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## The next big thing: A case report on Blood Pressure Variation encountered in my clinic

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### ABSTRACT

The role of high Blood Pressure levels on target organ damage and the protective effects of antihypertensive therapy have been extensively established in clinical practice [1]. Mortality from ischemic heart disease and stroke doubles every increment in 20 and 10 mmHg of systolic and diastolic blood pressure [1]. Nowadays, besides usual blood pressure other parameters contribute to TOD in hypertensive patients [2]. Blood pressure is a constant variable and it shows marked spontaneous oscillations over short-term (minutes to days) and long-term (month) periods [3]. Early reports from animal models of cardiovascular variability have clearly demonstrated the relationship between excessive fluctuation in blood pressure values and the development of target organ damage [4]. The initial hypothesis was further corroborated by clinical studies in hypertensive subjects showing that the assessment and quantification of Blood Pressure Variability (BPV) is of physio-pathological and prognostic importance [5]. In recent years, many preclinical and clinical studies have clearly identified the contribution of BPV to the cardiovascular complications associated with hypertension [6]. Moreover, preliminary data from retrospective analysis of clinical trials suggest that attenuation of BPV by antihypertensive agents contribute in the prevention of major cardiovascular events in hypertensive patients [7]. Considering the recent advances in the knowledge of the pathological role and clinical significance of BPV in cardiovascular diseases, the present case illustrates the Blood Pressure Variation in a routine OPD setting.

**Keywords:** Blood Pressure, Animal models

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## CASE REPORT

### **Patient presentation:**

A 29 year well-built male (BMI – 27Kg/m<sup>2</sup>), nonsmoker, social drinker, presented with elevated BP – 150/90mmHg. In the last one year, he was on Amlodipine 5mg OD with lifestyle modification advised by his physician. No Previous history of any illness. Both his parents were hypertensive and were on medication. On Random BP checks, he found his BP ranging from 160/100mmHg – 140/90mmHg and was very much concerned about his health. He expressed that despite strict adherence to lifestyle modifications, exercise, salt restriction, the BP was not under control. His CVS was normal without any murmurs. His CNS was well oriented. His routine blood reports, abdominal USG, fundoscopy, and ECG were all normal. Since the patient was young he was asked to check his ambulatory BP for 3 times a day (morning, afternoon and night) for 4 days. His BP readings were as follows: Day 1 (142/90, 148/90, 160/100), Day 2 (140/90, 150/90, 160/100), Day 3 (154/90, 140/90, 146/98) and Day 4 (144/90, 140/90, 158/94). BP measurements suggest that he was a non – dipper with consistent night BP – 160/100mmHg.

### **Treatment:**

Patient was switched to Olmesartan 20mg OD and was asked to maintain the BP chart. The second follow up in-clinic BP was 150/96mmHg and patient presented with a similar profile of fluctuating BP. So Olmesartan dose was titrated up to 40mg OD and BP monitoring was continued. His follow-up BP measurements were: Day 1 (150/90mmHg, 154/90 mmHg, 150/98 mmHg), Day 2 (146/94 mmHg, 144/92 mmHg, 148/90 mmHg), Day 3 (136/84 mmHg, 138/86 mmHg, 132/84 mmHg), Day 4 (132/86 mmHg, 130/80 mmHg, 130/80 mmHg). Addition of Olmesartan reduced both mean BP and BPV.

### **DISCUSSION:**

Many of the Indian patients have high sympathetic drive and it seems to have some connection with high BPV. Patients and physicians must be educated more on the use of HBPM and ABPM. Different classes of drugs such as ACEIs, ARBs and CCBs are regularly used to control high BP in heart patients.

There are lot evidences which illustrates blood pressure shows long-term variability (day-to-day, visit-to-visit, or seasonal) that has been associated with increased risk of cardiovascular disease. Nowadays, factors contributing in long-term BPV are relatively unknown; it has been suggested that behavioural changes play a central role in day-to-day variation [8]. More recently, increased arterial stiffness has been found to contribute in long-term BPV as a pathological mechanism. The Multiethnic Study of Atherosclerosis (MESA)

has recently demonstrated a reduction in aortic distensibility and arterial elasticity in patients while it increased in hypertensive patients with higher visit to- visit BPV <sup>[9]</sup>.

