



RENAL RISK EVALUATION IN CONTRAST MEDIA-INDUCED NEPHROPATHY

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Abstract. Contrast media-induced nephropathy (CIN) in patients receiving intraarterial iodinated contrast media is a chemotoxic adverse reaction that is often under-recognized in clinical practice due to the very low incidence of this morbidity. The renal impairment is usually temporary, but in a small number of patients acute renal failure can develop and dialysis may be necessary. Patients with both diabetes and pre-existing renal impairment are at the highest risk. Practices for identifying patients at risk vary: it may be possible to identify patients who may be at risk using screening questionnaires. The prevalence of CIN correlates with contrast media dose: therefore the amount of CM has to be minimized in all patients, especially in those with higher risk. Non-ionic monomers (low osmolar CM) are beneficial in comparison with ionic monomers (high osmolar CM) in patients with pre-existing renal impairment. Various drugs that have been used in attempts to prevent CIN have provided contradictory results in clinical trials and therefore their effectiveness remains to be proven. Still, adequate hydration pre- and postangiography remains the most efficient preventive therapy.

Keywords: adverse reaction, angiography, nephropathy

Introduction

Iodinated contrast media have been used on large scale since 1950. The first substances were ionic monomers with high osmolarity – 6 to 8 times plasmatic osmolarity – being responsible for a lot of the cases with adverse reactions.

The first non-ionic monomers were introduced during the 70's. They have an Iod: chemical particle ratio of 3 to 1 and that implies a smaller risk for developing any adverse reaction. These substances' osmolarity is approximately two times higher than plasmatic osmolarity, being similar to the next generation of contrast media – the ionic dimers.

During the late 80's the non-ionic dimers are developed, substances with an osmolarity similar to plasmatic values (300 mg/ml) and an Iod: active chemical particle ratio of 6 to 1.

Iodinated contrast media adverse reactions are classified based on the starting mechanism into anaphylactoid and chemotoxic types. The most important adverse reaction of the last category is nephrotoxicity – renal function impairment characterized by an increase in serum creatinine of more than 25% or 0.5 mg/dl (44µmol/l) over baseline.

This definition was adopted in 1999 by the Contrast Media Safety Committee of the European Urogenital Radiology Society. The prevalence reported by different studies varied significantly, from less than 5% in patients without associated morbidity to 50% in patients with very high risk [1]. Basically, the prevalence of CIN is undervaluated mostly because of the frequent lack of monitoring for serum

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creatinine values before and after arteriography. Nevertheless, despite the development during the past years of improved contrast media with very low risk of adverse reactions, CIN remains a very important issue in particular patient groups [2,3] and represents one of the most difficult to treat pathologies [4].

Risk factors

Finding the patients with higher adverse reactions risk is one of the most efficient methods of prevention in CIN. Several independent risk factors contribute to the likelihood of developing CIN linked both to the preexistent pathology and to the interventional radiological procedure. An insufficient renal function is the most important risk factor, determining an over 20-fold increase in CIN development. Until now, various studies were not able to demonstrate a strong correlation between diabetes and CIN but a preexistent nephropathy clearly represents a risk factor. Dehydration, older patients, congestive heart failure or the association with other nephrotoxic substances also increase the risk. On this list, we could include pathologies with insufficiently demonstrated influence such as multiple myeloma, hypertension, hyperuricemia or proteinuria [1,6].

Renal failure, the most important risk factor, presents the first clinical signs in advanced stages. That is why measuring serum creatinine and urea before any angiographic procedure is mandatory. Based on the fact that general population has insignificant predisposition for developing renal function impairment, an efficient classification of patients with preexistent risk factors can be done by measuring creatinine clearance – a much more sensitive analysis compared to measuring creatinine levels [7].

Creatinine clearance can be measured using the formula $[(140 - \text{age}) \times \text{weight}] / [\text{serum creatinine (mg/dl)} \times 72]$; for women, this formula is multiplied by 0,85.

In a study involving 1826 patients who underwent different angiographic procedures, those who had a clearance higher than 47 ml/min did not develop any CIN [2].

Type and volume of employed contrast media

The contrast media related risk factors include dose, osmolarity, previously administered iodinated substances or previous administration method (intraarterial use increases the risk of developing adverse reactions on later investigations).

Using small quantities (less than 100 ml) of low osmolarity contrast media importantly diminishes the risk of developing nephrotoxicity.

An extended analysis, based on 25 previous trials which compared the risk of nephrotoxicity of contrast media with different osmolarities injected to patients with preexistent renal insufficiency, showed that Iohexol (a non-ionic, hypoosmolar monomer) is significantly less nephrotoxic than Datzioat (a hyperosmolar ionic monomer) [5].

Recent studies have established that Iodixanol (an izoosmolar non-ionic dimer) is the substance with the lowest risk of developing CIN, diminishing it up to 9 times compared to hypoosmolar contrast media. CIN incidence consequent to Iohexol injection in patients with multiple risk factors (26%) is much higher than that after Iodixanol injection (3%).

Previous clinical studies weren't able to establish significant result differences between Iodixanol and non-ionic monomers injection [8,9], this conclusion being probably influenced by the small number of patients included.

Iodixanol advantages established through the latest studies favor its use in high risk patients; other studies are clearly necessary in order to confirm these results.

Prophylaxis

So far, the only prophylactic method with certain clear advantages was proper hydration (minimum 2 liters of isotone solution administered in fractions throughout the entire day of contrast media administration) [10].

The standard protocol uses perfusion of 100ml/h started 4 hours before and continued 24 hours after angiography.

Ultrior hemodialysis shows no clear benefits maybe because renal insufficiency tends to develop very rapidly [11].

Several drugs such as diuretics or vasodilators are not only ineffective but have in some cases increased the incidence of CIN [12-16].

Although clinical trials presented contradictory results on its efficiency, in recent years, N-acetylcysteine gained clinicians' attention especially because of small price, higher availability or minimal adverse reactions [17-21].

Conclusions

Although CIN implies prolonged medical surveillance and necessitates hemodialysis, it still continues to be underevaluated in clinical practice. In

order to determine patients at risk and thus avoid such complications, thorough anamnesis is mandatory. Any nephrotoxic drug administration must be stopped and proper hydration must be associated. Injection of minimum quantities of contrast media with good renal profile is best recommended.

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