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Metoprolol vs ivabradine in patients with mitral stenosis in sinus rhythm

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ABSTRACT

Background: Severe mitral stenosis is usually symptomatic and is treated by BMV or surgery, whereas mild to moderate mitral stenosis is usually asymptomatic or mildly symptomatic and managed medically. Patients in the later group may become symptomatic during episodes of exercise and increased heart rate. Beta-blockers are frequently used in patients with mitral stenosis to control the heart rate and alleviate exercise-related symptoms. The objective of our study was to investigate the comparative efficacy of ivabradine versus metoprolol in patients with mitral stenosis in sinus rhythm.

Methods: We studied 97 patients of mitral stenosis in sinus rhythm presented with exertional symptoms. The effectiveness of Metoprolol was compared with ivabradine in alleviating these exertional symptoms in a randomized, open label non crossover study. We also assessed various stress ECG parameters, 24 hour Holter parameters and 2D Echo parameters to objectively compare the effects of ivabradine and metoprolol in these patients.

Results: Ivabradine and metoprolol both were effective in controlling exertional symptoms. Significant improvement in objective parameters like TMT (work capacity, baseline heart rate and maximal heart rate) and 2D echocardiography (right ventricular systolic pressure) are seen with both drugs. Ivabradine controls the exertional symptoms significantly more than metoprolol. On head to head comparison there was a significant benefit of working capacity and heart rate at maximal exercise in favour of ivabradine.

Conclusions: Ivabradine should be strongly considered in medical management of mitral stenosis patients where beta blockers are contraindicated such as reactive airway disease. The cost of ivabradine is higher than metoprolol which might possess constraints as most of the rheumatic heat disease patients belong to low socio economic status.

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1. Introduction

Rheumatic mitral stenosis is a common problem in the young population in most of the developing world [1]. Severe mitral stenosis is usually symptomatic and is treated by balloon mitral valvuloplasty or surgery, whereas mild to moderate mitral stenosis is usually asymptomatic or mildly symptomatic and managed medically [2]. Patients in the latter group may become symptomatic during episodes of exercise and increased heart rate. As increase in heart rate occurs mostly at the expense of diastole, there is shortening of the diastolic filling period, and in the presence of obstruction at the mitral valve this results in increased left atrial pressure. Subsequently, pulmonary capillary wedge pressure rises, resulting in effort intolerance and dyspnea [3]. Theoretically, negative chronotropic agents such as beta-blockers and calcium channel blockers should be helpful in controlling tachycardia-related symptoms by improving diastolic filling and preventing rise in pulmonary capillary wedge pressure. However, associated negative inotropic effect on myocardium and effect on neuromuscular system may negate the beneficial effects of these drugs. Calcium channel blockers have little role in controlling heart rate when the patient is in sinus rhythm. Results from various clinical and hemodynamic studies with these agents have been conflicting [4–6].

Ivabradine is a new negative chronotropic agent that has selective action on sinus rate by acting on the If current with no effect on myocardial contractility [7]. It has a better safety profile than beta-blockers, and various trials have reported very few side effects [8]. Pure heart rate reduction with ivabradine, without any major cardiac or systemic effects, could be one of the reasons for better efficacy of this drug in improving effort tolerance.

Ivabradine therefore seems to be an attractive option for heart rate reduction in patients with mitral stenosis in sinus rhythm. One study showed that ivabradine decreases resting heart rate and is as effective as metoprolol in increasing exercise duration, reducing transmitral

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gradient and PASP in mild to moderate mitral stenosis with normal sinus rhythm [9]. Parakh et al. [10] studied the comparative efficacy of heart rate control with ivabradine or atenolol and its effect on effort tolerance in patients with mild–moderate mitral stenosis in normal sinus rhythm. They found ivabradine more effective than atenolol for effort related symptoms in patients with mild–moderate mitral stenosis and normal sinus rhythm.

In our study, we therefore set out to investigate the comparative efficacy of ivabradine versus metoprolol in patients with mitral stenosis in sinus rhythm.

2. Material and methods

This was a hospital based study conducted in the department of cardiology S.S. Hospital IMS BHU, Varanasi. Study subjects included 97 patients of mitral stenosis in sinus rhythm admitted or attended cardiology or medical ward or OPD during July 2014 to October 2014.

This was an interventional, randomised, open label, non cross over study. The study was approved by the institutional ethics committee.

