

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Use of Beta Blockers in Patients with Reactive Airway Disease and Concomitant Hypertension or Ischemic Heart Disease.

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ABSTRACT

Beta-adrenoreceptor antagonists can be safely prescribed and decreases mortality in patients with ischemic heart disease and cardiovascular risk factors. Some authors are of the opinion that there is underuse of beta blockers in this subgroup of patients. The objective of this study was to analyse drugs being prescribed and the effect beta blockers have on symptoms in asthmatics with concomitant reactive airway diseases and cardiovascular diseases. Data was collected from medical records of patients with reactive airway disease and concomitant hypertension and ischemic heart disease. It included demographic details of the patients, the clinical diagnosis, drugs prescribed and the patient outcome regarding whether there was exacerbation of asthma symptoms on taking beta blockers. Medical records of 250 patients were analysed. 13% of all patients was prescribed beta blockers. Among hypertensive's 12% , among patients with ischemic heart disease 16.6% and of patients with IHD and hypertension, 20% were prescribed beta blockers. Of the 33 (13%) patients who were on beta blockers, only 3 patients had exacerbation of bronchial asthma symptoms. Prescribing cardioselective beta blockers under supervision appear to be safe in patients with reactive airway disease and concomitant hypertension and ischemic heart disease

Keywords: beta blockers, hypertension, ischemic heart disease, asthma

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INTRODUCTION

The concept of paradoxical pharmacology has gained wider acceptance among the clinicians and hence, beta blockers which were once contraindicated in congestive heart failure, are now among the first line drugs. Despite the proven benefits of beta-adrenoreceptor antagonists (beta blockers) in treating hypertension, ischaemic heart disease and heart failure, clinicians, for obvious reasons, are reluctant to prescribe these drugs to such patients who have concurrent reactive airway diseases such as bronchial asthma or chronic obstructive airway disease (COPD). There are some studies which suggest that beta blockers can be safely prescribed in mild to moderate asthma and COPD. There are investigators who have even found in studies that cardio-selective beta blockers reduce mortality, exacerbations, and hospital admissions in patients with COPD [1]. Beta-blockers improve survival rates in patients with chronic systolic heart failure and after myocardial infarction, including in those patients with coexisting COPD. Though cardioselective beta blockers are the preferred drugs in this group of patients, caution and close follow-up in such patients is mandatory [2].

With this background, there is a need for research to find out the effect of beta blockers on reactive airway disease in patients with concomitant cardiovascular diseases. In this study, we analysed the drugs being prescribed and the effect beta blockers had on symptoms in asthmatics with concomitant reactive airway diseases and cardiovascular diseases

MATERIALS AND METHODS

This retrospective cohort study was started after taking clearance from the institutional ethics committee. The study was conducted at a 2100-bed tertiary care teaching hospital attached to a medical college in south India. The hospital provides health care services to surrounding urban, semi urban and rural areas. The case records of 250 in-patients, admitted in medical wards with a diagnosis of bronchial asthma with concomitant cardiovascular diseases like ischemic heart diseases or hypertension were accessed from the medical records department of the hospital. The study was conducted over a period of three months.

Inclusion criteria

- Patients diagnosed with asthma and concomitant ischemic heart disease (IHD) or hypertension.
- Patients in the age group 18 to 70 years were selected.
- Patients of both sexes.

Data Collection

Investigators collected the data from medical records department on a daily basis for two months. The data collected included demographic details of the patients, the clinical diagnosis, drugs prescribed and the patient outcome regarding whether there was exacerbation of asthma symptoms on taking beta blockers.

Statistical Analysis

The data was entered into predesigned pro forma and analysed using descriptive statistics.

RESULTS

Medical records of 250 patients were analysed. Females constituted 60% and males constituted 40% of the study group. The patients were in the age group of 20-70 years. Maximum number of patients was in the age group of more than 60 years followed by 50-60 years. (Figure 1).

