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REVIEW

Preoperative Use of Oral Beta-Adrenergic Blocking Agents and the Incidence Of New-Onset Atrial Fibrillation After Cardiac Surgery. A Systematic Review and Meta-Analysis

Paul Min Thein [a,b*], Kyle White [b], Khyati Banker [b], Carole Lunny [c], Sam Mirzaee [d], Arthur Nasis [d]

[a]Department of Medicine, Monash Medical Centre, Monash Health, Melbourne, Vic, Australia
[b]Monash University, School of Public Health and Preventive Medicine, Melbourne, Vic, Australia
[c]Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Cochrane Australia, Melbourne, Vic, Australia
[d]MonashHeart, Monash Cardiovascular Research Centre, Monash Health & Department of Medicine (MMC), Monash University, Melbourne, Vic, Australia

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Background Current epidemiological data suggests that postoperative atrial fibrillation or atrial flutter (POAF) causes significant morbidity and mortality after cardiac surgery. The literature for prophylactic management of POAF is limited, resulting in the lack of clear guidelines on management recommendations.

Aim To examine the efficacy of prophylactic rate control agents in reducing the incidence of new-onset POAF in patients undergoing elective cardiac surgery.

Methods Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and Medline were systematically searched for blinded randomised controlled studies (RCT) evaluating adults with no history of atrial fibrillation randomised to a pharmacological agent (either beta blocker, calcium channel blocker or digoxin), compared to placebo. Utilising Cochrane guidance, three reviewers screened, extracted and the quality of the evidence was assessed. We used a random effects meta-analysis to compare a rate-control agent with placebo.

Results Five RCTs (688 subjects, mean age 61 ± 8.9, 69% male) were included. Beta blocker administration prior to elective cardiac surgery significantly reduced the incidence of POAF (OR 0.43, 95%CI [0.30–0.61], $I^2 = 0\%$) without significant impact on ischaemic stroke (OR 0.49, 95%CI [0.10–2.44], $I^2 = 0\%$), non-fatal myocardial infarction (OR 0.76, 95%CI [0.08–7.44], $I^2 = 0\%$), overall mortality (OR 0.83, 95%CI [0.19–3.66], $I^2 = 0\%$), or length of stay (mean −0.96 days 95%CI [−1.49 to −0.42], $I^2 = 0\%$). An increased rate of bradycardic episodes was observed (OR 3.53, 95%CI [1.22–10.23], $I^2 = 0\%$).

Conclusions This review suggests that selective administration of prophylactic oral beta blockers prior to elective cardiac surgery is safe and may reduce the incidence of POAF.

Keywords Atrial fibrillation • Atrial flutter • New onset • Prophylaxis • Beta blocker • Cardiac surgery

*Corresponding author at: Monash Medical Centre, Monash Health, 246 Clayton Road, Clayton, Vic 3150, Australia, Tel.: +61 9594 6666.
Email: paul.thein@monashhealth.org

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Background

Description of the Condition

Atrial fibrillation (AF) is the most common form of tachyarrhythmia after major cardiothoracic surgery [1]. Postoperative atrial fibrillation (POAF) is often associated with structural heart disease and can lead to haemodynamic impairment and thromboembolic complications which, in turn, can result in significant morbidity, mortality and cost [2].

Atrial fibrillation occurs in 10% to 65% of patients after cardiac surgery, usually on the second or third postoperative day [3]. Independent clinical predictors of postoperative AF were identified in one study as increasing age, surgery for valvular heart disease and postoperative complications (stroke, infection and unstable haemodynamics) [4]

In our experience, there is no clear basis on which the decision to administer a rate-control agent preoperatively in patients undergoing cardiac surgery is made. We hypothesised that pharmacotherapy decisions for this particular cohort might be variable according to the involvement of specialists from different disciplines.

Furthermore, we hypothesised that the decision in choosing the most appropriate therapy might depend on 1) level of experience, e.g. junior trainees might choose the safest drug with minimal efficacy; 2) area of speciality, e.g. intensivists are more comfortable administering drugs which are available in intravenous form; and 3) availability of drugs, e.g. lack of availability can influence the choice of drug therapy even if the drug is highly efficacious.

Postoperative atrial fibrillation has been shown to be associated with increased morbidity and mortality and longer, more expensive hospital stays [5,6].

Beta blockers are the most commonly used medication in preventing atrial fibrillation, and the commonly used agents include atenolol, metoprolol, bisoprolol, and sotalol (a beta blocker with, additionally, potassium channel antagonism resulting in anti-arrhythmogenic properties) [7]. The second most commonly used class of drug is a calcium channel blocking agent, such as verapamil or diltiazem. Digoxin, an agent with rate-control and inotropic properties, is also used [7]. Amiodarone has antiarrhythmic properties and is used for rhythm control, therefore it was not included in our systematic review which focusses on a rate control strategy for prophylaxis of new onset POAF [8].

Description of the Intervention

Rate control agents such as beta blockers (metoprolol, atenolol, bisoprolol and sotalol), calcium channel blockers (verapamil and diltiazem) and digoxin have been recommended in the European Society of Cardiology (ESC) clinical guidelines in rate-controlling atrial fibrillation [7]. These agents control the ventricular rate of atrial fibrillation and possibly prevent atrial fibrillation with rapid ventricular rate thereby potentially reducing the incidence of postoperative atrial fibrillation related complications during inpatient stay.

How the Intervention Might Work

Given the high incidence of new onset atrial fibrillation post-cardiac surgery mentioned above [2], the number of in-hospital complications related to new atrial fibrillation could be significantly reduced if clinicians can prevent POAF with prophylactic rate-control agents during the preoperative period.

Why It Is Important To Do This Review

Evidence in supporting prophylactic rate control to prevent POAF prior or during the immediate postoperative period is largely based on studies performed prior to 2004 and hence the need to look for updated data in rapidly changing evidence-based medicine is of paramount importance [3,5,9–13].

Similarly, the optimal duration of maintenance rate control agents after hospital discharge is unknown. Among patients with new-onset AF after cardiac surgery, many will revert to, and maintain, normal sinus rhythm which makes the clinical decision process more complex [14].

A recent Cochrane review [15] studying pharmacotherapy for prevention of atrial fibrillation in cardiac surgery patients only included old trials that tested the efficacy of rate control agents prior to 2004. More recent trials have tested the efficacy of amiodarone and atrial pacing or ablation therapies up to 2010 in the review by Arsenault et al. [15]. However, in clinical practice, they are considered a rhythm control strategy which is a different approach in managing atrial fibrillation and there have been multiple studies published related to this approach [16–19].

Recommended beta blocking agents for rate-controlling AF in therapeutic guidelines include metoprolol, atenolol and sotalol [20]. In a 2013 Cochrane review (Arsenault 2013), trials of beta blockers that are not commonly used in clinical practice were included. This prompted the authors to plan a review on beta blockers which are commonly used in practice to evaluate their effectiveness. The beta blockers used commonly in clinical practice include metoprolol, atenolol, sotalol, carvedilol and bisoprolol. In brief, there is an obvious need for an updated systematic review which attempts to address prophylactic properties of rate control agents which are commonly used in a hospital setting in preventing new onset POAF [7]. Explicit descriptions of the objectives of the review are included in Appendix 1.

Methods

Search Methods for Identification of Studies

Database Searches

Our search strategy involved combining the following terms: procedure (cardiac surgery), intervention (beta blockers, calcium channel blockers and digoxin), and outcome (atrial fibrillation, atrial flutter). We searched CENTRAL (30

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