

## ORIGINAL ARTICLE

### Cost effectiveness and anti-hypertensive efficacy of Metoprolol and Nebivolol - A Comparative Clinical Study

Siddharth Sonkar

Assistant Professor, Department of Medicine, Prasad Institute of Medical Sciences Lucknow, Uttar Pradesh, India

#### ABSTRACT:

**Background:** Hypertension is an increasingly prevalent chronic condition that is associated with serious morbidity and mortality. The present study was conducted to compare metoprolol and nebivolol in management of hypertension. **Materials & Methods:** The present study was conducted on 128 patients (males- 64, females- 64) age ranged between 18-60 years. They were divided into 2 groups of 64 patients each. Group I (32) received 10 mg nebivolol and in group II received 25 mg metoprolol. All were recalled to record blood pressure on day 1, day 25 and day 45. **Results:** Mean age  $\pm$ S.D (years) in group I was  $46 \pm 5.5$  and in group II was  $44 \pm 5.6$ . BMI (Mean  $\pm$  S.D) (Kg/m<sup>2</sup>) in group I was  $24.2 \pm 2.6$  and in group II was  $26.2 \pm 2.6$ . The difference was non-significant ( $P > 0.05$ ). In group I, the mean SBP  $\pm$ SD was  $160.4 \pm 4.6$ , on 25<sup>th</sup> day was  $148.2 \pm 3.4$  and on 45<sup>th</sup> day was  $140.4 \pm 2.2$ . In group II, the mean SBP  $\pm$ SD was  $162.1 \pm 4.0$ , on 25<sup>th</sup> day was  $150.2 \pm 4.2$  and on 45<sup>th</sup> day was  $138.2 \pm 2.4$ . The difference was significant within the group ( $P < 0.05$ ) whereas on comparison between the both groups, the difference was non-significant ( $P > 0.05$ ). **Conclusion:** Both nebivolol and metoprolol found to have comparable effectiveness in patients with hypertension.

**Key words:** Hypertension, Metoprolol, Nebivolol

**Corresponding author:** Dr. Siddharth Sonkar, Assistant Professor, Department of Medicine, Prasad Institute of Medical Sciences Lucknow, Uttar Pradesh, India-

**This article may be cited as:** Sonkar S. Cost effectiveness and anti-hypertensive efficacy of Metoprolol and Nebivolol - A Comparative Clinical Study. J Adv Med Dent Scie Res 2015;4(4):210-213.

#### INTRODUCTION

Hypertension is an increasingly prevalent chronic condition that is associated with serious morbidity and mortality. Hypertension is part of the group of cardiovascular diseases that symbolize the highest proportion of diseases mortality causes such as cerebral vascular accident (CVA) and acute myocardial infarction, reaching about 2/5<sup>th</sup> of the adult population in developed countries. It is an important risk factor for the development and progression of cardiovascular disease (CVD), which is the leading cause of death and disability worldwide.<sup>1</sup>

It is well established that both genetic and environmental factors play an important role as a etiological factors. The majority of hypertensive patients have cardiovascular risk factors such as diabetes mellitus (DM), smoking habits, overweight, salt ingestion, sedentary lifestyle, among others. It is then reconsidered to modify these factors to maintain a controlled blood pressure.<sup>2</sup>

In India, 23.10% men and 22.60% women > 25 years suffer from hypertension. Treating systolic blood pressure (SBP) and diastolic blood pressure (DBP) to targets that are <140/90 mmHg is associated with a decrease in CVD complications. Blood pressure (BP) reductions of 10 mmHg systolic or 5 mmHg diastolic are associated with a 33-48% reduction in stroke and a 17-27% reduction in coronary heart disease (CHD) events. It is necessary to sensitize the population to adopt a healthy lifestyle, not only a balanced

diet and the practice of regular physical activity, but also by frequent monitoring of BP.<sup>3</sup>

Carlberg et al. described in their meta-analysis that the efficacy and effectiveness of atenolol was found to be as good as that of placebo. Moreover, they challenge the use of atenolol as a reference drug in outcome trials of hypertension.<sup>4</sup>

Metoprolol is the cardioselective beta-1-adrenoreceptor blocker conventionally used to treat hypertensive patients particularly in developing countries such as India. Nebivolol 5 mg is likely to have advantages over existing antihypertensive drugs and may have a role in the treatment of hypertension.<sup>4</sup> The present study was conducted to compare metoprolol and nebivolol in management of hypertension.

