Effect of atenolol on hemoglobin level in mild to moderate hypertension

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INTRODUCTION

Hypertension is one of the important public health problems worldwide. A recent report on the global burden of hypertension indicates that nearly one million adults had hypertension in 2000, and this is expected to increase to 1.56 million by 2025.1 A meta-analysis of hypertension prevalence rates in India showed a significant rise in the prevalence of the disease over the years and the disease burden in India are now almost comparable to those in the USA.2 Hypertension is the most common cardiovascular disease and major cardiovascular risk factor that cause significant morbidity and mortality. Complex interaction of multiple vascular effectors including the activation of the sympathetic nervous system, renin-angiotensin-aldosterone system and the inflammatory mediators is attributed to the pathophysiology of hypertension.

ABSTRACT

Background: Hypertension is the most common cardiovascular disease and a major cardiovascular risk factor that causes significant morbidity and mortality worldwide. Most common type is primary (essential) hypertension and is genetically determined. It affects many systems of the body and can also alter various hematological parameters. The study was undertaken to check the effect of atenolol on hemoglobin (Hb) level in mild to moderate hypertension.

Methods: The study was prospective and non-randomized. Thirty newly diagnosed hypertensives selected for atenolol therapy by medicine personnel were enrolled in the study based on inclusion and exclusion criteria. Patients were divided into pre-treatment (before starting atenolol therapy) and post-treatment group. Red blood cell (RBC) count, Hb, packed cell volume (PCV) and red cell indices were measured at the time of enrolment and then monthly after starting atenolol for next 3 months.

Result: Results were analyzed by repeated measure analysis of variance. Atenolol treatment was found to increase Hb and PCV significantly, whereas no significant change in RBC count and red cell indices.

Conclusions: Treatment with atenolol for mild to moderate hypertension has shown a significant increase in Hb and PCV level. This positive effect may be because of the decrease in sodium and water reabsorption by decrease in sympathetic overactivity and excretion of sodium and water by improvement in kidney functions. Atenolol has no any direct effect on Hb synthesis and erythropoiesis.

Keywords: Hemoglobin level, Hypertension, Packed cell volume, Sympathetic overactivity

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Lesser Hb concentration due to stress induced hypertension can lead to increased cardiac output and heart failure. Anemia in cardiovascular disease is associated with an increase in mortality, morbidity and hospitalizations.

There is the role of Hb while monitoring the prognosis of hypertensive patients. Atenolol is among the commonly used β-blocker for the treatment of hypertension, one of its mechanisms is by decreasing sympathetic activity. Considering all the above facts, relationship between sympathetic overactivity, hypertension and anemia is complex. Thus, this study was designed to check the effect of atenolol on Hb in mild to moderate hypertensive patients. If atenolol shows a positive impact on Hb in hypertensive patients, hypothesis about additional benefit of atenolol in these patients can be made and tested by further research.

METHODS

Study subjects

The study was conducted at the New Civil Hospital, Surat during the period from September 2012 to March 2013. The study was approved by the local Institutional Ethics Committee. Mean age of 30 male individuals participating in the study is 30.93±7.23 years. Informed consent of each participant was taken. The individuals participating in this study were divided into two groups: pre-treatment group (newly diagnosed hypertensive patients) and Post-treatment group (newly diagnosed hypertensive patients started on atenolol therapy). Selection of patient was based on inclusion and exclusion criteria.

Inclusion criteria

1. Essential hypertension defined according to the criteria of the VII Joint National Committee (JNC VII).
2. Patient with mild to moderate hypertension (JNC VII).
3. Never treated previously for hypertension before the beginning of the study.

Exclusion criteria

1. Any other cardiovascular diseases like myocardial infarction, CHF etc.
2. Neurological involvement.
3. Diabetes mellitus.
4. Renal diseases.
5. Any other medication is affecting Hb such as multivitamins, iron, food supplements etc.
6. History of hookworm infestation and malaria.
7. Active viral and bacterial infections.
8. Alcoholics.

After enrollment, hypertensive patients were treated with antihypertensive drug β-blocker (atenolol - 50 mg) and followed up through 3 month’s period. The blood samples were collected for the estimation of hemoglobin level, red blood cell count (RBCs) and other parameters like mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) at the time of the first evaluation before starting atenolol treatment and every monthly for next 3 months during the antihypertensive treatment. During atenolol treatment, the patient is on his or her regular diet.

Statistical analysis

All values are expressed as mean±standard deviation. Comparison of systolic blood pressure (SBP), diastolic blood pressure (DBP) and hematological parameters between pre-treatment group and post-treatment group (post-treatment group includes atenolol treated group at 1 month, 2 months and 3 months) is performed by repeated measures analysis of variance (ANOVA) test with Greenhouse–Geisser correction and post-hoc analysis with Bonferroni correction. p<0.05 is taken as statistical significant. All statistical analysis is by using International Business Machines Corporation (IBM) SPSS 17.0 software.