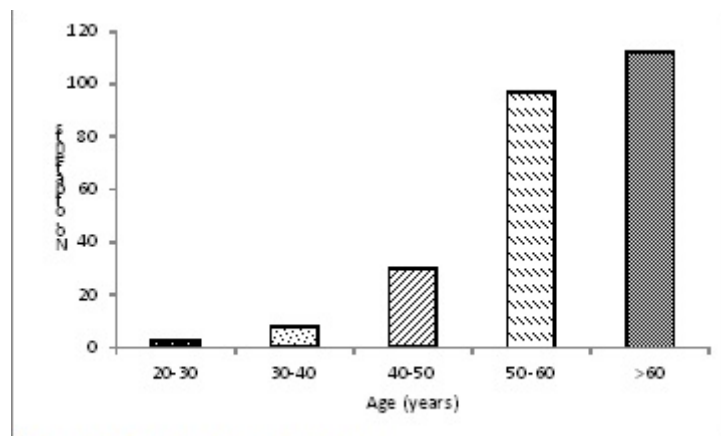


Figure 1 Age distribution of subjects

All patients were asthmatics and in addition 83% of them had hypertension, 7% had IHD and 10% had concomitant IHD and hypertension (Figure 2).

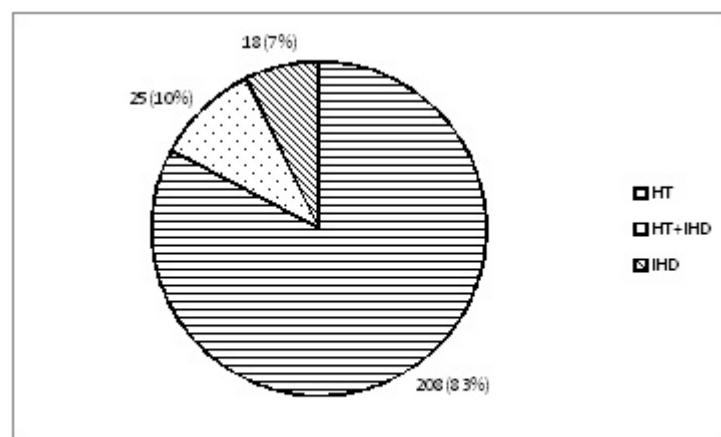


Figure 2 Distribution of cardiovascular comorbid conditions

IHD= Ischemic heart disease, HT= Hypertension

The patients were having other diseases like diabetes mellitus, anaemia, hypothyroidism, acute gastritis etc. Of these diabetes mellitus constituted the largest group (28%). The study patients were on different cardiovascular drugs as shown in figure 3.

Calcium channel blockers were the most frequently prescribed drugs for cardiovascular diseases. Amlodipine was the most frequently prescribed (85%) calcium channel blocker followed by diltiazem and nifedipine. A total of 13% (n=33) of study patients were on beta blockers (figure 3).

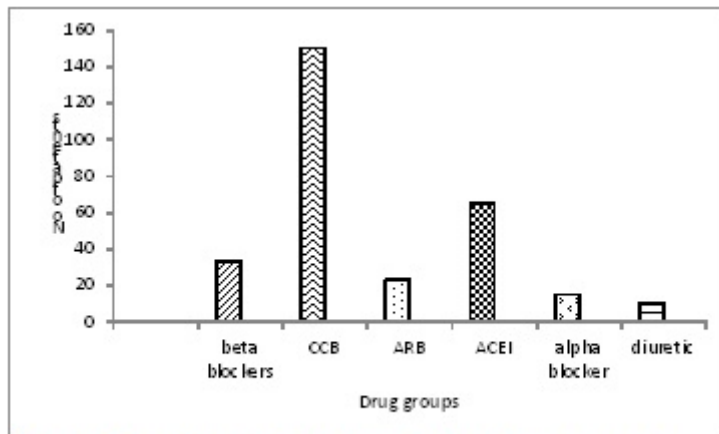


Figure 3 Different groups of cardiovascular drugs being prescribed

CCB- calcium channel blockers, ARB- Angiotensin receptor blockers
ACEI- Angiotensin converting enzyme inhibitors

Various beta blockers prescribed are shown in figure 4.

