

Postoperative Atrial Fibrillation and N-Acetyl Cysteine

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Postoperative Atrial Fibrillation

Postoperative atrial fibrillation (POAF) is the most common complication of cardiac surgery. It is associated with severe complications including stroke, hypotension and mortality and increased duration of hospitalization and costs of the procedure [1,2].

Recent investigations have suggested that cardiopulmonary bypass surgery may be associated with oxidative stress and inflammation, processes that are interrelated and have been implicated in the atrial remodeling and therefore the development and perpetuation of atrial fibrillation (AF) [3-15].

N-Acetyl Cysteine and Postoperative Atrial Fibrillation

N-acetyl cysteine (NAC) is a mucolytic agent and it has been used as an antidote for acetaminophen intoxication [16]. It has anti-oxidant and anti-inflammatory properties. It is a glutathione precursor, may scavenge reactive oxygen species and reduce oxidative damage [17,18]. Therefore, it seems that it is a promising agent that can be used for the prevention of POAF. In this review, we focus on the studies searching the association between POAF and NAC.

N-acetyl cysteine has been shown to reduce oxidative and inflammatory response [19-21], ischemia/reperfusion injury [22], and reperfusion arrhythmias [23].

In 20 patients undergoing by-pass surgery, Eren et al. [24] compared the patients receiving NAC to those receiving salt solution and found that the incidence of POAF was lower in the salt group (10%) than the NAC group (20%). Orhan et al. [22] also compared the NAC group with control group in a total of 20 patients and no difference was detected with respect to POAF rate between the groups. Haase et al. [25] also showed that the NAC group and the placebo group developed similar rate of POAF ($p=0.42$) in a phase II study performed in 60 cardiac surgery patients at high risk of postoperative heart failure. Although statistically insignificant, POAF rate was found to be lower in the NAC group as compared with the placebo group ($p=0.21$) in the study of Wijeyesundera, [26] who randomized 177 cardiac surgery patients with moderate renal insufficiency to NAC or placebo. On the contrary, El-Hamamsy et al. [27] indicate no beneficial effects of NAC on any end-points including POAF in a randomized study. POAF was not primary end-point in any of the above studies.

In only our randomized [28] study POAF was primary end-point. We included 115 patients undergoing by-pass and/or valve surgery and compared the effects of NAC or saline as placebo and found that POAF incidence was significantly lower in patients receiving NAC as compared to those receiving placebo. In an observational study including 590 patients, we obtained the similar positive results in similar patient group [29]. These findings were supported by two recent meta-analyses [30,31]. In the meta-analysis of Baker et al. [30] POAF was end-point in 6 studies and its risk decreased significantly (36%) with NAC. In the meta-analysis by Gu et al. [31] including 8 studies with 578 patients, it was shown that POAF was significantly reduced by NAC compared to controls. However, it was recognized that a large

randomized trial with POAF as primary endpoint was needed. On the other hand, another meta-analysis [32] including 1407 patients was unable to indicate any beneficial effects of NAC on POAF ($p=0.19$).

NAC has sulfhydryl group and therefore it may decrease ischemia-reperfusion injury and may have vasodilator actions [22]. Also, it may increase I_{to} and $I_{Ca,L}$ current, and may affect atrial remodeling [33,34].

Conclusions

Available data to date indicate that, although promising results have been obtained, there is no homogeneity in all the studies. Therefore, it is early to recommend NAC routinely for the prevention of POAF. Large randomized trials with POAF as primary endpoint comparing different doses and durations of treatment are needed.

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