic acidosis when contrast-medium–induced nephropathy occurs in a patient with diabetes who is receiving metformin, it is prudent to withhold this agent until the glomerular filtration rate is greater than

Table 2: *Predicting the risk of acute renal failure after per cutaneous coronary intervention*

Risk factors	Score	
Hypotension Systolic blood pressure <90 mmHg>1 hour or patients need ionotropic support, intra aortic balloon pump within 24 hr of procedure	5	
Use of Intra-aortic balloon pump	5	
Heart failure class III or IV, or history of pulmonary edema	5	
Age >75 yrs	4	
Hematocrit<39 for men or <36 for women	3	
Diabetes	3	
Volume of contrast	1 for each 100 cc	
Serum creatinine >1.5 mg/dl or GFR<60ml/min/1.73m2	42=40-<604=20-396=,<20	
Total score	Risk of CIN	Risk of Dialysis
≤5	7.5 %	0.04%
6-10	14 %	0.12%
11-15	26.1 %	1.09%
≥16	57.3 %	12.6%

40 ml per minute per 1.73 m^2 and for the 48 hours before exposure of the patient to the contrast medium [51]. In general, the expected rate of CIN is 30 to 40 % and need of dialysis dialysis occurs in 2 to 8 % in patients who have a GFR of 30 ml/min/1.73m2 [52].

PREVENTIVE STEPS

Protocols for Administration of Fluids

The majority of studies have recommended administration of fluids as first line therapy to reduce the risk of contrast-medium induced nephropathy. However, the optimal regimes for fluid administration remain unknown.

Trivedi et al have shown that serum creatinine levels increases by more than 0.5 mg per deciliter in 34.6 % patients given water orally as compared to 3.7% given intravenous saline for 24 hours beginning 12 hours before administration of the contrast medium [53]. Another study comparing the use of intravenous fluids for 12 hours before and after the procedure with oral fluids plus a single intravenous bolus of fluid showed a lesser mean decline in the glomerular filtration rate 18.3 compared to 34.6 ml/ min/1.73 m^2 at 48 hours, in the group receiving intravenous fluids after administration of the contrast medium [54]. However, this finding was not confirmed in the other trial [55].

Mueller et al have compared isotonic saline with 0.45 percent saline, and found that CIN was less likely in patients who were given isotonic saline (0.7 %) compared to 2% in 0.45% normal saline group (p=0.04) [56]. The fluid was given at 1 ml per kg/hr for 24 hours starting in the morning of the procedure involving the contrast medium.

Alkalinization of Urine:

Studies have shown that infusion of sodium bicarbonate has a beneficial effect in prevention of CIN. Alkalinization of tubular fluid causes reduction in the levels of pH-dependent free radicals and decreases the extent of injury. Merten et al [57] have shown that, CIN was less likely within two days after the administration of contrast medium in patients who were given an infusion of isotonic sodium bicarbonate than in those given a saline infusion.

In conclusion , it is reasonable to start volume supplementation with intravenous normal saline or sodium bicarbonate solution 3 to 12 hours before procedure at a rate of 1-2 ml/kg/hour [2,56,58]. A urine output of 150ml/h should be the target of hydration after procedure. When adequate urine flow rates were achieved in clinical trial setting, there was a 50% reduction in rate of observed CIN [58].

N-*acetylcysteine (NAC)*

More data is needed before *N*-acetylcysteine can be strongly recommended for the prevention of contrast-medium induced nephropathy. Recent meta-analyses [59-62] suggest some benefit to *N*-acetylcysteine (pooled odds ratio, 0.54 to 0.73).