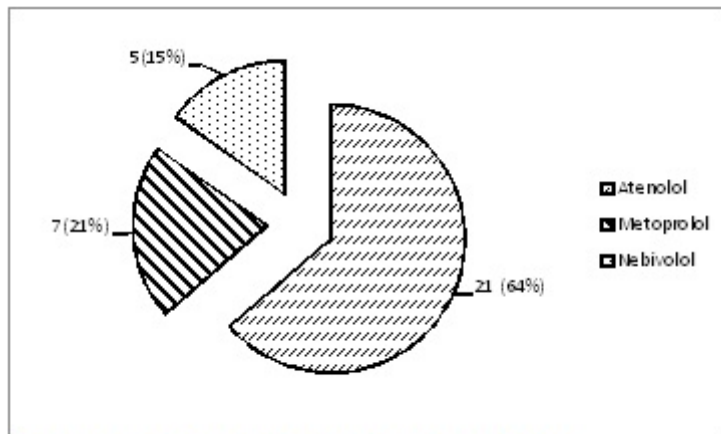


Figure 4: Various beta blockers prescribed to the patients

Disease-wise overall beta blocker administration is shown in figure 5.

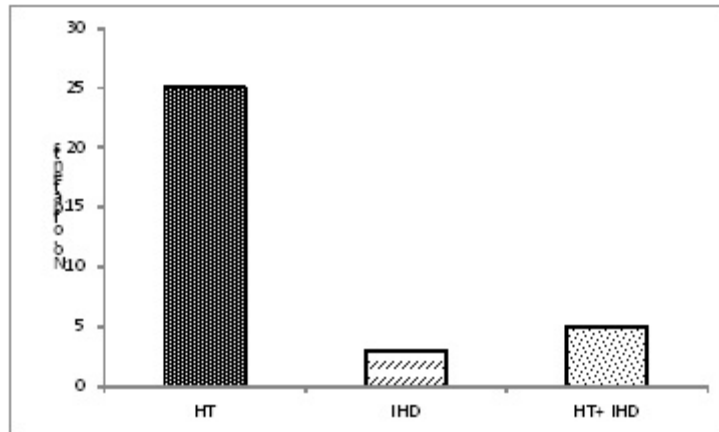


Figure 5: Disease-wise overall beta blocker usage

IHD= Ischemic heart disease, HT= Hypertension

12% of hypertensive patients, 16.6% of IHD patients and 20% of IHD and hypertension were prescribed beta blockers. Disease-wise individual beta blockers prescribed to patients with different diagnosis is shown in figure 6.

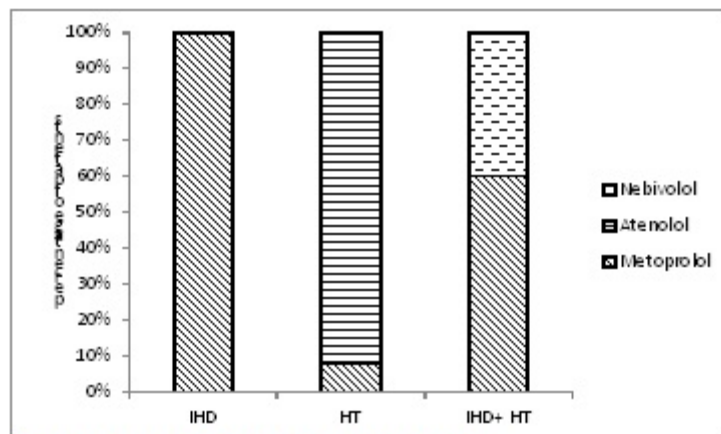


Figure 6: Disease-wise specific beta blocker usage

IHD= Ischemic heart disease, HT= Hypertension
 Ateno= Atenolol, Nebi= Nebivolol, Meto= Metoprolol

Of the 33 patients who were on beta blockers, 3 patients had exacerbation of bronchial asthma.

