A CASE REPORT OF ADVERSE DRUG INTERACTION OF LITHIUM AND FUROSEMIDE—A SERIOUS INTERACTION

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ABSTRACT

Drug interactions are said to occur when pharmacological activity of one drug is altered by concomitant use of another drug or by the presence of some other substances. A 45 years female patient was admitted in psychiatry ward with chief complaints of hyperactivity, uncontrolled thought and speech, excessive laughing since one week. Lithium was the first drug used for the treatment of mania. In our case, the patient was already known mania patient and she was on treatment with lithium, And suddenly she was developed pedal oedema and severe pain. So the patient was treated with inj. Furosemide and with NSAIDS for relieving pain oedema. On day 3, the patient was experienced symptoms like confusion, palpitations, and abnormal heart rhythms. As per scientific literature we have concluded that because of diuresis the patient was developed hyponatremia. For correcting sodium levels in the body, The sodium pump was activated in distal convoluted tubule and because of that the sodium reabsorption was taken place, As sodium is a monovalent cat ion and lithium also a monovalent cat ion. So, That the subsequent reabsorption of lithium also taken place. Because of that on day 3, Patient was experienced symptoms similar like acute lithium toxicity. Better vigilance is necessary for implementation of safe and effective treatment for each individual patient. In order to prevent serious adverse drug interactions need to consider thorough drug history and patient risk factors, knowledge about actions of drugs, close monitoring during treatment.
course, individualization of therapy, recognition of the problem, and careful management of all patients who experienced this type of interaction is essential.

KEYWORDS: Lithium, Sodium pump, vigilance, NSAIDS, Acute Lithium toxicity.

INTRODUCTION
Drug interactions are said to occur when pharmacological activity of one drug was altered by concomitant use of another drug or by the presence of some other substances. The drug whose activity is affected by such an interaction is called as the object drug and the agent which precipitates such an interaction is referred to as the precipitant. The net effect of the drug is generally quantitative i.e. increased or decreased effect, seldom qualitative i.e. Rapid or slower effect, precipitation of newer or increased adverse effects. Drug interactions are mostly undesirable and rarely desirable. Lithium was the first drug used for the treatment of mania, it reduces the motor activity, decrease euphoria, relieves insomnia & stabilises the mood. It produces narrow margin of safety, it causes wide variety of adverse effects from GI side effects to coma, either by drug alone or by interacting with some other drugs. Furosemide is one of the most commonly and extensively used diuretic in treatment of hypertension, renal, hepatic, cardiac oedema, acute pulmonary oedema etc. Our case describes the interaction between the lithium & furosemide as a “homeostatic drug interaction”.

CASE
A 45 years female patient was admitted in psychiatry ward with chief complaints of hyper activity, un controlled thought and speech, excessive laughing since one week. Patient past medical history includes-known mania patient diagnosed 6 months back. Patient past medication history includes she was on treatment with tab. lithium 450mg daily, two times in a day ,but she is on irregular treatment. Patient personnel history includes known alcoholic since 10 years (she was taking alcohol occasionally. During treatment course in psychiatry department the patient due to sudden fall down on iron metal, she developed oedema on right leg with severe pain, so, the patient was referred to orthopaedic department then the doctors prescribed, parenteral anti-inflammatory drugs(diclofenacsodium 75mg-two times in a day),parenteral diuretic(furosemide 20mg-two times in a day) for 5 days. On general examination the patient was conscious and coherent, and her pulse rate is 76beats for minute, blood pressure-110/80mg. On systemic examination cardiovascular system had S1S2+, central nervous system had no abnormalities and respiratory system was-clear, No other
laboratory investigations was performed. Based on the subjective and objective evaluation the patient was diagnosed with mania and on day 3, had right leg pain with pedal oedema. She was planned with following medications oral anti-mania drug (lithium 450mg) oral vitamin supplement (Tab. complex) oral haematinic (Tab. iron & folic acid) on day three with parenteral anti-inflammatory and diuretic (diclofenacsodium,furosemide).on day 5 the patient experienced confusion, altered mentalstatus,palpitations,abnormal heart sounds , pulse rate-56 beats per minute. Then as per scientific literature we are suspected that these may be the adverse drug interaction between lithium & furosemide and patient was referred to following laboratory examinations like ECG examination and Electrolyte levels as follows.

Electrolyte levels

Table1: Shows electrolyte levels of patient.

<table>
<thead>
<tr>
<th>S.NO</th>
<th>ELECTROLYTES</th>
<th>OBSERVED VALUES</th>
<th>NORMAL VALUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Sodium</td>
<td>90 meq/lit</td>
<td>135-145 meq/lit</td>
</tr>
<tr>
<td>2.</td>
<td>Potassium</td>
<td>3.0 meq/lit</td>
<td>3.5-4.5 meq/lit</td>
</tr>
<tr>
<td>3.</td>
<td>Chloride</td>
<td>98 meq/lit</td>
<td>96-106 meq/lit</td>
</tr>
</tbody>
</table>

Then, By using these information we have conformed these was the drug interaction between lithium and furosemide.

DISCUSSION

Lithium was the first drug used for the treatment of mania, recently anti-epileptic drugs such as carbamazepine, sodium valproate and gabapentin have been approved for the treatment of manic depressive psychosis, but lithium is the top most drug used in treatment of manic depressive psychosis still now also. Lithium is effective orally and it does not binds to plasma proteins and it is distributed throughout the body water. It is not metabolised and gets excreted in urine, saliva, sweat etc.[4] Lithium is a monovalent cat ion. The kidney handles lithium in the same way as Na⁺. About 80% of the lithium filtered lithium is reabsorbed in the proximal tubules. Sodium depletion reduces the rate of excretion of lithium and thus increases its toxicity.[5] Furosemide causes excretion of water and electrolytes by binding with Na’K’2Cl⁻ co transporter. In our case, the patient was already known mania patient, he was on treatment with lithium, and suddenly the patient was developed pedal oedema and severe pain. So the patient was treated with injection. Furosemide and with NSAIDS for relieving pain and oedema. Due to injection. Furosemide the patient had experienced diuresis action with loss of electrolytes. On day 3, the patient was experienced symptoms like confusion, palpitations, and abnormal heart rhythms. As per scientific literature we have
concluded that because of diuresis the patient was developed hyponatremia. For correcting sodium levels in the body, The sodium pump (Na+K+ATPase pump) was activated in distal convoluted tubule and because of that the sodium retention was taken place, As it is monovalent cat ion and lithium also a monovalent cat ion. So, That the subsequent reabsorption of lithium also taken place, that’s why on day 3, patient was experienced symptoms similar like acute lithium toxicity.

ADVERSE DRUG INTERACTION MANAGEMENT
Lithium and furosemide was stopped immediately.
Intravenous mannitol was given for promoting excretion of lithium.
Intravenous normal saline to restore Na+ levels which promotes excretion of lithium.

CONCLUSION
Lithium is used as a prophylactic drug for bipolar disorder. It decreases the frequency and severity of both manic and depressive attacks; hence it is called as a “mood stabilizer”. Better vigilance is necessary for implementation of safe and effective treatment for each individual patient. In order to prevent serious adverse drug interactions need to consider thorough drug history and patient risk factors, knowledge about actions of drugs, close monitoring during treatment course, individualization of therapy, recognition of the problem, and careful management of all patients who experienced this type of interaction is essential, if not identified these problem it can cause coma and death. Which can leads to morbidity and mortality.

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