N-acetylcysteine reduces the nephrotoxicity of CMs through its antioxidant and vasodilatory effects [63]. Tepel et al studied that CIN occurs in 2 percent of patients of *N*-acetylcysteine group as compared to 21 percent of patients in the control group (P<0.01) [64]. However, the event rate in the control group was unexpectedly high for patients who received low-dose intravenous low-osmolality contrast medium in this study. In the Rapid Protocol for the Prevention of contrast Induced renal Dysfunction (RAPPID) trial [65], CIN occurred in 5% in patients with NAC plus hydration compared to 21% in patients who had only hydration. Brigouri et al [66] in study of two dosage regime of NAC 600mg versus 1200mg, have shown less incidence of CIN 3.5% in 1200 mg regime compared to 11% in patients with 600mg regime. It was also observed that benefit of double dose NAC was greater in patients who have received a volume of at least 140 ml of radicontrast (5.4% versus 18.9%,p=0.039) than in those who had less than 140 ml of contrast. This study supports the hypothesis of dose dependent protective effect of CIN. For the most part, subsequent trials have involved patients with reduced kidney function who underwent coronary angiography. Some have shown a benefit and others have shown a lack of effect; many are limited by low power and a lack of blinding [59-62]. However, this estimate must be interpreted with caution, given the heterogeneous results of the individual trials, the possibility of publication bias, and the under representation of small negative studies. Also, the effect of *N*-acetylcysteine on outcomes other than minor changes in serum creatinine levels is unknown. However, another metaanalysis of group data of both blinded and non-blinded randomized trials, the overall risk ration was 0.41(95% confidence interval 0.22-0.79;p=0.007) on random effects model. Kshirsagar et al [59] have not supported the routine use of NAC for prevention of CIN in their review since they feel that the beneficial effect of NAC may be because of chance variation.

Theophylline

Theophylline and aminophylline have also been proposed as agents that may reduce the risk of contrast-medium induced nephropathy. In a study from authors center, theophylline has shown beneficial effect on prevention of CIN [67]. A recent meta-analysis found that the mean rise in serum creatinine levels was significantly lower (by 0.17 mg per deciliter [15 µmol per liter]) at 48 hours after administration of the contrast medium among patients receiving either of these medications than among those receiving placebo [68]. However, the clinical importance of this finding is questionable. Since, there was heterogeneity among studies with regard to changes in serum creatinine levels. Overall, no prophylactic agent has been shown conclusively to prevent clinically important contrast-medium induced nephropathy.

Other Approaches to Prophylaxis

Several other interventions have been proposed to reduce the risk of contrast-medium induced nephropathy with limited data support. *Forced diuresis* with furosemide, mannitol, dopamine, or a combination of these given at the time of exposure to the contrast medium has been associated with similar or higher rates of contrast-medium induced nephropathy when compared with prophylactic fluids alone [2,58-70]. Deleterious effects may be explained by negative fluid balance in some instances.

In general, small randomized trials, have failed to show the beneficial effect of the use of various *vasodilators*, including dopamine, fenoldopam, atrial natriuretic peptides, calcium blockers, prostaglandin E_1, or a nonselective endothelin-receptor antagonist, in reducing the risk of contrast-medium–induced nephropathy in comparison to fluid therapy [70-75]. A small randomized trial [76] showed a lower frequency of an increase of more than 0.5 mg per deciliter in serum creatinine levels in patients given captopril for three days as compared with those given placebo, but confirmatory trials are required.

In another small trial, serum creatinine levels were significantly less likely to increase (by >25 percent or >0.5 mg per deciliter) within two to five days of administration of the contrast medium in patients who received ascorbic acid as an antioxidant than in those who received placebo [77]. The baseline serum creatinine level was lower in the placebo group, and both groups reached a similar level after exposure to the contrast medium.

HEMODIALYSIS OR HEMOFILTRATION

The role of hemodialysis in patients at high risk for contrast-medium induced nephropathy remains uncertain. Vogt et al [78] evaluated prophylactic hemodialysis soon after the contrast procedure and continued for 3 hrs with the aim to remove contrast medium effectively through dialysis. However, this strategy did not show any significant benefit as compared to normal saline alone. Patients who were treated with hemodialysis were more likely to have a decline in renal function and further need of hemodialysis.

Among patients with advanced kidney disease (mean creatinine clearance, 26 ml per minute), an increase in serum creatinine levels of at least 25 percent was significantly less common in patients randomly assigned to prophylactic hemofiltration before and after the administration of contrast medium than in those assigned to receive fluid alone (5 percent vs. 50 percent, P<0.001) [79]. In-hospital death was also significantly less frequent in the hemofiltration group [80]. However, the serum creatinine level is directly altered by the intervention, and the relationship between the intervention and the reduced mortality rate is unclear. Thus, the results require confirmation. Given the resources to deliver the intervention, this approach would apply only to the most ill.