DISCUSSION

As beta blockers have life preserving effects in patients with cardiovascular disease, it has been suggested that they can in most circumstances, be judiciously administered in patients with reactive airway disease such as COPD[3].

As per Joint National Committee 7 (JNC 7), excellent clinical outcomes in patients with hypertension have been seen with ACE inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers and thiazide diuretics[4]. In the present study, in addition

to these drugs a small percentage of patients were prescribed alpha blockers. Calcium channel blockers were the most commonly prescribed anti-hypertensives in this study. Of calcium channel blockers, amlodipine was predominantly prescribed. Amlodipine because of long half-life has less peaks and thus has less adverse effects which could be the reason for its frequent use.

It has been found in a study that 28% of the 270 patients who were discharged from a university hospital after an acute exacerbation of COPD, were suffering from hypertension [5]. Beta-blockers are valuable agents in the treatment of hypertension but must be used with extreme care in patients with reactive airway disease such as asthma [6]. In our study, 12% of all hypertensives were prescribed beta blockers (Figure 5). However some studies have put forth that in the absence of concomitant cardiovascular disease, routine use of beta-blockers for the treatment of hypertension in patients with asthma should be avoided [7].

Beta-blockers are first line drugs for treatment of symptomatic stable ischemic heart disease and for reducing mortality post-MI[8]. In present study, in patients with IHD alone, 16.6% were prescribed beta blockers (Figure 5). But on considering all IHD patients in the study, the percentage was 36.6%, which was much more than that in hypertensive patients among which only 12% were taking beta blockers. The reason for more frequent use of beta blockers in IHD patients, despite the presence of bronchial asthma, could be the therapeutic benefits and relative lack of alternative drugs compared to hypertension.

In our study, atenolol was the most commonly prescribed beta blocker followed by metoprolol and then nebivolol (Figure 4). Atenolol and metoprolol are cardio selective beta blockers. Atenolol in the present study was being prescribed to hypertensive patients whereas metoprolol was prescribed to patients with hypertension alone, IHD alone and hypertension with IHD (figure 6). Nebivolol is also a cardio selective blocker with endothelial nitric oxide mediated vasodilatory activity and approved for hypertension. Nebivolol was prescribed to hypertensive and IHD patients (Figure 6). Nebivolol, which modulates the endogenous production of nitric oxide and affects oxidative cascade, proved clinically well tolerated in terms of respiratory outcomes in patients with reactive airway disease. Due to the substantial dissociation between its cardiac and pulmonary activity, nebivolol confirmed a very good safety profile when it was regularly administered to hypertensive subjects with obstructive respiratory comorbidities[9]. Prescribing cardio selective beta blockers in mild to moderate reversible airway diseases under medical supervision appears to be safe [10]. Studies show that metoprolol succinate and nebivolol are safe and can be used in patients with severe COPD and bronchial asthma with concomitant hypertension and/or COPD [11]. Some authors are of the opinion that a cautious approach (under specialist supervision) to beta-blocker use in patients with heart failure and airways disease can result in successful treatment. The implications of withholding these agents may have more serious consequences than their administration [12]. A meta-analysis of 29 randomized trials shows that cardio selective-blockers, do not significantly worsen respiratory symptoms in patients with mild to moderate reactive airway disease [13].

However, it has been reported in a case report that oral betaxolol had induced bronchospasm, although it is considered to be highly cardio selective and seems less likely

than other beta1-selective blocking agents to cause pulmonary adverse effects. Betaxolol should be administered with caution to patients with asthma or chronic pulmonary disease [14]. Many studies go in favour of beta blocker use and one of those suggests that cardio selective beta-blockers reduced long term mortality in patients with COPD, who underwent major vascular surgery [15]. Intensified dosing regimens appeared to be superior to low doses in terms of their impact on a 30-day mortality [15].

