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Case Report

First Dose Hypotension by Telmisartan: A Rare Adverse Effect in a Case of Partial Renal Artery Stenosis

Saif Zil Kibriya[1], Faiz Muqtadir[2], Sadaf Rakhshan[3], Shireen Rokodia[4], Anand Nagalikar[5]

[1]Senior Resident, Dept. of Medicine ESIC Medical College, Gulbarga.
[2]Senior Resident, Dept. of ENT, ESIC Medical College, Gulbarga
[3]Consultant Gynecologist.
[4]Assistant Professor Saptagiri Medical College, Bangalore.
[5]Assosiate Professor, KBNIMS, Gulbarga, Karnataka, India.

Corresponding Author: Saif Zil Kibriya

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ABSTRACT

Hypotensive actions of antihypertensive medication are accentuated in conditions of chronic heart failure and renal artery obstruction (unilateral or bilateral). Apart from angiotensin type 1 receptor blockers, almost all antihypertensives (including adrenergic alpha 1 receptor antagonist, adrenergic beta 1 receptor antagonist, calcium channel blockers and angiotensin converting enzyme inhibitors) have first dose hypotension as an adverse effect.

Telmisartan can cause first dose hypotension unlike other angiotensin type 1 receptor blocker due to its unique PPAR-gamma modulating activity. These effects are more pronounced in patients with renal artery obstruction (unilateral or bilateral). Hence prescription of this drug should be exercised with precaution in such patients.

Keywords- First dose hypotension, Telmisartan, PPAR-gamma, Renal artery stenosis

INTRODUCTION

Angiotensin 2 of the renin-angiotensin aldosterone system is implicated in the pathogenesis of essential hypertension, renovascular hypertension and congestive cardiac failure. [(1-3)]

Angiotensin converting enzyme inhibitors and angiotensin type 1 receptor blocker (which counteract effects of angiotensin 2) are thus the most effective medical therapy for renovascular hypertension. [(4)]

Angiotensin type 1 receptor blockers have a favourable adverse effect profile compared with angiotensin converting enzyme inhibitors similar to placebo. [(2)]

Telmisartan, the longest acting angiotensin type 1 receptor blocker has excellent tolerance.[(2)] No first dose hypotension has been reported with this drug. [(5)] The authors believe that this case report is the first case reported with such an adverse effect.

CASE REPORT

A 35 year old female patient, newly diagnosed hypertensive grade 2 was prescribed telmisartan 40 mg by a duty

doctor. After 30 minutes she was rushed to the medical emergency with complaints of giddiness, light headedness and syncope. The patient's attendees gave the history that the patient went pale and remained unresponsive for few seconds.

No previous history of cardiovascular disorder, including valvular heart disease or arrhythmias could be obtained and history suggestive of primary autoimmune degenerative disorders and peripheral neuropathy was absent. No history of any medication in the past was significant.

Vitals: Radial blood pressure was 140/100 in supine position and 100/80 in erect posture. Symptoms were exaggerated in erect position. Pulse rate was 76 per minute regular, normal rhythm in both supine and standing position.

Urine output was normal.

General physical and systemic examination did not show any abnormality.

INVESTIGATIONS

Total count was 5600 cells/mm^3, HB% 11.2gm%, RBS 102mg/dl, blood urea 36, serum creatinine 1.2 and urine examination was normal.

ECG and ECHO were found to be normal with no evidence of arrhythmias, valvular or ischaemic heart disease.

CT scan of brain was normal.

USG abdomen showed right kidney was (9 x 4 cms) (fig1) while the left kidney measured (10.2 x 4.6 cms), with the intrarenal echotexture showing grade 1 renal parenchymal disease of right kidney; the left kidney was normal(fig2).

Renal Doppler evaluation – right renal artery at hilum shows dampened flow with increased acceleration time (pulsus parvus form) and high resistivity index (0.9) implying haemodynamically significant stenosis at hilar portion of right renal artery(fig3).