PERITONEAL DIALYSIS

Intermittent automated peritoneal dialysis removes 43-72% of contrast volume over 16-18 hour. Continuous ambulatory peritoneal dialysis has also been shown to remove 54% (range 36-80%) of administered dose of contrast medium in patients with end stage renal failure [81,82].

CHOICE OF CONTRAST MEDIUMS

Iodinated contrast mediums can be classified by osmolality (e.g., high-osmolar contrast mediums, such as sodium diatrizoate; low-osmolar mediums, such as iohexol; and iso-osmolar mediums, such as iodixanol). In a meta-analysis of comparative trials, an increase in serum creatinine levels of more than 0.50 mg per deciliter after administration of the contrast medium in patients with reduced kidney function was less frequent with low-osmolar than with high-osmolar mediums (odds ratio, 0.50; 95 percent confidence interval, 0.36 to 0.68) [83]. Because of the small number of events, no conclusion could be reached about the effects of osmolality on the need for dialysis.

Iso-osmolar contrast mediums have been proposed as an alternative. One randomized trial involving patients with diabetes who have renal impairment showed a significantly lower frequency of increases in creatinine levels of at least 0.5 mg per deciliter with the iso-osmolar agent iodixanol, than with a low-osmolar agent [6]. However, the rate of renal deterioration in the group receiving a low-osmolar contrast medium was higher than expected. Similarly, in an open-label trial, a maximal increase in serum creatinine levels of greater than 25 percent within a week after the administration of contrast medium was less common with iodixanol than with iohexol (3.7 percent vs. 10 percent), but a lack of consistent timing for measuring creatinine levels in the two groups may have biased the results [30]. In contrast, other trials have revealed no significant differences between iodixanol and low-osmolar agents in the rates of renal failure requiring intervention or prolonging hospitalization [31] or in mean changes in creatinine levels

Table 3: *Recommendations of interventions commonly used to reduce the risk of Contrast medium induced nephropathy*

Intervention	
Intravenous saline therapy	Rate 0.9% normal saline at 1ml/kg/hr, beginning 2-12 hr before administration of contrast medium
Contrast medium of choice	• Low or Iso osmolar contrast agents • Evidences support lower nephrotoxicity of low and Iso-osmolar contrast media over high osmolar contrast media. Further data are needed to show relative nephrotoxicity of iso osmolar contrast agents over low osmolar contrast agents. Experimetal studies does not support it • Dose; lowest dose is preferred, dose of 5 ml × kg of body weight÷ serum creatinine (mg/dl) is associated with higher risk
Sodium bicarbonate solution	154mmol/l 3ml/kg/hr before administration of contrast agents followed by 1ml/kg/hr for 6 hours after administration. Evidence is based on randomized trial but further data are needed.
N acetyl cysteine	Dose 600 mg BID -4 doses starting before contrast administration. Evidences are based on multiple randomized trials and metanalysis but furher data are needed.

after administration of contrast medium [32]. Further studies are needed before iso-osmolar contrast mediums can be recommended in place of low-osmolar mediums. Experimental studies also did not support the use of iso osmolar contrast as compared to low osmolar contrast agent.

Exceeding a volume of contrast medium of 5 ml per kilogram of body weight divided by the serum creatinine level in milligrams per deciliter strongly predicts nephropathy requiring dialysis [15]. Table 3 summarizes recommendations regarding interventions commonly used to prevent contrast-medium–induced nephropathy.

RECOMMENDATIONS

The risk evaluation should be done in every patient as per suggestion in table 2. The assessment of risk factors including dehydration, heart failure, age greater than 70 years, and concurrent use of nephrotoxic drugs, along with measurement of serum creatinine levels in those at risk for reduced kidney function are mandatory.