Among patients without reactive airway disease (RAD), beta-blocker prescription rates were 78.3% at admission and 88.7% at discharge; in patients with a RAD history, rates were 65.6% at admission and 77.2% at discharge [16]. RAD history was the most significant predictor of likelihood of not receiving a beta blocker at admission or discharge. Receipt of beta blockers within 24 hours after admission was associated with a lower in-hospital mortality rate for patients with RAD and authors are of the opinion that careful assessment of beta-blocker safety and RAD severity by physicians is needed to improve beta-blocker prescription rates in large group of patients with acute coronary syndrome[16].

Cardio selective beta-blockers appear to be safe even in elderly male patients with mild-to-moderate COPD in whom there is a compelling indication for same. They improve mortality in older patients with coexisting cardiovascular disease and COPD. Nonselective beta-blockers, on the other hand, should be avoided except in patients with heart failure in whom carvedilol is beneficial [17]. Evidence supports improved mortality after MI with beta-blocker use [18]. However in current guidelines there are no specific recommendations as to beta-blocker type or duration [19]. Analysis confirms the efficacy of prophylactic beta-blockers against post-CABG atrial fibrillation. Authors recommend continuing perioperative beta-blockers in the open heart surgery patients in the absence of contraindications [20].

A single-centre analysis of 825 patients admitted with acute exacerbation of COPD found a 40% reduction in mortality in patients who received beta-blocker therapy during hospitalisation, raising the possibility that the common practice of withholding beta blockers may be harmful[21]. A recent meta analysis suggests that cardio selective beta-blockers should not be contraindicated in patients with COPD [22]. In a retrospective study which examined the association between beta-blocker therapy and in-hospital mortality among patients with IHD, CHF or hypertension, has put forth that continuing cardio selective beta blockers during hospitalisation for COPD was safe and clinicians should consider choosing cardio selective beta-blockers rather than non-selective beta-blockers in these patients [23]. Along with asthma and IHD or hypertension, 28% of the total patients had diabetes mellitus in present study. Patient with diabetes and cardiovascular risk factors have more stringent blood pressure targets. Unlike conventional beta-blockers, vasodilatory beta-blockers have favourable tolerability and metabolic profiles [24].

Three of the 33 patients taking beta blockers in our study had exacerbation of asthmatic symptoms. One of these patients was on anti-asthmatic drugs from five years. The patient was diagnosed to have hypertension and was prescribed amlodipine and atenolol combination. The patient developed acute exacerbation of bronchial asthma after which beta blocker was replaced. Other two patients in atenolol group had exacerbation of symptoms soon after starting beta blocker and need to stop beta blockers. It has been seen that single dosing with a beta-blocker may cause acute broncho constriction; chronic

administration may produce beneficial effects including attenuated airway hyper responsiveness [25]. In 50 patients with coronary artery disease and chronic obstructive pulmonary disease no side effect was seen which could be attributed to beta blocker, metoprolol [26]. In patients with COPD and cardiovascular disease, use of cardio selective beta blockers appears to be safe and benefits of the drugs exceed the risks of exacerbation of COPD [27]. Another recent study puts forth that β blockers in addition to reducing cardiovascular risks, reduces mortality and COPD exacerbations [1].

To summarize, beta blockers reduce morbidity and mortality in patients with diseases like CHF, MI, IHD. Also non-selective beta blockers can accentuate the bronchospasm in patients with reactive airway disease. Cardio selective beta blockers do not induce bronchospasm in patients with reactive airway disease [28]. A study in patients admitted with acute coronary syndrome and concomitant COPD [29] has put forth that beta blockers should be tried in such patients and a safe approach is to start with cardio selective beta blockers at a low dose and titrate up as tolerated with close observation to ensure that these patients are not denied of useful and efficient treatment.

As large numbers of patients with reactive airway disease have concurrent CHF, hypertension and IHD, studies should be undertaken to assess the risk–benefit ratio of beta blockers in this population. Most of the studies on beta blocker use in reactive airway disease include patients with COPD. Hence, more studies are required to understand the effects of beta blockers in asthmatics.

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