In addition, large variation in visit-to-visit BPV could be a consequence of poor BP control in treated patients or inconsistent office BP readings <sup>[8]</sup>. Therefore, patient compliance with the prescribed therapeutic regimen and correct dosing and titration of blood pressure lowering medication can influence day-to-day and visit-to-visit BPV. Measurement of day-to-day BPV can be performed using ABPM over consecutive days or by HBPM. Although utility of self-measurement of blood pressure for long-term BPV is limited by its standardized conditions, it can be used to monitor BP changes over several days in patients with stable treatment regimen <sup>[8]</sup>. Visit-to-visit BPV can be assessed by Office Blood Pressure Monitoring or between-visit Ambulatory Blood Pressure Monitoring; however, estimation of long-term using OBPM requires a consistent number of visits to achieve a meaningful value. In addition, measurement of BP at the office does not provide data regarding BP during usual activities and has limited value as indicator of BP control [8]. The use of 24 h ABPM overcomes limitations of OBPM considering that it provides extensive information on BP levels within a given 24 hour period. Nevertheless, ABPM cannot be routinely used to assess visit-to-visit BPV <sup>[8]</sup>.

Expanding evidence has clearly demonstrated the influence of short-term and long-term BPV on target organ damage and cardiovascular events in hypertensive patients. Degree of short-term BPV is independently associated with target organ damage and rate of cardiovascular events in both the general population and in subjects with hypertension <sup>[5]</sup>. Parati et al. first demonstrated the existence of an independent association between both 24 hour mean BP and 24 hour BPV with the prevalence and severity of target organ damage in 108 mild-to-severe essentially hypertensive patients <sup>[9]</sup>. Moreover, for any given 24 hour mean BP value, the prevalence and severity of target organ damage were linearly related to the extent of short-term BPV <sup>[10]</sup>. In another study, the prognostic relevance of short-term BPV was assessed in 73 hypertensive patients using intra-arterial BP measurement. After a follow-up period of 7 years, baseline BPV was found to be a contributor for the development of cardiovascular complications, particularly left ventricular hypertrophy <sup>[11]</sup>. Daytime systolic BPV estimated by SD obtained from 24 hour ABPM has been found to be associated with increased vascular damage and left ventricular hypertrophy in over 700 subjects with normotension or hypertension of different degrees of severity <sup>[12]</sup>. In addition, the European Lacidipine Study on Atherosclerosis (ELSA) has shown that carotid intima media thickness was related with 24 h systolic BPV assessed by SD suggesting the relationship between short-term BPV and alterations of large artery structure in hypertension <sup>[13]</sup>.

In another, a large-scale study involving 635 patients with mainly mild to moderate hypertension were randomised to 8 weeks of treatment with either Olmesartan medoxomil 20 mg/day or candesartan cilexetil 8 mg/day. Changes from baseline during the last 4 and 2 hours of ambulatory BP measurement (ABPM) after 1, 2 and 8 weeks of treatment were compared between the two groups., in which 635 patients with mainly mild to moderate hypertension were randomised to 8 weeks of treatment with either Olmesartan medoxomil 20 mg/day or candesartan cilexetil 8 mg/day. Changes from baseline during the last 4 and 2 hours of ambulatory BP measurement (ABPM) after 1, 2 and 8 weeks of treatment were compared between the two groups. In addition, the proportions of patients who achieved various ABPM goals, including those suggested by the European Society of Hypertension/European Society of Cardiology (ESH/ESC) [ $<125/80$ mm Hg] and the Japanese Society of Hypertension (JSH) [ $<135/80$ mm Hg], over 24 hours, during the daytime and at the last 4 and 2 hours of ABPM measurement were also compared. After 8 weeks, significantly greater proportions of patients treated with Olmesartan medoxomil 20mg achieved 24-hour and daytime ABPM goals recommended by the guidelines of the ESH/ESC (25.6% and 18.3%, respectively) and JSH (37.5% and 26.6%, respectively) compared with candesartan cilexetil 8mg (24-hour ESH/ESC goal = 14.9%,  $p < 0.001$ ; 24-hour JSH goal = 26.6%,  $p = 0.003$ ; daytime ESH/ESC goal = 9.6%,  $p = 0.002$ ; daytime JSH goal = 16.4%,  $p = 0.002$ ). During the last 4 hours of 24-hour ABPM, the proportions of patients who achieved the ESH/ESC and JSH ABPM goals were significantly greater with Olmesartan medoxomil (33.3% and 39.1%, respectively) than with candesartan cilexetil (22.9%,  $p < 0.001$  and 31.6%,  $p = 0.047$ , respectively). Similarly, during the last 2 hours of 24-hour ABPM, the proportions of patients who achieved these BP goals were either significantly greater (JSH) or approached statistical significance (ESH/ESC) with Olmesartan medoxomil (26.9% and 19.9%, respectively) compared with candesartan cilexetil (19.6%,  $p = 0.028$  and 14.3%,  $p = 0.061$ , respectively). Even in our case that adding Olmesartan has shown a significant reduction of Blood Pressure Variation and help the patient to achieve the BP goal.

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