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N-acetyl cysteine and acute kidney injury after cardiac surgery

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Abstract

Acute kidney injury (AKI) is a very common and important complication of cardiac surgery. It is associated with severe complications including mortality. Cardiac surgery may induce oxidative stress and inflammation and both of these processes may be associated with AKI. N-acetyl cysteine (NAC) is a mucolytic agent and it has antioxidant and anti-inflammatory properties. Although positive results have been obtained in animal studies, however; no significant beneficial effects of NAC on AKI have been found in randomized studies and meta-analyses. Currently available data do not support to recommend NAC for the prevention of AKI after cardiac surgery.

Introduction

Acute kidney injury (AKI), defined as an absolute increase in serum creatinine level of >0.5 mg/dL or relative increase >25% from baseline level, is a very common and important complication of cardiac surgery. It is associated with severe complications including mortality (1).

Cardiac surgery may induce oxidative stress and inflammation and both of these processes may be associated with complications of the procedure including AKI (3-5). Metabolic factors, ischemia, toxins, neurohormonal activation and increased renal vascular resistance occurring secondary to pump, emboli, and low cardiac output syndrome may predispose the patients to have AKI (1, 5).

N-acetyl cysteine (NAC) is a mucolytic agent with antioxidant and anti-inflammatory properties (6). In this review, we focus on the animal and human studies and meta-analyses evaluating the effects of NAC on AKI.

Animal studies: N-acetyl cysteine decreased kidney injury after cardiopulmonary by-pass (7, 8) and renal ischemia-reperfusion injury (9, 10) in animal models.

In a rat model, it was shown that combination of NAC and spironolactone improved renal function more as compared with NAC alone (11). Similarly, in a dog model combination of NAC, sodium nitroprusside, a nitric oxide donor and phosphormidon, an endothelin-1 converting enzyme inhibitor, attenuated renal ischemia-reperfusion injury (12).

Human studies: NAC decreased MDA levels in patients undergoing hemodialysis , ameliorated ischemic renal failure and enhanced early outcomes of deceased donor renal transplantation by attenuating oxidative stress (13,8,14).

Barr et al. have shown that the change in creatinine clearance from preoperative to postoperative day 3 was significantly less for single use of NAC or fenoldopam, which is stimulator of the DA-1 dopamine receptor that increases the renal blood flow, but there was a trend for their combination compared with control group in patients with chronic kidney disease undergoing cardiac surgery (5).

Sisillo et al. indicated a non-significant trend to a reduction in AKI with administration of intravenous NAC in patients with chronic kidney disease undergoing cardiac surgery. Similarly, Fischer et al. have shown that NAC reduce rise in serum creatinine and improved creatinine level non-significantly in patients with normal baseline renal function undergoing cardiac surgery (15-16). In patients with preexisting moderate renal dysfunction undergoing cardiac surgery, Wijeysundera et al. have found the similar findings: there was a trend to the preservation on postoperative estimated glomerular filtration rate and a significant reduction in mortality with NAC (17).

On the other hand, Haase et al. found no effect of NAC on prevention of AKI in high-risk cardiac surgery patients (18). Ristikankare et al. also found no difference in postoperative creatinine levels between patients receiving and not receiving NAC in those with serum creatinine levels >100 µmol/l but <400 µmol/l. Adabag et al. have found that serum creatinine levels, incidence of AKI, requirement of hemodialysis, mortality and length of hospital stay were similar between patients receiving oral NAC and control group in those with

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baseline chronic kidney disease undergoing cardiac surgery (19,20). Burns et al. performed a large study including 295 patients and found no beneficial effects of NAC on postoperative renal dysfunction (21). El-Hamamsy et al. found the similar findings (22).

Meta-analyses: Adabag et al. were unable to show any beneficial effects of NAC on the incidence of AKI and maximal increase of creatinine after cardiac surgery in a meta-analysis including 10 RCTs (1). In another metaanalysis including 7 RCTs (n = 1000) no improvement in postoperative creatinine increase, requirement of renal replacement therapy and mortality has been found by Naughton et al. Metaanalysis of Nigwekar and Kandula comprising 12 studies showed that NAC did not reduce the risk of AKI, requirement of haemodialysis, mortality and length of intensive care stay (23,24). Similarly, in the meta-analysis of Ho et al, NAC did not decrease AKI, hemodialysis or mortality in patients undergoing cardiac or abdominal surgeries (25).

Wang et al. also showed in their metaanalysis that NAC did not decrease acute renal failure requiring renal replacement therapy. Similarly, Baker et al. including 13 studies were unable to show any beneficial effects of NAC on AKI. Park et al. were also unable to show any beneficial effects of anti-inflammatory agents including NAC on AKI after cardiac surgery (26-28).

Conclusion

Currently available data do not support to recommend NAC for the prevention of AKI after cardiac surgery.

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