26453 - N-ACETYLCYSTEINE FOR REDUCING RENAL INJURY IN CARDIAC SURGERY

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INTRODUCTION: Acute renal failure is an important complication of cardiac surgery that is associated with increased mortality and morbidity. N-acetylcysteine (NAC) may prevent renal insufficiency after cardiac surgery by reducing free-radical-mediated renal injury and improving renal perfusion.

METHODS: Following REB approval, patients who were (1) undergoing aortocoronary-bypass and/or valve surgery under cardiopulmonary bypass (CPB) and (2) had preoperative renal insufficiency (creatinine clearance < 60 mL/min) were recruited into a randomized triple-blinded placebo-controlled single-centre trial. Allocation was concealed through central randomization with drugs prepared by the pharmacy. Following informed consent, participants received either intravenous NAC (100 mg/kg bolus prior to CPB and 20 mg/kg infusion until 4 hours after surgery) or placebo. Participants were followed for 60 days after surgery. The primary outcome in intention-to-treat analyses was the percent 72-hour decline in creatinine clearance following surgery.

RESULTS: Between 2003 and 2005, 177 participants were randomized (88 NAC, 87 placebo). Overall, the participants were at high-risk for perioperative morbidity and mortality (mean Euroscore 5.8). Participants in the NAC arm had poorer preoperative renal function and a higher prevalence of diabetes; in contrast, individuals in the control arm were more likely to have poor ventricular function and undergo complex surgical procedures. No patients were lost to follow-up. There was a non-significant trend ($P = 0.46$) towards slightly improved 72-hour renal function in the NAC arm (Figure). NAC caused a significant reduction in all-cause mortality (0% versus 8%, $P = 0.009$). In addition, it was associated with trends toward reduced dialysis (1% versus 4%, $P = 0.37$), reduced atrial fibrillation (57% versus 67%, $P = 0.21$), and reduced postoperative inotropic requirements (16% versus 22%, $P = 0.31$).

DISCUSSION: This triple-blinded placebo-controlled concealed-allocation randomized trial demonstrated that high-dose NAC is safe in high-risk patients undergoing cardiac surgery. In comparison to a recent trial, this present study employed a higher dose of NAC and recruited higher-risk patients (1). NAC did not cause significant improvements in perioperative renal function in the present study. With regard to secondary outcomes, NAC caused a significant reduction in all-cause mortality and trends towards reduced cardiac morbidity. High-dose NAC should be further evaluated among high-risk patients in a large multi-centre randomized trial.

REFERENCES:

(1) JAMA. 2005 294:342-350.