

# A Prospective Real World Experience of Moxonidine Use in Indian Hypertensive Patients—Prescription beyond Current Guidelines

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## ABSTRACT

**Objective:** The primary objective of this study was to assess the use of moxonidine, a centrally acting anti-hypertensive agent in real world practice.

**Material and Methods:** Patients who attended out-patients clinic with diagnosis of hypertension were enrolled in the study. Demographics with co-morbid illnesses of all patients were recorded. Patient's prescriptions were recorded and anti-hypertensive medications were also analysed.

**Results:** A total of 990 patients were eligible during the study period. Moxonidine was used in 4.54% of patients. Two groups could be identified in moxonidine users – one Group with resistant hypertension (30 patients, 3.03% of total, 66.66%

of moxonidine users) on multiple drugs to control BP and another Group with intolerance to conventional, first line drugs (15 patients 1.51% of total, 33.33% of moxonidine users). Moxonidine was not used in newly diagnosed hypertension cases. Resistant hypertension and renal failure predicted the use of moxonidine. Majority of drug used was as per current guidelines.

**Conclusions:** Our study results reflected real world practice of current anti-hypertensive therapy. Patients generally receive medications in accordance with current recommendations and guidelines. Small but significant proportion of patients may require use of drugs like moxonidine to control high BP. Guidelines need to incorporate these real world practices.

**Key words:** Hypertension, Drugs, Moxonidine, Monotherapy, Polytherapy, Guidelines

## INTRODUCTION

Arterial hypertension affects approximately 25% of the global adult population and its prevalence and consequent health cost is predicted to rise above 1.5 billion hypertensive patients in 2025 [1]. Hypertension is common among Asians and the incidence is increasing in the Indian population, especially in the urban areas [2,3]. According to a WHO report on Global Status of Non-Communicable Diseases 2010, 33% of the adult Indian men and 30% of adult Indian women have high BP, implying that one in every three adult Indians is hypertensive. This increase in prevalence can be attributed to risk factors associated with urbanization, such as physical inactivity, smoking, high fat and low fruit/vegetable intake, obesity and diabetes. In a recent Indian Heart Watch study which took place over a period of five years (2006-2010) and involved 6,000 men and women from 11 cities across various regions of India, approximately one-third of the study participants had hypertension [4,5], of which only about half (57%) were aware of their high BP. Of these, only 40% were on treatment and only 25% had adequate control. This is in contrast to >75% awareness found in most high- and middle income countries, where >50% of people have their BP under control.

There is a linear relationship between Blood Pressure (BP) values and cardiovascular risk [6,7] and according to worldwide analysis, 7.6 million premature deaths (about 13.5% of total deaths), 54% of strokes and 47% of events occur due to coronary artery disease are attributed to high BP [8]. Most importantly, even modest BP reduction is accompanied by significant reduction in overall cardiovascular morbidity and mortality, irrespective of initial BP level [9-12]. Despite appropriate anti-hypertensive treatment, BP goals are not achieved in a large proportion of patients.

Majority of hypertensive patients cannot be controlled by using one drug. JNC 7, as well as the European Society of Hypertension

and Cardiology and the German Hypertension League have stated that large proportion of hypertensive patients will require a combination of two or more antihypertensive agents to achieve desired target BP [13-17].

Based on various guidelines, Calcium Channel Blockers (CCBs), Angiotensin Converting Enzyme Inhibitors (ACEIs), angiotensin Receptor Blockers (ARBs), diuretics (thiazide type), Beta Blockers (BBs) are prescribed to treat the hypertension, either alone or in combination. Therapeutic choice is guided by age and other co-morbid illnesses and evidence available with the molecule. However, in real world situation, drugs which are centrally acting are used due to various reasons. One such drug, Moxonidine, is available and is used to treat hypertension. Moxonidine is a centrally acting imidazoline receptor agonist that has been well tolerated as an effective anti-hypertensive agent [18-22]. However, its use in real world situation has not been reported previously. This study was intended to assess use of moxonidine in Indian hypertensive patients.

## MATERIAL AND METHODS

This prospective study was conducted at Navodaya Medical College and Hospital, Raichur, in Northern Karnataka, part of India, during the period from January 2011 to June 2012. Hypertensive male and female patients, aged >18 years, attending out-patient clinics of investigators were evaluated for inclusion in the study. Hypertension was diagnosed if patients were on anti-hypertension medications or their office BP was more than >140/90 mmHg as per guidelines. Each patient's demographics and BP medications were recorded along with co-morbid illnesses. Only new registrations were considered for inclusion. Pregnancy associated hypertension cases were excluded from the study.

This study was conducted according to Good Clinical Practice

guidelines and the Declaration of Helsinki, and the protocol was approved by the ethics committee of the hospital. Written informed consents were obtained from all the patients prior to their inclusion into the study.

## STATISTICAL ANALYSIS

Basic descriptive statistics were calculated and expressed as mean  $\pm$  SD. Statistical analysis was performed by using software MINITAB 16.

