Does hydration prevent radiocontrast-induced acute renal failure?

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Introduction

A decline of renal function after the administration of contrast media (CM) is a frequent cause of hospital-acquired acute renal failure. This so-called contrast-media-induced nephropathy (CMIN) includes a haemodynamic response to contrast media and tubulotoxicity. Although the clinical features of CMIN have been well described, uncertainties concerning the prophylaxis and clinical relevance of this form of nephrotoxicity persist. The purpose of this article is to review the role of a hydration strategy in the prevention of this condition.

From a theoretical point of view prehydration of patients may have the following beneficial effects on the kidney:

- decreased activity of the renin–angiotensin system,
- downregulation of the tubuloglomerular feedback,
- augmentation of diuresis and sodium excretion,
- dilution of the contrast media and thus prevention of renal cortical vasoconstriction,
- reduced pre-constriction of the vessels,
- avoidance of tubular obstruction, and
- reduction of endothelin and other intrarenal vasoconstrictive mediators (e.g. vasopressin).

Historical background

Approximately 30 years ago several studies documented that dehydration accentuates the risk of renal failure especially in patients with diabetes mellitus or pre-existing renal failure [1]. The incidence was higher in summer at a time when no special hydration was performed and patients had to thirst before excretory urograms in order to maximize the concentration of contrast media in the urinary tract. Sometimes patients were given laxatives before intravenous pyelography, a factor further aggravating dehydration. Observations comparing hydrated patients with a historical population gave the first clues that a fluid load might prevent CMIN [2–4]. So far, no controlled systematic study has been published addressing the question which sort of fluid, how long, how often and how much should be given in order to minimize the risk of CMIN.

Experimental studies

In a rabbit model of CMIN involving low-sodium diet and administration of indomethacin, the infusion of isotonic saline or isotonic mannitol (both given at a rate of 20 ml/h/kg, equal to 4% of the animal’s body weight over a 2-h period) parallel to the infusion of the contrast media was not able to prevent acute renal failure, while pre-treatment of the animal with chronic high sodium intake and DOCA administration did [5]. As plasma renin activity is reduced by administration of DOCA as well as by an acute infusion of saline and mannitol, the authors concluded that apart from lowering of intrarenal renin and plasma renin activity, the increase of urinary sodium and solute excretion per se (and probably the plasma volume expansion) contributed to the prevention of CMIN. These data were confirmed by our own study in rats with high intravascular resistance due to chronic NO inhibition. DOCA pre-treatment completely reversed the haemodynamic response to contrast media [6]. Yoshioka et al. [7] showed that water-deprived rats (72 h) had reduced activities of catalase and superoxide dismutase and were highly sensitive to the application of diatrizoate which caused a significant and persistent fall in GFR 72 h after CM application. After injection of saline water-deprived rats gradually normalized GFR by 72 h.

Clinical studies

Most studies dealing with the issue of hydration in the prevention of CMIN addressed the role of mannitol
or the role of vasodilators such as dopamine, atrial natriuretic peptide, Ca antagonists, or ACE inhibitors with regard to the protection of the kidney from contrast media damage [8–13]. The authors found that hydration alone was as effective or even better than additional administration of hypertonic mannitol or the administration of one of the vasodilative agents. Other investigators compared results in patients submitted to special hydration protocols with historical control groups [2,3] or data reported in the literature [4,14,15] whereby with hydration alone the incidence of acute renal failure was lower. So far only one controlled, randomized study compared saline administration alone (0.45% saline over 24 h, starting 12 h before administration of radiocontrasts) with mannitol (25 g of mannitol given 60 min before administration of radiocontrasts) or frusemide (80 mg i.v.) [8]. In this study administration of saline alone was the most successful strategy. In numerous studies dealing with the nephroprotective effect of non-ionic contrast media prehydration of the patients was included in the protocol [16,17], but patients with cardiac failure, liver cirrhosis or oedema have mostly been excluded from the studies in order to avoid overhydration.

Conclusion

So far no controlled prospective study addressed the issue, which hydration strategy is optimal in order to prevent CMIN. Presently, it seems appropriate to start hydration at least 12 h before administration of contrast media in order to induce volume expansion with concomitant suppression of the renin system. This could be continued for 12–20 h after the procedure. The best route of fluid administration, the amount and the type of fluid have to be clarified. Whether this strategy is safe in patients with heart failure, liver cirrhosis and edema has to be shown in future studies. The use of loop-active diuretics should be avoided as no benefit in preventing CMIN has been proved and hypovolaemia could be enhanced.