#### MATERIALS & METHODS

The present study was conducted on 128 patients (males- 64, females- 64) diagnosed with hypertension. Patient age ranged between 18-60 years of age. Patients with pregnancy and/or lactation, patients with anuria, progressive and severe oliguria, hepatic coma, hypernatremia (sodium <135 mEq/ml), hypokalemia ( $K^+ < 3.5$  mEq/ml), hyperuricemia (uric acid >6 mEq/ml), systemic lupus erythematosus were excluded from the study. All were informed regarding the study and written consent was obtained. Ethical clearance was obtained prior to the study.

General information such as name, age, gender etc. was recorded. They were divided into 2 groups of 64 patients each. Group I (32) received 10 mg nebivolol and in group II

received 25 mg metoprolol. All were recalled to record blood pressure on day 1, day 25 and day 45.

**RESULTS**

**Table I Demographic data of patients**

Parameters	Group I	Group II	P value
Mean age ±S.D (years)	46± 5.5	44± 5.6	0.25
BMI (Mean± S.D) (Kg/m <sup>2</sup> )	24.2± 2.6	26.2± 2.6	0.42

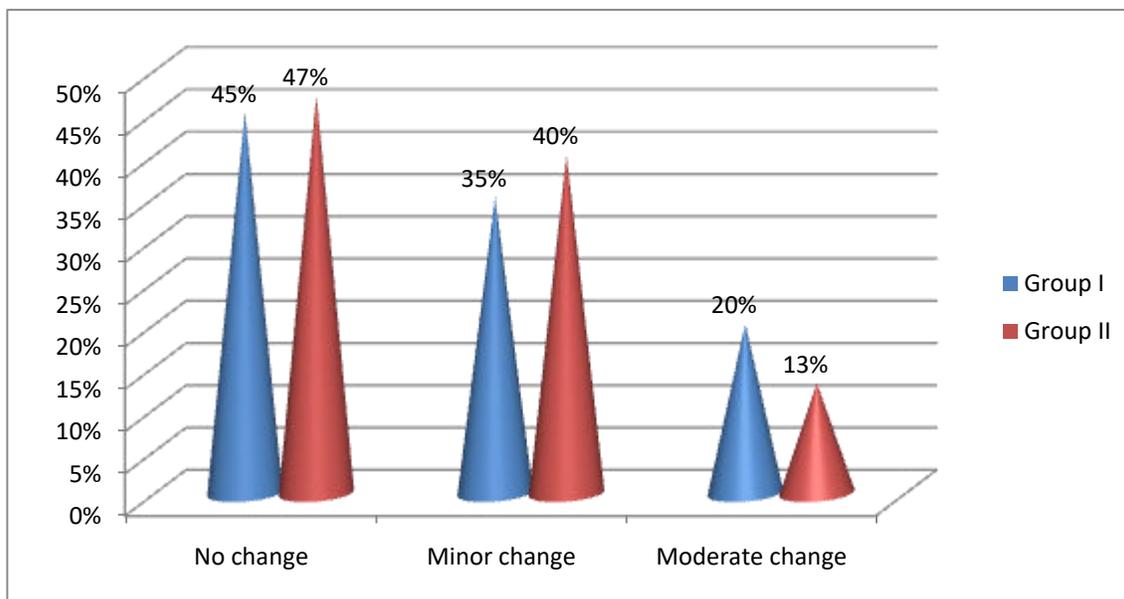
Mean age ±S.D (years) in group I was 46± 5.5 and in group II was 44± 5.6. BMI (Mean± S.D) (Kg/m<sup>2</sup>) in group I was 24.2± 2.6 and in group II was 26.2± 2.6. The difference was non- significant (P> 0.05).

