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REVIEW ARTICLE

Use of Beta Blocker in COPD Patient: A Dilemma to Prescribe

Mohammad Ashiqur Rahman[1], Md. Abdur Rouf[2], Nazifa Tasnim[3]

Abstract:

Cardiovascular disease, which is common in patients with chronic obstructive pulmonary disease (COPD), has a profound effect on morbidity and mortality. Despite the clear evidence of beta blockers effectiveness, there is a general reluctance of physicians to use them in patients with COPD due to a perceived contraindication and fear of inducing adverse reactions and bronchspasm. But it is seen that Beta blockers are well tolerated in patients with cardiac disease and concomitant COPD. The cumulative evidence from trials and meta-analysis indicates that cardioselective Beta blockers should not be withheld in patients with reactive airway disease or COPD. Patients with COPD have a high incidence of cardiac events necessitating careful consideration of prophylactic treatment. The benefits of beta blockade in this group appear to outweigh any potential risk of side effects according to the available evidence. In this article, we will discuss the effect of Beta blockers in patients with COPD with and without cardiac indication and review the result of these two groups.

Keywords: COPD, Beta blocker, Heart failure, MI.

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Introduction:

Beta-blockers have an established position in the management of coronary artery disease and heart failure. COPD management strategies also state that the benefits of selective beta-1 blocker treatment in heart failure clearly outweigh any potential risk associated with treatment even in patients with severe COPD [1]. Despite this guidance there is a reluctance of physicians to prescribe even cardioselective beta-blockers in COPD, even in the presence of known cardiac disease, because of persistent concerns regarding potential bronchoconstriction, especially in more severe patients.

Cardiovascular comorbidity, including coronary artery disease and heart failure, commonly coexists in chronic obstructive pulmonary disease (COPD) due to the effects of smoking, systemic inflammation, hypoxaemia and other shared risks. COPD may also be associated with impaired diastolic filling due to lung hyperinflation, which may be compounded by the negative lusitropic effects of hypoxaemia and left ventricular hypertrophy. The use of beta-blockers in COPD has been proposed because of their known cardioprotective effects as well as reducing heart rate and improving systolic function.

1. Registrar, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka.
2. Professor, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka.
3. Medical Officer, Upazila health complex, Sonaimuri, Noakhali, Chittagong.

Correspondence to: Dr. Mohammad Ashiqur Rahman, MBBS, MRCP (UK), Registrar, Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka. Email:ashique49@yahoo.com

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Effect of Beta blockers:

Beta-blockers have positive effects on morbidity and mortality in patients with heart failure and in those who have had a myocardial infarction. Most retrospective observational studies have suggested that such positive effects also occur in patients with COPD who have cardiovascular disease. [2] Along with their potential cardiac effects, beta-blockers have noncardiac targets with potential beneficial effects in patients with COPD, such as reducing systemic inflammation, the number of goblet cells, and mucus release. Thus, beta-blockers may have beneficial effects in patients with COPD who do not have clear cardiac indications.

Potential cardiac targets for beta-blockers in COPD

- Improved left ventricular systolic and diastolic function
- Reduced left ventricular dilatation
- Protection against myocardial ischaemia
- Reduced left ventricular mass
- Reduced heart rate
- Anti-arrhythmic effects
- Inhibition of myocyte apoptosis
- Protection against hypoxic sympathetic drive
- Protection against adverse effects of beta-agonists

Potential non-cardiac targets for beta-blockers in COPD

- Inhibition of endothelin-1 release
- Reduction in circulating pro-inflammatory cytokines
- Inhibition of neutrophil chemotaxis and respiratory burst
- Reduction in goblet cell number and mucus release

Box: *Cardiac and non-cardiac effect of Beta Blocker*

Now question is what will be the outcome if beta blocker is given to the patient of COPD with cardiac indication in comparison to patients without cardiac indication.

Study Result:

In this article here is given two different study discussion where beta blocker was given to one group patient of COPD with cardiac indication and another group was beta blocker to the COPD patients without any cardiac indication.

