(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume2, Issue 2, Page No: 314-318
March-April 2019

Clinical Impact of Rifampicin In A Patient Of Hypertension With Chronic Kidney Disease And Tubercular Pleural Effusion: A Case Report

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Type of Publication: Case Report
Conflicts of Interest: Nil

ABSTRACT

A 40 years old male with severe hypertension, chronic kidney disease and tubercular pleural effusion on category 1 anti-tubercular drugs was admitted. Inspite of using six different classes of Anti- Hypertensive drugs including diuretics, BP was not reduced to target level. BP responded after stopping Rifampicin. This highlights importance of drug interaction in a multi treatment regimen.

Keywords: hypertension, rifampicin, diuretics, drug interaction

INTRODUCTION

Refractory hypertension is defined as uncontrolled blood pressure despite use of ≥5 antihypertensive agents of different classes, including a long-acting thiazide-like diuretic and an MR (mineralocorticoid receptor) antagonist, at maximal or maximally tolerated doses. [1] The management of patients with resistant hypertension requires a gratifying combination of clinical acumen and implementation of evidence-based medicine.

We present a case of refractory hypertension.

Case report

A 40 year old right handed married Muslim male, male nurse by occupation, resident of Sawai madhopur, Rajasthan presented with complaints of headache 15-20 days and restlessness 4-5 days.

History of present illness: Patient was apparently asymptomatic 15 days back then he developed headache which was insidious in onset, continuous in nature, mild and in occipital region, not associated with any aggravating factor and not relieved with medication. There wsa no history of fever, chest pain, palpitation, cough, nausea, vomiting, head injury and obstructive sleep apnoea.

Past history: He is known case of hypertension (HTN) and chronic kidney disease (CKD) since 1year and tubercular pleural effusion on ATT category I since 2 months. There is no history of type 2 DM, COPD and thyroid disorder

Family history: not significant

Personal history: Non alcoholic, non smoker, non vegetarian, normal bowel and bladder habits. Normal sleep pattern

General physical examination

- Patient was concious, cooperative, well oriented to time, place and person, moderately built and nourished. Skin, conjunctivae, tongue and nails were pale, Sclera white, no clubbing, no icterus, cynosis, edema feet, no significant lymphadenopathy. JVP was not raised. Afebrile (98.4^0F)
- His BP was 230/130 mm hg in both upper arms in supine position and 240/140 mm hg in both lower limbs in supine position.
- Pulse 96/minute, regular, high volume, no radio radial and radio femoral delay, All peripheral pulses palpable and arterial wall not thickened. Respiratory rate 20/minute abdomino thoracic

Systemic examination

- CVS - S1S2 normal, tachycardia present, no murmur
- Respiratory - bilateral air entry normal & equal, Normal vesicular breath sounds, No crepts and wheezes
- CNS- No neurological deficit, No abnormal gait, Plantar bilateral flexor, Pupil bilateral round, regular and reactive, Superficial and deep tendon reflexes normal, No sign of meningeal irritation, Fundoscopic examination normal.
- GIT - Abdomen soft and nontender, Liver and spleen not palpable, Kidneys are non ballotable, Bowel sounds were present. No bruit were present.

Investigation

The patient's Hemogram showed Hb to be 8.2 gm%, TRBC 2.26 million/cubic mm, PCV 24.8% with normocytic normochromic anemia. Other blood indices were in normal range. Fasting blood sugar was 102 mg/dl, urea 139 mg/dl, creatinine 4.3 mg/dl, electrolyte sodium 135, potassium4.4, chloride 102, calcium 6.61mg/dl, phosphorus 9.26 mg/dl, S uric acid 12.3 mg/dl.

LFT, lipid profile and viral markers were normal.

Urine examination showed proteinuria 2+ with 24 hour urinary protein as 200 mg. There was 6-8 RBC in urine. 24 hour urinary sodium was 136 mEq/L and VMA was 4.6 mg. GFR was 55 ml/min/1.73 m.

PTH was 176 pg/ml.

ECG and 2 D echocardiography were unremarkable.

USG Abdomen was normal except kidney size. Rt kidney -91 x 36 mm, left kidney – 92x 39 mm. Both kidneys were bright and showed poor corticomedullary differentiation suggestive of medical renal disease. No renal artery stenosis was noted on Doppler studies.

Patient's BP was well controlled on tab. Nifedipine 20 mg BID, Clonidine 100 ug TID, Prazosin 5 mg OD and torsemide 10 mg OD when he was treated for CKD about 2 months back.

Thus on the basis of history, clinical examination & investigation we were dealing with a case of: CKD with Tubercular pleural Effusion on ATT category 1 with Accelerated Hypertension & normocytic normochromic anemia.

Treatment

Patient was managed accordingly for CKD, Tubercular pleural effusion and anemia.

Treatment of hypertension is summarized in Table 1

So at the end of Day 20 we were using:

- 1 Calcium Channel Blocker – Nifidipine 160mg/day in divided doses
- Diuretic 1 loop diuretic - Torsimide 120 mg/day in divided doses
- 1 Thiazide diuretic – Chlorthalidone – 25 mg/day in divided doses
- 1 Mineralocorticoid Receptor Antagonist- Spironolactone 100 mg/day in divided doses
- 1 Angiotensin Receptor Blocker – Telmisartan 80 mg/day in divided doses
- 1 central sympatholytic –Clonidine 1200 ug/day in divided doses
- 1 beta blocker- Metoprolol 100 mg/day in divided doses &
- 1 alpha + beta blocker –labetalol 800 mg/day in divided doses
- 1 alpha blocker – Prazosin 15 mg/day in divided doses

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Inspite of using six different classes of Anti-Hypertensive drugs including diuretics BP was not reduced to target level.