Inclusion criteria:

1) Age 18–70 years
2) Documented mitral stenosis (mild, moderate or severe*)
3) Normal sinus rhythm
4) Need heart rate controlling agents (e.g. digoxin, beta blockers, or calcium channel blockers) for their effort/tachycardia related symptoms.
5) Competency to give consent

*Not willing/fit for intervention e.g. unfavourable valve morphology, LA clot.

Exclusion criteria:

1) Atrial fibrillation;
2) Other significant valvular lesions (more than mild aortic stenosis/aortic regurgitation/mitral regurgitation);
3) Inability to perform treadmill test (TMT)/contraindication for TMT
4) Need for surgical treatment or BMV;
5) Presence of significant noncardiac comorbidities, e.g., chronic obstructive pulmonary disease, renal failure, malignancy, etc.;

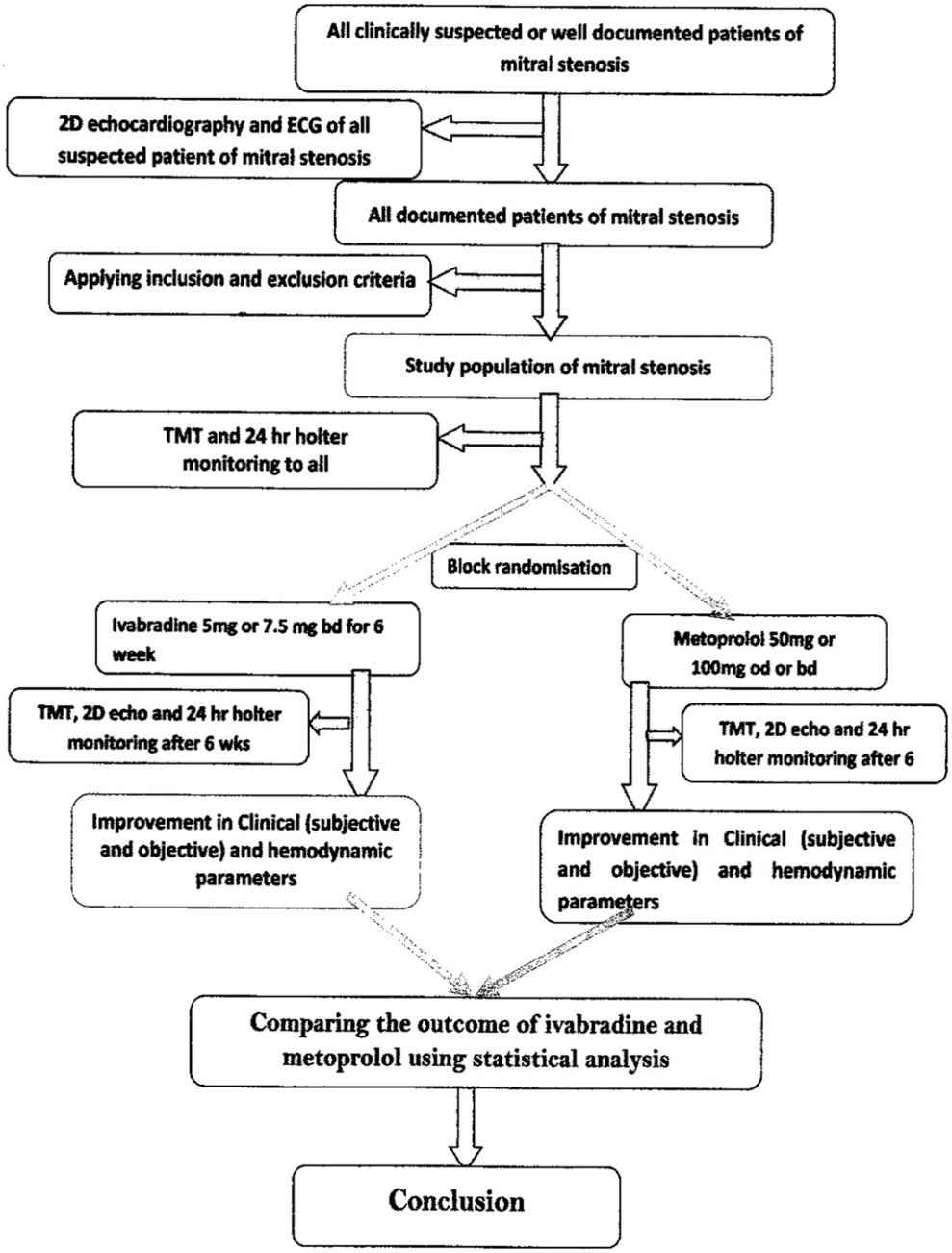

Fig. 1. Trial protocol flow chart.

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