## RESULTS

During the study period, total, 990 [Table/Fig-1], (60% males and 40% females) patients were enrolled. Majority were under middle age ( $54.88 \pm 9.57$  years, range 28 to 72). Diabetes was present in 20% of the patients, known coronary artery disease was present in 18.18% patients, chronic renal failure was seen in 8.08% patients and current smoking was noted in 20% patients. Forty five (4.54%) patients were on moxonidine. Two groups could be identified in moxonidine users – one group with resistant hypertension [Table/Fig-2], 30 patients, 3.03% of total, 66.66% of moxonidine users) on multiple drugs to control BP and another group with intolerance to conventional, first line drugs (15 patients 1.51% of total, 33.33% of moxonidine users). Majority in first group had chronic renal failure (20 patients, 2.02% of total, 44.44% of moxonidine users  $p < 0.05$ , 66.66% of first group). Newly diagnosed patients or patients with diagnosis of heart failure were not on moxonidine. Monotherapy was noted in 240 (24.24%) patients and majority of them received multiple drugs (750, 75.75%). Monotherapy was common in newly diagnosed hypertensives (110 patients, 11.11% of total,  $p < 0.05$ ). ACEI and ARB use was more in younger patients ( $< 55$  years, 89.78%  $p < 0.05$ ) and CCB and diuretics were used more in older patients (81%  $p < 0.05$ ). Only 40% of patients previously diagnosed were well controlled by medications.

Age (N, Mean $\pm$ SD)	990	54.88 $\pm$ 9.57
Sex (M:F, N)	594:396	60:40
Diabetes (N, %)	198	20
CAD (N, %)	180	18.18
CKD (N, %)	80	8.08
Smoking (N, %)	198	20
Newly diagnosed HTN (N, %)	140	14.14

**[Table/Fig-1]:** Clinical characteristics

Monotherapy – newly diagnosed (N, % total)	110	11.11
Monotherapy – follow-up (N, % total)	110	11.11
ACEI & ARB in newly diagnosed (N, %)	75	53.57
CCB & Diuretics in newly diagnosed (N, %)	65	46.42
ACEI & ARB $< 55$ yrs (N, %)	423	89.78
ACEI & ARB $> 55$ yrs (N, %)	315	60.57
CCB & Diuretics $< 55$ yrs (N, %)	290	61.7
CCB & Diuretics $> 55$ yrs (N, %)	421	81
Moxonidine use total (N, %)	45	4.54
Moxonidine use – Monotherapy (N, %)	15	1.51
Moxonidine use – Polytherapy (N, %)	30	3.03

**[Table/Fig-2]:** Drug use

## DISCUSSION

Hypertension is one of the most important risk factors in the management of cardiovascular disease. Untreated hypertension leads to higher incidences of heart failure, myocardial infarction, stroke and renal disease. Pharmacological therapies remain the mainstay of anti-hypertensive treatments. Various guidelines are available for choosing anti-hypertensive agents [13-17]. It

is primarily based on age and co-morbid conditions. ACEIs or low cost ARBs are recommended as first line drugs in younger hypertensives, while CCBs and diuretics are recommended for older patients. However, in real world situation, due to various reasons (adverse reactions, side effects, drug-drug interactions, co-morbid illnesses, resistance cases, etc), drugs belonging different classes are used either alone or in multiple combinations, which are beyond the recommended guidelines at times.

We assessed moxonidine (which is a centrally acting imidazoline receptor agonist) use in patients attending out-patient clinic, representing real world practice. In our study, 4.5% patients were receiving moxonidine as antihypertensive agent. This appears to be significant finding. We identified two groups of patients who received moxonidine – first, with resistant hypertension, requiring multiple drugs and second, with intolerance to recommended first line drugs.

Majority of hypertensive patients (75.75%) were on combination of drugs to control high BP, which was in accordance with earlier reports. Only 40% in ALLHAT trial, 60% of those whose BP was controlled to  $< 140/90$  mmHg received two or more agents, and only 30% overall were controlled on one drug. In hypertensive patients with lower BP goals or with substantially elevated BP, three or more anti-hypertensive drugs may be required [23].

None of the newly diagnosed patients received moxonidine, which was also in accordance with recommended guidelines and also, patients with diagnosis of heart failure did not receive moxonidine, as adverse mortality effects of central sympathetic inhibition with sustained release moxonidine had been reported earlier [24]. Presence of resistance hypertension and renal failure appears to predict the use of drug like moxonidine. Patients with chronic renal failure have difficulty in controlling the hypertension, thus requires multiple medications with maximum tolerated doses.

**Limitations:** Our study population represented patients attending general medical out-patients clinic who were under physicians' care. General population meeting general practitioners or family physicians may be different. Also, patients attending speciality clinics (like hypertension clinic, nephrology clinic or cardiology clinic) may receive different combinations of medications. Further studies are required to assess those patient populations. Only new registrations were included in this study. Significant medication changes in hypertensive patients is not uncommon.

## CONCLUSIONS

Our study results reflect real world practice of current anti-hypertensive therapy. Patients generally receive medications in accordance with current recommendations and guidelines. Small proportion of patients may require use of drugs like moxonidine to control high BP. Guidelines need to incorporate these real world practices.

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