So, A final diagnosis of Refractory hypertension with CKD with Tubercular pleural effusion with normocytic normochromic anemia was made.

Per se**,** CKD causes resistant hypertension but in view of relatively stable renal functions this did not seem to be a cause of resistant hypertension. Diet and compliance were checked on many occasions and other concomitant diseases and drugs causing hypertension were ruled out.

As the patient was not responding to anti hypertensive drugs we thought of stopping rifampicin after a search of scientific literature.

ON day 21: **Rifampicin was stopped**. Same anti hypertensive treatment was continued. Patient's BP was 180/110 mm hg. 5 days after Rifampicin stoppage, BP reduced to 154/94 mm hg prompting us to gradually decrease the doses of antihypertensive drugs.

On 28th day patient was discharged on BP 118/82 mm of hg with the following treatment-

- Antihypertensive - Tab nifidipine 20 mg bid, Tab clonidine 100 ug tid, Tab prazosin 5mg bid, Tab labetalol 100 mg tid, Tab telmisartan 40 mg plus chlorthalidone 12.5 mg od.
- Modified ATT category 1 without Rifampicin.
- Conservative m/m for CKD and Anemia.

Discussion:

Resistant hypertension is defined as blood pressure that remains above goal despite concurrent use of three antihypertensive agents of different classes, commonly including a long-acting calcium channel blocker, a blocker of the renin-angiotensin system (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker), and a diuretic [2-4]. Patients whose blood pressure is controlled with four or more medications are considered to have resistant hypertension. Refractory hypertension is defined as uncontrolled blood pressure despite use of ≥5 antihypertensive agents of different classes, including a long-acting thiazide-like diuretic and an MR (mineralocorticoid receptor) antagonist, at maximal or maximally tolerated doses. [1]

Several factors have been identified as contributors to resistant hypertension. Poor patient adherence, physician inertia, inadequate doses or inappropriate combinations of antihypertensive drugs, excess alcohol intake, and volume overload are some of the most common causes of resistance [5-7]. Secondary forms of hypertension may be due to endocrine, renal, neurological disorders, acute stress or drug-induced hypertension.

Tuberculosis continues to be a major health problem in India. [8] With rapid urbanization, changes in lifestyle and dietary habits, there is also increase in non-communicable diseases such as diabetes, malignancies and cardiovascular diseases. [9] It is believed that hypertension may have effect on the immune system which could increase the risk of TB. [10]

Rifampicin is a first line antitubercular drug and shows pharmacokinetic interactions with numerous drugs. Rifampicin is a potent inducer of hepatic cytochrome P 450 (CYP) 3A4 in the liver and small intestine. [11] It also induces P-glycoprotein in the liver and small intestine. The P-glycoprotein functions as cellular efflux pumps. [12]

Sharma et al in their study observed an increase in antihypertensive medications in 60 % of patients in the TB group and a two-fold increase in drug requirement. [13] Agarwal A et al in their study stated that Rifampicin should be avoided in patients of CKD with hypertension as far as possible. [14]

Rifampicin causes a decrease in blood levels of commonly used antihypertensives and therefore a very close watch is required on BP measurements in hypertensive patients who are on rifampicin.

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Table 1: Treatment of hypertension

Medication	On admission	Day 1	Day 2	Day 3-6	Day 7-9	Day 10-13	Day 14-20
BP (mm Hg)	240/130	240/122	220/120	210/120	220/130	190/110	180/110
Tab nifidipine	20 mg BID	40 mg TID	40 mg TID	40 mg TID	40 mg TID	40 mg QID	40 mg QID
Tab clonidine	100 ug TID	200 ug TID	200 ug TID	200 ug TID	200 ug QID	300 ug QID	300 ug QID
Tab prazosin	5 mg OD	5 mg BID	5 mg BID	5 mg BID	5 mg BID	5 mg TID	5 mg TID
Inj torsemide	10 mg OD	10 mg BID	10 mg BID	30 mg TID	30 mg TID	40 mg TID	40 mg TID
Inj Labetalol	-	1 mg/min IV infusion for 5 hr	20 mg IV TID	20 mg IV TID	20 mg IV TID	20 mg IV TID	Stopped
Inj Nitroglycerine	-	-	16 ug/min infusion	stopped	-	-	-
Inj Sodium nitropruside	-	-	-	-	0.4ug/kg/min	stopped	-
Tab Metoprolol	-	-	-	-	50 mg BID	50 mg BID	50 mg BID
Tab Telmisartan	-	-	-	-	-	40 mg BID	40 mg BID
Tab Spironolactone	-	-	-	-	-	50 mg BID	50 mg BID
Tab Chlorthalidone	-	-	-	-	-	12.5 mg BID	12.5 mg BID
Tab Isosorbide mononitrate	-	-	-	-	-	-	20 mg BID
Tab Labetalol	-	-	-	-	-	-	200 mg QID

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