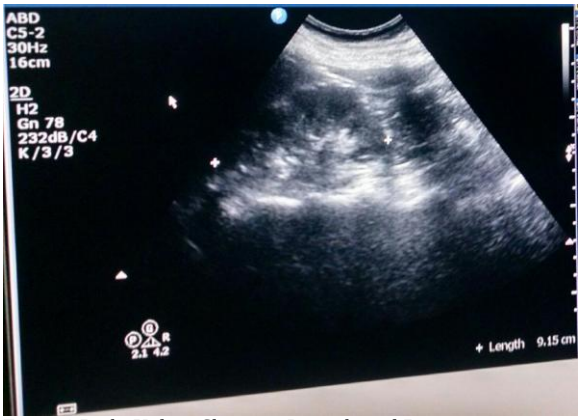

Figure 1.Right Kidney Showing Parenchymal Disease

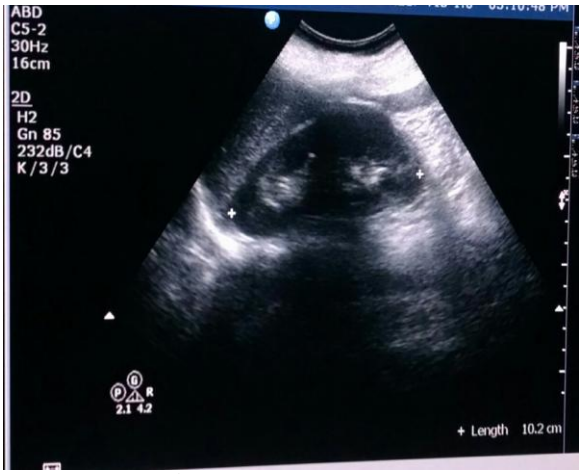

Figure 2.Normal Left Kidney

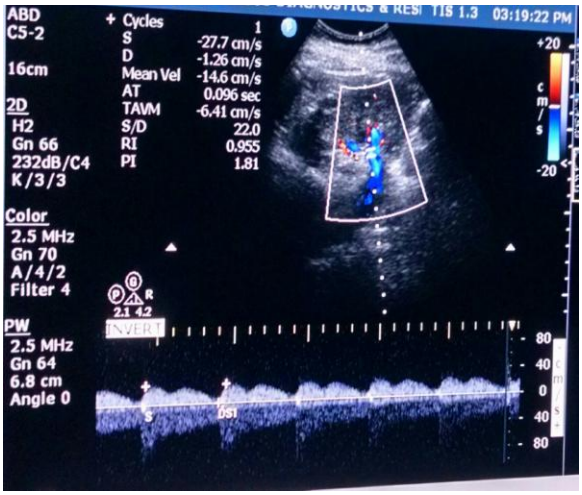

Figure 3.Right Renal Artery Doppler Showing Heamodynamically Significant Stenosis at Hilar Portion and Pulsus Parvus Form.

The left renal artery at both hilum and origin, right renal artery at origin and intrarenal branches of both right and left

renal arteries show normal flow with resistivity index (0.5).(fig4 and fig5)

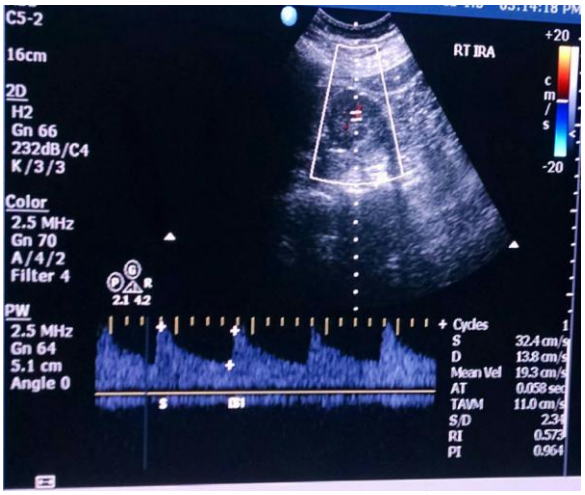

Figure 4.right intrarenal vessels showing normal flow.

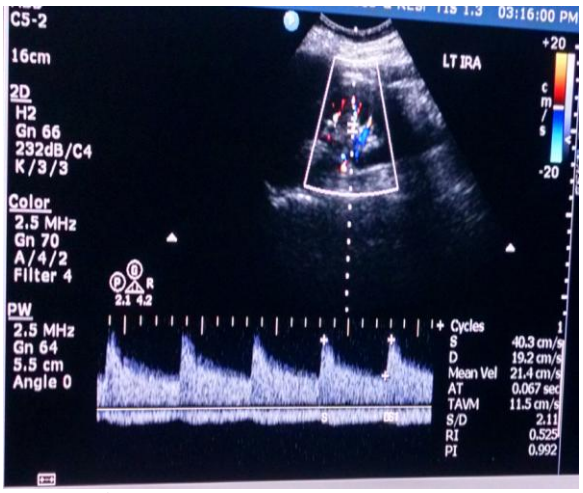

Figure 5.Left Intrarenal Vessels Showing Normal Flow

DISCUSSION

First dose hypotension is a sudden and severe fall in blood pressure occurring when changing from a lying down to standing posture the first time an antihypertensive drug is used. [6] Classically orthostatic hypotension is a reduction in Systolic blood pressure of at least 20 mm of mercury or diastolic blood pressure of at least 10 mm of mercury within 3 minutes of standing or head up tilt. [7]

In our case this 35 year old hypertensive female developed orthostatic hypotension within 30 minutes of administration of telmisartan. As per casualty assessment of Narango algorithm with a score of 6, the present adverse drug reaction can be labelled as probable. [8]

The present adverse drug reaction could not be explained with the mechanism of angiotensin antagonism, this unpredictable reaction cannot be labelled as type A or type B.

The USG report of the patient indicated significant unilateral right renal artery obstruction, while other causes of secondary hypertension were ruled out (ECHO, ECG, CT scan, thyroid profile, vanillylmandellic acid level in urine were normal). Digital angiography was not done as facilities were not present in our hospital.
G Manacea and Schmacher reported that the incidence of serious adverse effects with telmisartan was less compared to Angiotensin converting enzyme inhibitors and tolerance of patients in case of telmisartan was better. [9] Similar reports by Mazzoli et al indicated that first dose hypotension phenomenon was not seen with angiotensin type 1 receptor blocker. [5]

Thus, the pathophysiological phenomenon remains unknown, not fully explained by angiotensin antagonism. The proposed mechanism of PPAR modulating activity was first reported by Stephen et al highlighting this unique characteristic of telmisartan which can cause direct vasodilation. [10] A report by Vladmir et al that PPAR-GAMMA controls renin expression supports this concept. [11]

Therefore, in our study case with renal artery obstruction with hyperreninemia and over expression of renin gene due to renal hypoperfusion, [12] telmisartan can cause severe hypotension by PPAR-GAMMA partial agonist action.

There is a need for further studies both in animals and human beings to subject this hypothesis to test. The case report

assumes significance as a pointer to an alternate pathway to control hypertension in human beings.

CONCLUSION

First dose hypotension can follow prescription of telmisartan in patients with partial renal artery obstruction. Precaution should be exercised while prescribing telmisartan in such patients.

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