In a meta-analysis of 15 retrospective studies involving patients of COPD with cardiac indication, those who received beta-blockers had a 28% lower frequency of death and a 38% lower frequency of exacerbation than those who did not receive a beta-blocker. [3] These studies indicate positive role of beta blocker in COPD with cardiac disease patient.

The second group of study was the BLOCK COPD (Beta-Blockers for the Prevention of Acute Exacerbations of Chronic Obstructive Pulmonary Disease) trial, where moderate or severe COPD patients were chosen who did not have an established indication for beta-blocker use. Patients with COPD were randomly assigned to receive a beta-blocker (extended-release metoprolol, dose 25–100 mg daily, depending on heart rate and blood pressure) or placebo, with a primary outcome of the first exacerbation of COPD.

During average follow-up of nearly 1 year, no significant difference was observed between groups in overall exacerbation rates. However, metoprolol recipients were significantly more likely to be hospitalized for COPD exacerbations (0.45 vs. 0.28 exacerbations per person-year). At routine follow-up visits, metoprolol recipients reported more dyspnea than did placebo recipients, but no differences in FEV_1 were noted. On the basis of these data, current COPD management strategies indicate that beta-blockers should be prescribed in patients with COPD who have cardiovascular indications, even in those with severe COPD.[4]

Prescribing Information:

Initiating treatment with beta-blockers is not simple as it requires dose titration over a period of weeks along with monitoring of heart rate, blood pressure and perhaps spirometry, all of which take time, incurring extra healthcare costs. Moreover beta-blockers may be less well tolerated in older patients with coexisting comorbidities such as diabetes, peripheral vascular disease and renal impairment, who are more prone to postural hypotension.

- Beta-1 selective antagonists including metoprolol, bisoprolol and nebivolol exhibit dose related beta-2 receptor blockade.

- Bisoprolol has a licensed indication for use in heart failure and coronary artery disease and has a beta-1:2 receptor selectivity ratio of 14:1, which is higher than either atenolol (5:1) or metoprolol (2:1) [5]
- Nebivolol has been shown to exhibit greater *in vitro* beta-1/2 receptor selectivity than bisoprolol in human myocardium [6] and also suppresses endothelial nitric oxide [7].
- Carvedilol is a nonselective beta-antagonist that is more likely to cause bronchoconstriction than beta-1 selective antagonists.
- Slowly titrate the dose of beta-blockers at 1–2 weekly intervals up to the usual maintenance dose.
- Monitor supine and erect blood pressure, heart rate and spirometry during dose titration.
- Concomitant long-acting muscarinic antagonists may obviate potential bronchoconstriction.
- Symptomatic bradycardia may occur if beta-blockers are used with other rate-limiting drugs such as calcium blockers (*e.g.* verapamil and diltiazem), ivabradine or anti-arrhythmic agents (*e.g.* digoxin, amiodarone and flecainide)
- Symptomatic hypotension may occur when beta-blockers are used with other vasodilatory drugs (*e.g.* angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers and alpha receptor blockers)

Conclusions:

There are compelling reasons to use cardioselective beta-blockers in patients with COPD who have coexistent heart failure or are post-myocardial infarction. Current evidence would suggest that there remains a reticence to prescribe beta-blockers in such patients because of a fear of adverse events, particularly worsened lung function. Cardioselective â-blockers remain appropriate for COPD patients who have valid cardiovascular indications for their use, but this study suggests that COPD patients without such indications should avoid these drugs.

Key messages:

- The main indications for beta-blockers in patients with COPD are post-myocardial infarction and heart failure with reduced ejection fraction
- Meta-analyses of retrospective studies with beta-blockers in COPD have shown pooled estimates for reductions in mortality of 28% and exacerbations of 38%.
- Initiating treatment with beta-blockers requires careful dose titration and monitoring. Slowly titrate the dose of beta-blockers at 1–2 weekly intervals up to the usual maintenance dose.
- Beta-1 selective antagonists such as bisoprolol, nebivolol and metoprolol are preferred to the nonselective carvedilol as they are less likely to produce bronchoconstriction in COPD. Among them nebivolol has the highest selectivity to the beta 1 receptor.
- Long-acting muscarinic antagonists, which are commonly used in COPD, protect against the potential for bronchoconstriction due to dose related beta-2 receptor antagonism.

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