

# Management of Hypertension at Crossroads – What is the Current Status of Beta Blockers?

A George Koshy

Department of Cardiology, Medical College, Thiruvananthapuram\*

## ABSTRACT

Published on 29<sup>th</sup> June 2009

The rationale of drug management for systemic hypertension is discussed. The role of various drug classes like beta blockers, thiazides diuretics and calcium channel blockers are discussed. The relative advantages and disadvantages of each group is discussed. The importance of following periodic guidelines for the management of hypertension is also discussed.

**Keywords:** Systemic hypertension, Anti hypertensive drugs, Beta blockers, Thiazides

\*See End Note for complete author details

Over the last half a century, several significant changes have happened in the understanding and management of Systemic Hypertension. The only options available in the early 1950s for the management of systemic hypertension were rigid low sodium diet, surgeries like sympathectomy and bilateral adrenalectomy and a few drugs with significant side effects prohibiting their wide spread use. Studies demonstrating the benefits of treating severe or malignant hypertension became available in the 1950s. Several well conducted trials between 1960s and 1980s confirmed that even milder elevations of blood pressure are associated with long term adverse outcome and that bringing down blood pressure to normal levels does reduce the associated risk and complications. As more information accumulated, it became apparent that the benefits of treating less severe degrees of hypertension far outweighed the risks especially in the high risk elderly population.

The exciting era of beta blockers was initiated by Sir James Black. Propranolol was synthesised in 1963, was shown to be effective in hypertension in 1964 and was marketed in England a year later. Sir James Black was awarded Nobel Prize in Physiology/ Medicine in 1988. Several drugs became available for the treatment of hypertension but no systematic approach was available till the JNC guidelines came in 1978. Initially only diuretics were recommended as first line drugs for hypertension. It was in 1984 report (JNC 3) that beta blockers were first recommended along with diuretics as first line treatment for hypertension. Based on the newer data and scientific information that accumulates, these recommendations are periodically updated and the last

recommendations came in May 2003 (JNC 7 report). European Society of Cardiology, British Hypertension Society and WHO also give periodic up dated guidelines on the management of hypertension.

Recent controversy about beta blockers in hypertension was initially triggered by a meta analysis by Carlberg, Samuelsson and Lindholm on “Atenolol in hypertension” published in Lancet 2004. They identified 4 studies that compared Atenolol with placebo or no treatment and 5 studies that compared Atenolol with other antihypertensive drugs. Despite major differences in BP lowering, there were no outcome differences between Atenolol and placebo in the 4 studies, comprising 6825 patients, who were followed up for a mean of 4.6 years on all cause mortality, cardiovascular mortality or myocardial infarction. The risk of stroke however tended to be lower in the Atenolol than in the placebo group. When Atenolol was compared with other anti hypertensives, there were no major differences in BP lowering between the treatment arms. But the meta analysis showed a significantly higher mortality with Atenolol treatment compared with other active treatment. Cardiovascular mortality as well as stroke was more frequent with Atenolol treatment compared to treatment with other classes of drugs. There have been lot of discussions and speculations as to why Atenolol failed to perform as expected. The possible reasons are<sup>1</sup> Atenolol being non lipophilic will not cross the blood brain barrier and hence does not suppress the central sympathetic outflow like a lipophilic beta blocker. Hence it does not offer protection from sudden cardiac death.<sup>2</sup> Though conventional beta

### Corresponding Author:

Dr. A George Koshy, MD, DM, Professor, Department of Cardiology, Medical College, Thiruvananthapuram.  
Phone: 9847250246. E-mail: tvm\_agkoshy@sanchamnet.in

blockers lower the brachial blood pressure, the central aortic blood pressure is not lowered to the same extent. This may not be true about the newer vasodilatory beta blockers.<sup>3</sup> Atenolol given as a once daily formulation might not have controlled blood pressure effectively throughout 24 hours.<sup>4</sup> The metabolic side effects of beta blockers on insulin resistance, metabolic syndrome and glucose metabolism as well as the adverse effects on the lipid profile are increasingly recognized.<sup>5</sup> Studies have shown that regression in left ventricular hypertrophy with beta blockers is less compared to other hypotensive agents, especially ACE inhibitors and ARBs.<sup>6</sup> Conventional beta blockers do not lower the peripheral vascular resistance and may not have a significant role in improving endothelial dysfunction.

Thiazides and conventional beta blockers increase the risk of “new onset diabetes”. The most frequently recommended combination in most of the trials has been Atenolol 50 to 100 mgms with a diuretic, usually hydrochlorothiazide. In a 6 year prospective study reported in NEJM 2000 on 12250 hypertensives, beta blockers alone increased the risk of new diabetes by almost 28%. The combination of Atenolol with thiazide diuretic was associated with higher diabetes compared to the combination of ACE inhibitor, Perindopril and calcium channel blocker, Amlodipine in the ASCOT trial. The diabetogenic potential of diuretics was also observed in the ALLHAT trial.

