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Drug –Drug interaction between Promethazine and Olanzapine induced paralytic ileus

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Abstract

The aim of this study is to demonstrate drug—drug interaction between olanzapine and promethazine which leading to paralytic ileus. Results: A diagnosis of paralytic ileus secondary to drug _drug interaction between promethazine and olanzapine was made. Conclusion: It is important to review the medications of psychiatric patients , monitor and continues follow up of patients using antipsychotic drugs to avoid unwanted side effects of the drugs.

Keywords: Drug, Promethazine, Olanzapine

INTRODUCTION

Ileus is a clinical syndrome caused by impaired intestinal motility and characterized by symptoms and signs of intestinal obstruction in the absence of a lesion-causing mechanical obstruction [1].The most frequent encountered factors for developments of paralytic ileus were abdominal operations, infection and inflammation, electrolyte

abnormalities and drugs like anticholinergic, opiates, phenothiazine's, calcium channel blockers and tricyclic antidepressants [1].

It represents 20% of acute abdominal pain cases [2].All of the psychotropic drugs with anticholinergic side effects can result in a change in bowel movements, which may result in paralytic ileus [2]. Paralytic ileus cases have been reported related to the anticholinergic side effects in the use of antidepressants such as amitriptyline, clomipramine and imipramine; and first-generation antipsychotics such as chlorpromazine, thioridazine and flupenthixol. Second generation antipsychotics can cause a very rare paralytic ileus .[2]

The aim of this study is to demonstrate drug—drug interaction between olanzapine and promethazine which leading to paralytic ileus.

Case report:

A 36 years old single male presented to accident and emergency department complaining of abdominal distention and absolute constipation for 3 days, no vomiting or abdominal pain. He did not report change in bowel habits, bleeding per rectum or past medical history of surgical operations prior to admission. Patient was known to have schizophrenia. He had treated with carbamazepine 200mg, olanzapine 10mg and promethazine 25mg for 45 days.

O/E: Patient looked ill, not pale or jaundiced. Abdomen is grossly distended, no abdominal tenderness or masses, hernial orifices were intact. He had a tympanitic note on percussion and no bowel sounds on auscultation. DRE: empty collapsed rectum.PR: 140 bpm, RR: 26 bpm, BP: 120/70.Initial biochemical investigations for electrolytes, renal profile and a full blood count were normal.

Initial management consisted of nothing per mouth, IV fluids, IV antibiotics, NG tube and suction, urinary catheter and monitoring of the vital signs with follow up chart. Erect and supine abdominal x-ray showed distended bowel loops as shown in figure 1&2.

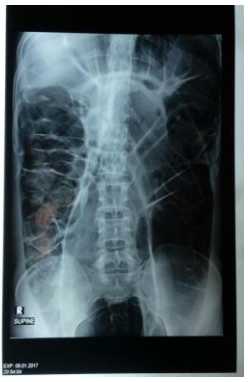
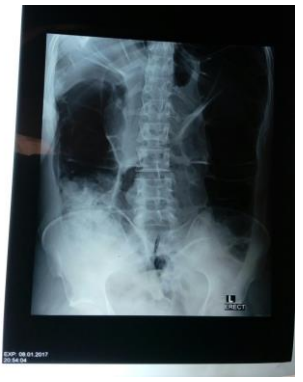

Fig (1). Supine abdominal X ray Fig (2) erect abdominal X ray

3days later while patient stopped his medications he passed flatus and stool. A diagnosis of paralytic ileus secondary to drug _drug interaction between promethazine and olanzapine was made. After discussion with psychiatrist, his medications were stopped and changed to fluphenazine decanoate injection 25mg monthly. Patient was follow for 3 months, and he did not have similar condition.

Discussion:

Promethazine is an antiemetic, a histamine H1 antagonist, first generation phenothiazine derivative. it blocks postsynaptic mesolimbic dopaminergic receptors in the brain, exhibits a strong alpha adrenergic blocking effect and depresses the release of hypothalamic and hypophyseal hormones, competes with histamine for H1 receptor, muscarinic blocking effect may be responsible for antiemetic activity, reduce stimuli to the brainstem, reticular system[3].Anticholinergic effects: constipation, blurred vision, urinary retention so it used with caution in patients with decreased gastrointestinal motility, urinary retention [3].

Olanzapine is a thienobenzodiazepine atypical antipsychotic. It has affinity for serotonin, muscarinic, histamine (H_1), and adrenergic (α_1) receptors as well as various dopamine receptors. Olanzapine is use for the management of schizophrenia and for the treatment of moderate to severe mania associated with bipolar disorder[4].

Anticholinergic effects are constipation, blurred vision, and urinary retention. Used with caution in patients with decreased gastrointestinal motility, paralytic ileus, urinary retention, relative to other neuroleptics, olanzapine has a moderate potency of cholinergic blockade [3].The largest study investigating the risk factors of ileus in patients with schizophrenia showed that increasing age and treatment with clozapine and anticholinergic were associated with an increased risk of fatal ileus[5].

Clozapine's highest anticholinergic property is thought to be the main cause of paralytic ileus. Patients receiving clozapine and/or other psychotropic associated with significant muscarinic properties should undergo careful monitoring of bowel function and timely use of laxatives, and early referral of constipated patients, because early recognition can prevent life threatening pathologic process and fatal outcomes and enable appropriate management. A limitation of the current study was in that[6].

Sometimes serious intensification takes place with the use of antipsychotic, with antimuscarinic, for the sake of clarity these have been subdivided here into heat stroke, constipation and a dynamic ileus, atropine-like psychoses, antagonism of antipsychotic effects and miscellaneous effects[7]. Concomitant use of two or more of these drugs may increase the risks associated with anticholinergic activity. So caution is warranted[8].Patients receiving psychotropics associated with significant muscarinic properties should undergo careful monitoring of bowel function and timely use of laxatives and early referral of constipated patients, because early recognition can prevent life-threatening pathologic process and fatal outcomes and enable appropriate management [8].

Management of this interaction: The concomitant use of two or more drugs that have anticholinergic activity (either as a therapeutic intention or as a side effect) is often clinically appropriate. However, it is important to recognize that the risk of unwanted effects may increase with such use .monitor for additive anticholinergic effects if two or more of these agents are concomitantly used[3].

Conclusion:

It is important to review the medications of psychiatric patients, monitor and continues follow up of patients using antipsychotic drugs to avoid unwanted side effects of the drugs. Patients receiving psychotropic associated with significant muscarinic properties should carefully monitored for changes in bowel habits and advised to take laxatives regularly and early report of constipation to avoid life threatening condition like paralytic ileus. In addition, we have to remember to exclude other causes of intestinal obstruction such as hypokalemia due to lack of oral intake and ingestion of foreign bodies in psychateric patients.

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