**Table II Comparison in blood pressure in both groups**

Day	Group I	Group II	P value
1 <sup>st</sup>	160.4± 4.6	162.1± 4.0	0.1
25 <sup>th</sup>	148.2± 3.4	150.2± 4.2	0.5
45 <sup>th</sup>	140.4 ± 2.2	138.2 ± 2.4	0.4
P value	0.01	0.001	

In group I, the mean SBP ±SD was 160.4± 4.6, on 25<sup>th</sup> day was 148.2± 3.4 and on 45<sup>th</sup> day was 140.4 ± 2.2. In group II, the mean SBP ±SD was 162.1± 4.0, on 25<sup>th</sup> day was 150.2± 4.2 and on 45<sup>th</sup> day was 138.2 ± 2.4. The difference was significant within the group (P< 0.05) whereas on comparison between the both groups, the difference was non- significant (P> 0.05).

**Graph I Quality of life in both groups**



In group I, there was no change in quality of life in 45%, minor change in 35% and moderate change in 20% whereas in group II, there was no change in 47%, minor change in 40% and moderate change in 13%. The difference was non-significant (P> 0.05).

## DISCUSSION

Hypertension is defined as a SBP of 140 mmHg or more or a DBP of 90 mmHg or more or taking antihypertensive medication. Hypertension is classified as either essential hypertension (EH) or secondary hypertension, and EH accounts for about 90-95% of the cases characterized by high blood pressure with no obvious underlying medical causes. In developing countries, it is a major medical concern that the high rate of undetected and untreated EH. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence, averaging 35-40%; myocardial infarction (MI), averaging 20-25%; and HF, averaging >50%. In present study we compared metoprolol with nebivolol.<sup>5</sup>

We observed that Mean age  $\pm$ S.D (years) in group I was  $46 \pm 5.5$  and in group II was  $44 \pm 5.6$ . BMI (Mean  $\pm$  S.D) ( $\text{Kg}/\text{m}^2$ ) in group I was  $24.2 \pm 2.6$  and in group II was  $26.2 \pm 2.6$ . The difference was non-significant ( $P > 0.05$ ). In group I, the mean SBP  $\pm$ SD was  $160.4 \pm 4.6$ , on 25th day was  $148.2 \pm 3.4$  and on 45th day was  $140.4 \pm 2.2$ . In group II, the mean SBP  $\pm$ SD was  $162.1 \pm 4.0$ , on 25th day was  $150.2 \pm 4.2$  and on 45th day was  $138.2 \pm 2.4$ . The difference was significant within the group ( $P < 0.05$ ) whereas on comparison between the both groups, the difference was non-significant ( $P > 0.05$ ). This is in agreement with Uhlir et al.<sup>6</sup> The efficacy and safety of 2 cardioselective  $\beta$ -blockers, metoprolol 100 mg twice daily and nebivolol 5mg once daily, were compared in ISS patients with mild to moderate hypertension in a double-blind multicentre parallel-group study, which comprised an initial placebo phase followed by 3 months of active treatment. Complete normalization of blood pressure was achieved in 79% of patients in the nebivolol group and 66% in the metoprolol group. There were fewer adverse reactions in the nebivolol group and only those patients receiving metoprolol ( $n = 3$ ) had to discontinue treatment because of adverse effects. Nebivolol has the advantages of low dosage and once-daily administration which aid patient compliance; this is particularly important as treatment for hypertension is prolonged.