RESULTS

Effect on SBP, DBP, packed cell volume (PCV) and Hb level

Atenolol treatment significantly reduces systolic and DBP as compared to pre-treatment group with p<0.05 (Figure 1). Repeated measure ANOVA with Greenhouse–Geisser correction reveals statistically significant difference in Hb
Effect on RBC count, MCV, MCH and MCHC

RBC count, MCV, MCH and MCHC does not differ significantly at different time points on repeated measure ANOVA (Tables 1 and 2, Figures 2-4).

DISCUSSION

Elevated BP is a strong, independent, and modifiable risk factor for stroke and heart disease, CAD and renal failure. Most common variant of hypertension is essential hypertension, where increased sympathetic overactivity is responsible for the majority of cases.10 Patients of hypertension have a hyperdynamic circulation driven by increased efferent sympathetic nerve firing to skeletal muscles and elevated levels of norepinephrine in heart and kidneys. Sympathetic activation stimulates heart, elevating cardiac output, causing naturally mediated vasoconstriction, and augmenting renin secretion and tubular reabsorption of sodium, increasing total body fluid volume.11 Sustained sympathetic activation contributes to long-term BP regulation because the renal sympathetic nerve potently stimulates the renin release by stimulation of β1 adrenergic receptor and renal sodium reabsorption. Radiofrequency ablation of renal sympathetic nerves markedly lowers BP in refractory hypertensives.12,13

In high-risk population with isolated systolic hypertension and left ventricular hypertrophy, lower Hb at baseline was associated with higher probability of cardiovascular death, and decrease in Hb over time was associated with higher probability of cardiovascular death or stroke.14 Recently, studies have shown that hypertensives have tendency for lesser Hb level when compared to normotensives.8,9 There are multiple factors responsible for lesser Hb level in cardiovascular disease such as hemodilution,15 pro-inflammatory cytokines, malnutrition due to right-sided heart failure, iron deficiency, decreased bone marrow perfusion and drug therapy for hypertension (like angiotensin converting enzyme inhibitors, aspirin), decreased erythropoietin production and decreased iron supply for erythropoiesis. Several of these mechanisms act simultaneously, and the anemia is the result of a complex interaction between them.16,17 Long-standing high BP affects kidney, heart and many organs leading to chronic anemia.18,19 Anemia can worsen the consequences of hypertension (precipitate HF) and treatment of anemia with erythropoietin or with iron preparations has a favorable impact on long-term complications of hypertension.20,21 Previous studies have showed stress associated increased sympathetic activity is culprit behind lesser Hb in hypertensives.8,9

### Table 1: RBC, Hb and PCV before and after atenolol treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Atenolol treated group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>After 1 month</td>
</tr>
<tr>
<td>RBC count/μL</td>
<td>4.240±0.403</td>
<td>4.298±0.45</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>13.32±1.03</td>
<td>13.41±1.00*</td>
</tr>
<tr>
<td>PCV%</td>
<td>35.16±2.88</td>
<td>35.65±2.52*</td>
</tr>
</tbody>
</table>

*p<0.05 versus baseline. RBC: Red blood cell, Hb: Hemoglobin, PCV: Packed cell volume

### Table 2: MCV, MCH and MCHC in newly diagnosed hypertensive patients and effect of atenolol therapy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Atenolol treated group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>After 1 month</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>83.58±9.67</td>
<td>83.85±7.99</td>
</tr>
<tr>
<td>MCH (Pg)</td>
<td>31.66±3.57</td>
<td>31.35±3.07</td>
</tr>
<tr>
<td>MCHC (g/dL)</td>
<td>38.08±3.86</td>
<td>37.76±3.60</td>
</tr>
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</table>

MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular hemoglobin concentration
Sympathetic overactivity associated increase in β₂ mediated renin release results in hemodilution via the aldosterone. This sympathetic-adrenal axis induce hemodilution is responsible for lesser Hb in hypertensives when compared to normotensives. In CHF pseudo anemia is mainly because of hemodilution besides other factors. Atenolol is one of the commonly prescribed drugs in young hypertensives without other compelling indications. It is an inexpensive and effective drug for the treatment of hypertension especially for developing countries like India. In this study, atenolol treatment in mild to moderate hypertension increases the Hb and PCV, but has no effect on RBC count, MCV, MCH and MCHC. Change in Hb and PCV is seen for initial 2 months of treatment but not after 2 months. Possible explanation is decrease in sympathetic overactivity induced hemodilution by β-blocker. This is evident after 1 and 2 months of atenolol treatment, but not after 3 months because β-blockers take several weeks to develop their full-fledged actions. Sympathetic overactivity is the primary cause in essential hypertension. Hypothalamic-adreno-sympatho activity mediated increased sympathetic drive influences renin-angiotensin-aldosterone system and is responsible for low Hb in hypertensives. In the true sense, this pseudo increase in Hb and PCV is mainly because of improved blood circulation and decreased in sodium water reabsorption. Other parameters like MCH, and MCHC not affected as atenolol has no any direct effect on Hb synthesis and erythropoiesis.

CONCLUSIONS

Treatment of atenolol in mild to moderate hypertension has a positive impact on Hb and PCV level. This positive impact is because of improvement in blood circulation and decreases in sodium water reabsorption by decrease in sympathetic overactivity. Atenolol has no any direct effect on Hb synthesis and erythropoiesis.

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