The NICE (National Institute for Health and Clinical Excellence) and British Hypertension Society came out with the revised guidelines for management of hypertension in June 2006. In hypertensive patients aged 55 years and over or black patients of any age, first choice of initial therapy should be either a calcium channel blocker or a thiazide type diuretic. In patients younger than 55 years, the preferred initial drug is ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated). If initial therapy was with a calcium channel blocker or thiazide diuretic and a second drug is required, the preferred drug is an ACE inhibitor or an ARB. If initial therapy was with an ACE inhibitor, CCB or thiazide type diuretic can be added as a second drug. If treatment with three drugs is required, the combination of ACE inhibitor/ ARB, calcium channel blocker and thiazide type diuretic should be used. The beta blockers have been degraded to the fourth position in the current NICE guidelines. But this has not been endorsed by the recent European guidelines who continue to recommend beta blockers along with the other drugs for initial treatment.

Though beta blockers many not be the initial choice in

many patients with un complicated systemic hypertension, one should not forget the value of this drug in those with Coronary Heart Disease, angina, post MI status and heart failure. Beta blockers continue to have a role in young anxious hypertensive individuals with hyperdynamic circulatory state and resting tachycardia.

It should be clearly understood that many of the adverse effects observed with the traditional beta blockers like Propranolol and Atenolol may not be shared by the newer beta blockers. Beta blockers differ in many significant pharmacologic aspects like cardio selectivity, lipophilicity, duration of action, metabolic side effects, intrinsic sympathomimetic activity and vasodilatory potential. “The Black and Whyte of Beta blockers” has been extensively reviewed by Dr. S. Harikrishnan in this issue of KMJ. Currently long acting lipophilic beta blockers are preferred over Atenolol. Though Metoprolol and Bisoprolol are commonly used in management of hypertension, data is less compared to Atenolol. In addition, Metoprolol has been extensively studied in acute coronary syndrome, post MI secondary prophylaxis and in heart failure and has been found to be useful. The newer beta blocker Nebivolol is highly selective for the beta 1 receptor and is lipophilic. It has nitric oxide mediated vaso dilatory action and hence has a salutary effect on improving endothelial dysfunction. It is devoid of any major adverse metabolic abnormalities. Carvedilol is another promising drug. In addition to beta blocking effect, it has alpha blocking action as well as anti oxidant properties. It is lipid friendly and does not cause insulin resistance. Several trials of Carvedilol in heart failure are available. Nebivolol was tried in the SENIORS trial in elderly heart failure patients. Large outcome trials of newer beta blockers in systemic hypertension are not yet available.

Based on the available evidence, it seems to be preferable to avoid prescribing Atenolol. If beta blockers are indicated, it may be wiser to change over to a long acting lipophilic beta blocker. Metoprolol is the preferred drug in acute coronary syndrome and post M I scenario. Carvedilol, Metoprolol and Bisoprolol are good options in heart failure. Nebivolol can be considered in elderly heart failure patients, especially if they have obstructive airway disease also. Metoprolol Succinate has the advantage of patient compliance in management of hypertension as it is available as once daily sustained release formulation. Available limited data with Nebivolol, Bisoprolol and Carvedilol look very promising.

Extreme care should be taken when beta blockers are discontinued in those who were taking the drug for a

long time. The dose should be reduced gradually before the beta blocker is weaned off. Abrupt discontinuation of beta blocker can produce uncomfortable palpitation and can even precipitate an acute coronary syndrome.

## END NOTE

### Author Information

Dr. A George Koshy, MD, DM, Professor,  
Department of Cardiology, Medical College,  
Thiruvananthapuram. Phone: 98472 50246  
E-mail: tvn\_agkoshy@sancharnet.in

**Conflict of Interest:** None declared

**Cite this article as:** A George Koshy. Management of Hypertension at Crossroads – What is the Current Status of Beta Blockers? Kerala Medical Journal. 2009 Jun 29;2(2):33-35

## REFERENCES

1. Carlberg B, Samuelsson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? *Lancet*. 2004 Nov 6;364(9446):1684–9.
2. Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet*. 2005 Nov 29;366(9496):1545–53.
3. Dahlöf B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*. 2005 Sep 10;366(9489):895–906.
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003 May 21;289(19):2560–72.
5. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*. 2002 Dec 18;288(23):2981–97.
6. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J*. 2007 Jun;28(12):1462–536.