DRUG INDUCED DYSELECTROLYTEMIA – A CASE REPORT

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Abstract:
Spiranolactone and Eplerenone were belongs to the class of potassium sparing diuretics where as Torsemide belongs to the loop diuretic class, they mainly acts by blocking the function of aldosterone hormone to retain the sodium and excrete potassium. By irrational use of these drugs induced dyselectrolytemia like hyperkalemia and hyponatremia. A 55 years female patient was admitted in cardiology department with the chief complaints of drowsiness and slow response to commands by using of the diuretics (Spiranolactone, Eplerenone and Torsemide) causes the electrolytes induced hyperkalemia and hyponatremia. These electrolytes abnormalities will causes the cardiac arrhythmias, muscle paralysis and sometimes death also. Whereas both rechallenge and dechallenge was done and the ADR assessment scales like Naranjo and WHO gives certain ADR and it can be managed by stopping of the above drugs. So, clinical pharmacist plays a major role in detecting, monitoring and managing of ADRs.

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Please cite this article in press as S.Kusuma Kumari et al, Drug Induced Dyselectrolytemia – A Case Report, Indo Am. J. P. Sci, 2017; 4(07).
INTRODUCTION:
Spironolactone and Eplerenone belongs to potassium sparing diuretic class it’s mainly bind to mineralocorticoid receptor blocking the functions of aldosterone hormone to retain sodium and excrete potassium. Torasemide or torsemide is a pyridine-sulfonlurea type loop diuretic. Torasemide inhibits the Na+/K+/2Cl- -carrier system (via interference of the chloride binding site) in the lumen of the thick ascending portion of the loop of Henle, resulting in a decrease in reabsorption of sodium and chloride. Spironolactone, eplerenone and torsemide are associated with electrolytic imbalances like hyperkalemia and hyponatremia. Hyperkalemia is life threatening metabolic disorder occurs when serum potassium levels is greater than 5 meq/l [1,2]. Symptoms of hyperkalemia is divided into mild, moderate and severe in mild to moderate includes generalized weakness fatigue, nausea vomiting and diarrhea whereas severe hyperkalemia causes cardiac arrhythmias and muscle paralysis. Causes of hyperkalemia medication induced hyperkalemia, insufficiency of aldosterone hormone and distribution of potassium between intracellular and extracellular was impaired [1]. Treatment for hyperkalemia includes intravenous administration of calcium lowers the risk of cardiac arrhythmias and stabilizing the causing of myocardial infarction. Metabolic acidosis is reduced by giving sodium bicarbonate that lowers the potassium where as insulin and beta 2 agonist are helpful for shifting of potassium intracellularly. The use of loop diuretics along with polystyrene resins reduces risk of volume overload because of sodium exchange for that potassium by resins. Long terms treatment includes restriction the potassium diet (1), Whereas hyponatremia occurs when the sodium in serum is less than 136 meq/l [2]. Symptoms of hyponatremia is divided into acute symptoms and chronic symptoms in acute symptoms occurs less than in 48 hrs it includes seizures and impaired mental status where as chronic symptoms occurs in greater than 48 hrs it includes GIT symptoms like nausea, vomiting and loss of appetite and second symptom is neurological abnormality. Causes of hyponatremia are medication induced dehydration and liver, heart and kidney problems [5].

Treatment for hyponatremia: To correct the hyponatremia, tolvaptan and conivaptan was administered intravenously or orally [2].

Incidence: The incidence of hyperkalemia is about 1% to 8% due to its life threatening arrhythmias. Whereas for hyponatremia incidence is 4% in hospitalized patients [2].

