



Editorial

Prevention of contrast-induced renal dysfunction by N-acetylcysteine

Truth or myth?

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There is an increase in the use of radiographic contrast agents in cardiovascular medicine for diagnostic and therapeutic interventions. However, these interventions are becoming more and more popular in elderly and polymorbid patients, thereby increasing the risk of contrast-induced complications such as renal dysfunction and delayed allergic reactions. A particular risk for renal dysfunction has been attributed to pre-existing renal dysfunction, diabetic nephropathy, dehydration, drug interactions and the use of large amounts of contrast, etc. The reduction in renal function by contrast agents may cause substantial morbidity and mortality and can lead to end-stage renal disease.

In an attempt to reduce contrast-associated morbidity and mortality, several interventions and drugs have been advocated such as hydration with saline, the use of isotonic and non-ionic contrast agents as well as administration of nephroprotective drugs such as theophylline, dobutamine and atrial natriuretic peptides. The largest experience exists, however, with the antioxidant N-acetylcysteine (NAC).

The mechanism of renal dysfunction after exposure to contrast media is not clear, but seems to be an interplay of renal haemodynamics, toxic effects on tubular epithelial cells and enhanced oxidative stress. Therefore, the use of antioxidants such as NAC has been recommended to protect the kidney and to prevent renal dysfunction.

In this issue of the *European Heart Journal* Briguori et al.¹ report on the prophylactic administration of NAC in patients undergoing coronary angiography with a low dose of a non-ionic, low osmolarity contrast medium.

They tested the hypothesis of a protective effect of high dose (2×1200 mg) vs standard dose (2×600 mg) NAC given orally along with saline hydration to prevent contrast-associated nephrotoxicity. Serum creatinine concentrations were similar in the two groups, but there was an increase in creatinine of at least 0.5 mg/dl after angiography in 12 of 109 (11%) patients in the standard dose group and 4 of 114 (3.5%) in the double dose group, respectively ($P=0.04$). Furthermore, the amount of contrast used (larger or smaller than 140 ml) had a significant effect on renal dysfunction, i.e. NAC had no effect on renal function in those with low contrast dose (<140 ml), whereas in those with high dose (>140 ml) NAC significantly reduced renal dysfunction from 18.9% to 5.4% ($P=0.04$). The authors concluded that the use of double dose of NAC seems to be more protective in preventing contrast-induced renal dysfunction especially in patients with high doses of contrast medium.

In the second paper of this issue of the *European Heart Journal*, Goldenberg et al.² examined the effect of NAC in prevention of contrast-induced renal dysfunction. In this study somewhat higher doses of NAC than standard dose were given (3×600 mg). Both groups received hydration with saline (1 ml/kg/h over 24 h). An increase of more than 0.5 mg/dl in serum creatinine after angiography was observed in 10% of the NAC and in 8% of the control group, respectively ($n=ns$). The authors concluded that prophylactic administration of oral NAC to prevent contrast-associated nephrotoxicity in patients with renal insufficiency undergoing coronary angiography is not justified.

These two contradictory studies have to be seen in the light of the complex interplay of pharmacology and contrast toxicity. Apparently, Briguori et al. make the point that beside the adjunctive therapy with saline the amount of contrast (>140) and the dose of the antioxidative NAC play an important role for nephroprotection,

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whereas Goldenberg et al. state that the effect of NAC in patients with mild to moderate renal insufficiency is of limited value and benefits may be observed only when appropriate hydration is not possible.

Apart from other studies without saline infusion^{3,4} most reports⁵⁻⁸ in patients undergoing cardiac catheterization have shown no beneficial effect of NAC as adjunctive therapy to saline infusion. Beneficial effects of NAC as adjunctive therapy to saline have been reported only by two other studies namely Briguori and Shyu.^{1,9} Shyu et al. reported a protective effect of NAC in patients with high serum creatinine levels (mean 2.8 mg/dl). Assuming the observation of Briguori and Shyu are correct following recommendations for preventing renal dysfunction in patients undergoing cardiac catheterization can be given:

- Hydration with saline in all patients (1 ml/kg/h 12 h before and 12 h after the intervention)
- Use of a modern non-ionic, low osmolarity contrast agent
- Use of high dose NAC (2×1200 mg) in patients with high creatinine levels (>2.5 mg/d) and large contrast doses (>140 ml)

In conclusion, patients with renal insufficiency undergoing diagnostic and therapeutic angiography are at high risk for developing contrast-induced renal dysfunction. The use of small amounts (<140 ml) of non-ionic, low osmolarity contrast media with appropriate hydration 12 h before and 12 h after the intervention

helps to reduce the risk of renal dysfunction. The addition of the antioxidant NAC (2×1200 mg) may be useful in patients with high serum creatinine levels (>2.5 mg/dl) and the use of high doses of contrast material (>140 ml).

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