Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

MECHANISMS FOR AN EFFECT OF ACETYLCYSTEINE ON RENAL FUNCTION AFTER EXPOSURE TO RADIOGRAPHIC CONTRAST MATERIAL

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Background and Aim
Patients who have had a heart attack commonly undergo a procedure called coronary angiography in which a heart doctor squirts a dye that shows up on x-rays into heart blood vessels to look for blockages. Unfortunately, the dye may injure the patient's kidneys, especially if they are already diseased. Since 2000, a medicine called acetylcysteine ('NAC', long used to prevent liver damage from paracetamol poisoning) has been used to protect kidneys from this injury. However, the evidence that it really benefits patients is weak, in part due to the lack of basic clinical studies to tell us how it works and the best way to give it to patients. In this study, we aimed to identify the effect of NAC tablets and of an injection of a higher dose of NAC on normal & diseased kidneys, with or without contrast dye.

This resulting information could be used to design better trials with which to assess the ability of NAC to protect kidneys during coronary angiography

Project Outline/Methodology
We studied kidney function in volunteers with no kidney disease and patients with moderately severe chronic kidney disease (CKD stage III), after giving them NAC (or not), with or without the contrast dye. Volunteers came to the Clinical Research Ward where they received NAC tablets or a larger dose given by injection, or dummy tablets and injection. In the first three parts of the study, eight volunteers came three times to the ward, each time receiving a different NAC treatment. We then observed the effect on their kidney function by measuring proteins and sugars (called biomarkers) in blood and urine samples collected regularly over 10 hrs, and the next day, and then 2 days later. In the 3rd part of the study, eight volunteers with normal kidneys received these same treatments on different days plus contrast dye to see how NAC might stop the dye causing injury. Finally, in the 4th part, 66 patients with CKDIII undergoing coronary angiography were randomised to receive the NAC injection, tablets or dummy. Each of these patients received only one treatment.

Key Results
In volunteers with healthy kidneys, an injection of NAC (but not the tablets or dummy) increased blood flow to the kidneys. This effect on blood flow was increased further when the patients were given the dye - a positive effect and one that should in theory protect kidneys. Unfortunately, in patients with diseased kidneys - who are most in need of this protection - the injection of NAC did not cause any rise in kidney blood flow. NAC tablets had no effect at all. In patients receiving contrast during coronary angiography, the injection of NAC again did not increase kidney blood flow. In addition, by studying the biomarkers in urine and blood, we were not able to find any evidence of a protective effect on kidneys

Conclusions
High doses of NAC given by injection increase blood flow to kidneys in healthy volunteers. Unfortunately, this protective effect does not occur in patients with moderate kidney damage, a group that might benefit from such an effect of IV NAC. We found no evidence that NAC given by injection or tablets provides any protective benefit to patients with kidney disease.

What does this study add to the field?
This is the first study to look in detail at the effect on kidneys of NAC given by different routes and in different doses. It found that NAC is unlikely to offer any benefit to patients at high risk of injury from the contrast dye.

Implications for Practice or Policy
Dye-induced damage remains a significant problem in the NHS. Until new methods of prevention are identified, the NHS should focus on ensuring patients are not dehydrated before they receive dye and forms of dye that cause relatively little injury are used. The NHS should not commit resources to further testing the role of NAC in this disease.

Where to next?
Effective methods of preventing injury are required

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