CASE REPORT:
A 55 years female patient was admitted in cardiology department with chief complaints of drowsiness since 3 days followed by slow response to commands. She was a known case of diabetes mellitus since 3 years, hypertension since 2 years, hypothyroidism since 1 year and coronary artery disease since 1 month. She was under regular medication for Diabetes mellitus Glimipiride, Hypertension Telmisartan, Hypothyroidism m-thyroxine and Coronary artery disease spironolactone, eplerenone, torsemide, clonazepam , metalozone , Rabeprazole ,ambroxol, buclizine, sodium picosulphate, desloratidine + montelukast. She was using the following drugs for her disease condition they are metolazone (used as diuretic), eplerenone + spironolactone (used for heart failure), telmisartan (used for hypertension), Rabeprazole (for gastric discomfort), thyroxine (hypothyroidism), clonazepam (used for sleep), ambroxol (used for cough), buclizine(used as antiemetic), torsemide (used as diuretic), glimepiride (used for diabetes mellitus), desloratidine + montelukast (used for allergy).

Investigations: On examination vitals shows that BP: 100/60 mm of hg, PR: 77 Bpm, T: 98.6 °f where as systemic examination includes CVS: S1, S2+ and RS: Clear. Her renal functions shows increased BUN (146 mg/dl) and serum creatinine values (1.8 mg/dl) Where as electrolytes indicates increased in potassium (5.8 mmol/l) and chloride (140mmol/l) levels with low serum sodium concentration (107 mmol/l). Based on subjective and objective evidence the patient is newly diagnosed with spironolactone , eplerenone and torsemide induced dyselectrolytemia. The following figure shows abnormalities in ECG like Long QT interval, abnormal QRS-T angle and marked ST Depression, possible subendocardialinjury(V4,V5).
DISCUSSION:
Spironolactone and eplerenone are both androgen receptor antagonists. The pharmacology of spironolactone is structurally similar to the progesterone molecule and produces antiandrogenic effects where as eplerenone is a derivative of spironolactone. It does not produce much antiandrogenic effects compared to that of spironolactone. The major pharmacokinetic effects of eplerenone inhibit aldosterone binding by 50% whereas only half by that spironolactone undergoing with rapid metabolism of 3 active metabolites of prolonged half lives (13.8-16.5 hrs) similarly the eplerenone undergoes extensive metabolism with short elimination half life (4-6hrs) [3]. Spironolactone induced hyperkalemia is happened by blocking the potassium excretion by binding directly with the mineralocorticoid antagonist is seen in patients treated with potassium sparing diuretics within 10 days[4]. Torasemide Rapidly absorbed following oral administration. Absolute bioavailability is 80%. Volume of distribution 12 to 15 L. Metabolized via the hepatic CYP2C8 to 5 metabolites. The major metabolite, M5, is pharmacologically inactive. There are 2 minor metabolites, M1, possessing one-tenth the activity of torasemide, and M3, equal in activity to torasemide. Overall, torasemide appears to account for 80% of the total diuretic activity, while metabolites M1 and M3 account for 9% and 11%, respectively. half life 3.5 hours. Symptoms of overdose include dehydration, hypovolemia, hypotension, hyponatremia, hyperkalemia, hyperchloremic alkalosis, and hemoconcentration[6].

ADR ASSESSMENT: CASUALITY ASSESSMENT OF SUSPECTED ADR
Both dechallenge and rechallenge was done.

Fig 1: shows the following abnormalities in ECG
<table>
<thead>
<tr>
<th>S.NO</th>
<th>SUSPECTED DRUG</th>
<th>SUSPECTED ADR</th>
<th>NARANJO SCALE</th>
<th>WHO-UMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Spironolactone, Eplerenone and Torsemide</td>
<td>Dyselectrolytemia</td>
<td>Certain</td>
<td>Certain</td>
</tr>
</tbody>
</table>

**ADR management:** Attempts are made to treat spironolactone, eplerenone and torsemide induced dyselectrolytemia by stopping of these drugs and correcting the electrolyte imbalance of sodium by supplying normal saline.

**CONCLUSION:**
The irrational use of diuretics like Spironolactone, Eplerenone and Torsemide causes electrolytic imbalances like Hyperkalemia and Hyponatremia and in severe conditions it may leads to cardiac arrhythmias, muscle paralysis and death. So clinical pharmacist plays a major role in detecting, monitoring and managing of ADRs.

**REFERENCES:**