References


Which fluid and when to start?

Most investigators administer 0.45% saline in combination with 5% dextrose intravenously in various amounts (around 1000–1500 ml starting 12 h before administration of radiocontrasts). There is no controlled study which assessed oral hydration in these patients. How long hydration should be continued has also not been investigated so far. In accordance with the experimental data good results in humans have been obtained with hydration prior to and up to 12 h after contrast media exposure [2,4,8]. Only a minor beneficial effect could be seen when fluid was administered during the procedure [3,15]. From a theoretical point of view the use of hyperosmolar fluids (such as 15% mannitol) in addition to the administration of the hyperosmolar contrast media may have adverse effects. Therefore it is not surprising that most studies failed to observe a beneficial effect of mannitol in this setting [2,8,9].

Use of diuretics?

No conclusive evidence is available to support a protective role of loop-active diuretics in regard to the prevention of CMIN. From the theoretical point of view it has been claimed that reducing the ‘workload’ of the tubular cells by decreasing the rate of sodium reabsorption might be tubuloprotective. Additionally there might be a dilution effect by an increment of diuresis after frusemide. Most investigators dealing with this point showed no benefit or sometimes even worse results after administration of frusemide [8,18,19]. The adverse effect of frusemide could be due to reduction of cortical resistance causing redistribution of renal blood flow and reduced perfusion of the medulla. In combination with the contrast-media-induced vasoconstriction, partial pressure of oxygen in the medulla could thus be reduced below a critical point. Consequently, if it is used at all, frusemide should be administered with caution, rigorously avoiding dehydration, which, by itself, would definitely enhance the nephrotoxicity of contrast agents.
Vitamin D receptor polymorphisms as a determinant of bone mass and PTH secretion: from facts to controversies

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Introduction

During recent years, powerful molecular biology techniques such as restriction enzymes and positional cloning have been used to identify genetic diseases even before the responsible genes were characterized. However, clinical studies have shown that bone mineral density (BMD) is under genetic control, probably polygenic in origin, and several candidate genes, namely oestrogen and vitamin D receptors (VDR), as well as collagen type I z 1 among others, may mediate important differences in bone mass and bone metabolism. Since the first description by Morrison et al. [1], several groups have shown that genetic polymorphisms at the 3-untranslated region of the VDR gene may account for at least some of the genetic variation in bone mass. These polymorphisms are defined by the presence or absence of a restriction site for the enzymes BsmI, ApaI and TaqI. Since that initial report, VDR gene polymorphisms have been associated with BMD, peak bone density, bone turnover and the serum levels of some biochemical bone markers, as well as the rate of bone loss, risk of osteoporotic fracture and the relative response to several treatments of osteoporosis such as vitamin D or calcium.

VDR polymorphisms in patients without renal failure

According to the most widely analysed BsmI restriction site—B absence, b presence of a cleavage site—several studies have documented that in patients without chronic renal failure (CRF), the presence of two copies of the allele b (genotype bb) is associated with a greater BMD than the heterozygous genotype Bb, whereas the genotype BB is associated with the lowest BMD [1]. Generally speaking, the BBAAtt genotype has usually been related to a lower bone mass. However, there is not general agreement and several reports have failed to confirm such a relationship. A recent meta-analysis provided evidence for an effect of the VDR polymorphisms on BMD, but it was quantitatively modest [2]. It has also been shown that environmental factors may influence the effect of genetically determined BMD. Thus, VDR genetic polymorphisms have been linked to differences in intestinal fractional calcium absorption. As such, individuals with the bbbaTT haplotype showed a higher rate of radio calcium absorption [3]. Conversely, individuals with the BB genotype had a lower efficiency of calcium absorption after dietary calcium restriction and had a lower BMD than those with the bb genotype [4]. This finding would be consistent with the presence of functional differences in the intestinal VDR among different VDR genotypes. However, the mean increase of BMD after treatment with vitamin D was significantly higher in individuals with the BB and Bb genotypes compared with the bb genotype [5]. A more pronounced suppression of PTH concentration by calcitriol has also been described in individuals with the bb genotype. Furthermore, VDR polymorphisms have been associated with urinary calcium excretion, but in this specific study they were not related to BMD [6]. Consequently, VDR polymorphisms seem to represent one of the genetic factors affecting BMD, but they account only partially for the overall genetic effect on bone mass and this effect is not observed in all the screened populations.

VDR polymorphisms in primary and secondary hyperparathyroidism

The VDR genetic polymorphisms have also been linked to the development of primary and secondary hyperparathyroidism...