Christine Espinola-Klein et al. carried out a study to evaluate the effects and tolerability of nebivolol in comparison with metoprolol in these patients. In conclusion,  $\beta$ -blocker therapy was well-tolerated in patients with intermittent claudication and arterial hypertension during a treatment period of  $\approx 1$  year. In the direct comparison, there was no significant difference between nebivolol and metoprolol.<sup>7</sup>

We observed that there was no change in quality of life in 45%, minor change in 35% and moderate change in 20% in group I, whereas there was no change in 47%, minor change in 40% and moderate change in 13% in group II. The difference was non-significant ( $P > 0.05$ ). This is in agreement with Patel et al.<sup>8</sup>

Several studies also indicated that arterial hypertension is a disease with high prevalence in the elderly population,

becoming a determining factor in the high rates of morbidity and mortality of these individuals.<sup>9,10</sup> It affects nearly 60% of the elderly and is often associated with other diseases such as arteriosclerosis, diabetes mellitus and metabolic syndrome, conferring to this group a high cardiovascular risk. Dietary factors include sodium, potassium and obesity, which are the most frequently cited as being important risk factors for AH in most studies. As for sodium, there is a well-documented relationship between sodium intake and arterial hypertension in humans. Some studies have also shown that, associated with the genetic factor, sodium intake leads to a rapid increase in blood pressure<sup>11,12</sup>

## CONCLUSION

Both nebivolol and metoprolol found to be equally effective in patients with hypertension. Lifestyle and habits play an important role. The limitations of the study include the small sample size and recall bias commonly associated with survey-based studies. Similar studies on a larger scale would help remove this error and help make a categorical conclusion about the superiority of nebivolol over metoprolol.

## REFERENCES

1. Roman MJ, Devereux RB, Kizer JR, Okin PM, Lee ET, Wang W, Umans JG, Calhoun D, Howard BV. High central pulse pressure is independently associated with adverse cardiovascular outcome the Strong Heart Study. *J Am Coll Cardiol.* 2009; 54: 1730–1734.
2. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: Meta-analysis of 147 randomized trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009; 338:1665.
3. Ormond BA, Spillman BC, Waidmann TA, Caswell KJ, Tereshchenko B. Potential national and state medical care savings from primary disease prevention. *Am J Public Health* 2011; 101:157-64.
4. Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension. A meta-analysis? *Lancet.* 2005;366:1545–53.
5. Espinola-Klein C, Weisser G, Jagodzinski A, Savvidis S, Warnholtz A, Ostad MA, et al. Beta-blockers in patients with intermittent claudication and arterial hypertension: Results from the nebivolol or metoprolol in arterial occlusive disease trial. *Hypertension* 2011; 58:148-54.
6. Uhlir MF, Havránek K, Leffl erová J, Vojáček J, Widimský J, Winterová KZ. Nebivolol versus metoprolol in the treatment of hypertension. *Drug Investig* 1991; 3:107-10.
7. Espinola-Klein C, Weisser G, Jagodzinski A, Savvidis S, Warnholtz A, Ostad MA, et al. Beta-blockers in patients with intermittent claudication and arterial hypertension: Results from the nebivolol or metoprolol in arterial occlusive disease trial. *Hypertension.* 2011;58:148–54
8. Patel, Kamal H. Sharma, Nitisha A. Kamath, Nirav H. Patel, Ankita M. Thakkar. Cost-effectiveness analysis of nebivolol and metoprolol in essential hypertension: A pharmacoeconomic comparison of antihypertensive efficacy of beta blockers. *Indian Journal of Pharmacology* 2014; 46: 485- 490.

9. Ogden LG, He J, Lydick E, Whelton PK. Long-term absolute benefit of lowering blood pressure in hypertensive patients according to the jnc vi risk stratification. *Hypertension* 2000; 35:539-43.
10. The sixth report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1997; 157:2413-46.
11. Chalmers J, Zanchetti A. The 1996 report of a World Health Organization expert committee on hypertension control. *J Hypertens* 1996; 14: 929-33.
12. Chalmers J. Treatment guidelines in hypertension: Current limitations and future solutions. *J Hypertens Suppl* 1996; 14: 3-8.