In the presence of risk factors, consideration of alternative imaging techniques, discontinuation of nephrotoxic drugs, and use of low-osmolar or iso-osmolar contrast mediums in limited doses are recommended. Maintaining adequate hydration and the administration of additional fluids are also recommended. Multiple infusions of contrast medium within a short period of time and the use of mannitol or diuretics are to be avoided. *N*-acetylcysteine or other potential prophylactic drug therapies may be of help in some of these patients.

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LITERATURE REVIEW

VASCULAR ERECTILE DYSFUNCTION IN CHORNIC RENAL FAILURE

Guido, Vincenzoand Domemico

Semin Nephrol 26:42-45

The prevalence of erectile dysfunction (ED) has increased dramatically worldwide in parallel with the aging of the population. In 1995, ED was estimated to be present in more than 150 million men. Considering population aging in Western Countries, estimates predict that more than 300 million men will be affected by ED by the year 2025. ED is a common and often distressing side effect of renal failure. It is present 30% of patients with chronic renal failure and in 50% of patients undergoing dialysis treatment. Uremic men of different ages report a high variety of sexual problems including sexual hormonal pattern alterations, reduced or loss of libido, infertility, and impotence, thereby influencing their well-being. The release of sildenafil citrate, the relationship between ED and the presence of cardiovascular disease (CVD) has been evaluated in several studies. Many of the risk factors for Ed are the same as those for cardiac disease. CVD and ED are closely interrelated disease processes. Indeed, ED can be considered a symptom of vascular endothelial damage. Therefore, it can be excepted that impotence will appear along with CVD, and the presence of ED suggests the existence of CVD. An accurate evaluation of sexual histories of all men who present to internists, cardiologists, and also nephrologists for early detection of ED may allow for early diagnosis and management of CVD.

LITERATURE REVIEW

Diuretic Use, Residual Renal Function, and Mortality Among Hemodialysis Patients in the Dialysis Outcomes and Practice Pattern Study (DOPPS)

Jennifer L. Bragg-Gresham, Rachel B. Fissell, Nancy A. Mason et.al. *Am J Kidney Dis 49:426-431, 2007.*

The role of diuretics in the management of hemodialysis (HD) patients has not been clearly defined, and guidelines for their use in patients with end-stage renal disease (ESRD) do not exist. Use of diuretics was shown to increase urine volume and sodium and potassium excretion in patients on continuous ambulatory peritoneal dialysis therapy. Management of volume status with may reduce the risk of fluid overload and minimize episodes of hypotension during dialysis. In addition, improved overall fluid balance could slow the development of cardiovascular disease and minimize complications of existing cardiovascular disease. The larger urine volume that accompanies diuretic use in both continuous ambulatory peritoneal dialysis and HD patients may allow for a more liberal fluid intake and perhaps allow for a more liberal diet, thus facilitating improved nutrition.

Diuretic use was investigated in 16,420 hemodialysis patients from the Dialysis Outcomes and Practice Patterns Study, a prospective observation of hemodialysis patients selected from nationally representative facilities on 3 continents. Logistic regressions were used to investigate associations between diuretic use and patient characteristics. Outcomes of interdialytic weight gain ,increased serum potassium and phosphorus levels, and odds of RRF after 1 year were investigated. Cox regression was used to analyze the association between mortality and diuretic use. Facility diuretic use varied substantially from 0% to 83.9% of patients. Diuretic use decreased sharply after the start of dialysis therapy. Loop diuretic use ranged from 9.2% in the united states to 21.3% in Europe. Where use within 90 days of starting dialysis therapy ranged from 25.0% in the United States to 47.6% in Japan. Diuretic use was associated with lower interdialytic weight gain and lower odds of hyperkalemia (potassium>6.0mmol/L). Patients with RRF on diuretic therapy had almost twice the odds of detaining RRF after 1 year in the study versus patients not on diuretic therapy. Patients administered diuretic had a 7% lower all-cause mortality risk (p=0.12) and 14% lower cardiac-specific risk (p=0.03) versus patients not administered diuretics.

Variation exists in facility practices of diuretic use. In patients with RRF, there may be benefit associated with continuing diuretic use rather than automatically discounting diuretic therapy at dialysis initiation.