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# METOCLOPRAMIDE – MERITS CAUTIOUS USE IN CIRRHOTIC.

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***Abstract:*** ***Background:*** Metoclopramide is used to treat nausea, vomiting, gastroesophageal reflux disease (GERD), and diabetic gastroparesis. It works by blocking dopamine receptors in the brain and increasing muscle contractions in the upper digestive tract. Its available in both oral and injectable routes. Orally, it is taken 30 minutes before meals and at bedtime. The maximum dosage is 10 mg thrice daily and treatment is generally limited to 4 to 12 weeks to minimize the risk of side effects like drowsiness, fatigue, dizziness, diarrhea or restlessness. The rare and serious side effects include extrapyramidal manifestations which can occur even after a single dose and include acute dystonias, akathisia, Parkinsonism, and tardive dyskinesia, dysarthria which can mimic hepatic encephalopathy in cirrhotic patients. ***Case report:*** We are reporting a seventy- five-year-old female, a known case of chronic hepatitis C related cirrhosis with features of decompensation, as evidenced by gross ascites, pedal edema and jaundice. She has already been fully treated with 24 weeks directly acting antiviral (DAA'S) treatment and achieved 12 weeks sustained virological response. She was on regular follow-up for chronic liver disease (CLD). Now, she was admitted with increased decompensation with increase in abdominal distension and pedal edema. The patient biochemical labs revealed deranged liver function tests with bilirubinaemia, transaminitis with ratio reversal of AST/ALT, hypoproteinaemia and hypoalbunemia. The renal function, blood sugar, thyroid profile, serum electrolytes were normal but there was hypocalcaemia with lower serum vitamin D3 levels. The serum phosphorus levels, alpha-feto protein levels, urine complete examination, ECG and chest x-ray were normal and ultrasonogram abdomen showed altered echotexture of liver with splenomegaly, increased portal vein diameter, collaterals and gross ascites. She was stable during admission but developed vomiting in night for which she was started on injectable metoclopramide by on duty junior resident. After few hours of this injection, she developed difficulty in articulation of words. On morning rounds, the difficulty in articulation of words persisted and there was thought of she being in hepatic encephalopathy but point against it was that she was fully conscious, oriented, without any tremors or reversal of sleep pattern with normal serum ammonia level. Hence, she was not started on hepatic encephalopathy treatment (Rifaximin, lactulose) and immediately injection metoclopramide was stopped. She recovered within six hours and remained stable for next three days. Then again, she developed vomiting and due to change of duty doctor, she was again given oral metoclopramide and within 3-4 hours, developed dragging sensation in throat, along with stiffness in the neck. The extra-pyramidal side effects of metoclopramide were immediately thought and metoclopramide was stopped. In the indoor file, notes were documented that she is having rare extra-pyramidal side effects due to metoclopramide, hence not to be used in future. ***Conclusion:*** The extra-pyramidal side effects of metoclopramide are rare and older age group are at more risk for it, and in cirrhotic patients, they can mimic hepatic encephalopathy which is an indication for liver transplantation. Hence, a cautious approach of using metoclopramide in them is need of time.

***Keywords:*** Metoclopramide, Dysarthria, Side effects, Hepatic Encephalopathy, Serum Ammonia.

## INTRODUCTION

Metoclopramide is a widely used antiemetic and gastroprokinetic agent, but it is well-known for causing extrapyramidal symptoms (EPS), particularly acute dystonia, often manifesting within 24 to 48 hours of starting the medication. It is useful in the preoperative phase to reduce gastric contents and increase lower esophageal sphincter tone, for pharmacologic pulmonary aspiration prophylaxis. Metoclopramide can precipitate extrapyramidal symptoms (EPS)/drug-induced movement disorders (DIMD). Tardive dyskinesia and Parkinsonism are generally seen after long-term use, whereas dystonia and akathisia can occur after a single dose of metoclopramide. [1]

These reactions are more frequent in patients receiving high doses of metoclopramide especially in female patients, children, and older patients. [2] The acute dystonic response is an acute neurological condition characterized by involuntary contractions of muscles in the extremities, face, neck, abdominal, pelvis, or larynx that occur in either persistent or intermittent rhythms, resulting in repetitive jerks and abnormal posture [3].

This condition is attributed to a number of drugs. One of the most frequent medications associated with this condition is metoclopramide. Extrapyramidal symptoms related to metoclopramide are encountered by about 0.2% of people receiving 30–40 mg of metoclopramide per day. A detailed history helps in differentiating it from other diseases like tetanus, strychnine poisoning, hypocalcaemia, hypomagnesemia, focal seizures, or other primary neurological causes such as Wilson's disease [4].

## CASE REPORT

We are reporting a seventy- five-year-old female, a known case of chronic hepatitis C related cirrhosis with features of decompensation, as evidenced by gross ascites, pedal edema and jaundice. She has already been fully treated with 24 weeks directly acting antiviral (DAA'S) treatment and achieved 12 weeks sustained virological response. She was on regular follow-up for chronic liver disease (CLD). Now, she was admitted with increased decompensation with increase in abdominal distension and pedal edema.

The patient biochemical labs revealed deranged liver function tests with bilirubinaemia, transaminitis with ratio reversal of AST/ALT, hypoproteinaemia and hypoalbunemia. The renal function, blood sugar, thyroid profile, serum electrolytes were normal but there was hypocalcaemia with lower serum vitamin D3 levels. The serum phosphorus levels, alpha-feto protein levels, urine complete examination, ECG and chest x-ray were normal and ultrasonogram abdomen showed altered echotexture of liver with splenomegaly, increased portal vein diameter, collaterals and gross ascites. She was stable during admission but developed vomiting in night for which she was started on injectable metoclopramide by on duty junior resident.

After few hours of this injection, she developed difficulty in articulation of words. On morning rounds, the difficulty in articulation of words persisted and there was thought of she being in hepatic encephalopathy but point against it was that she was fully conscious, oriented, without any tremors or reversal of sleep pattern with normal serum ammonia level. Hence, she was not started on hepatic encephalopathy treatment (Rifaximin, lactulose) and immediately injection metoclopramide was stopped. She recovered within six hours and remained stable for next three days. Then again, she developed vomiting and due to change of duty doctor, she was again given oral metoclopramide and within 3-4 hours, developed dragging sensation in throat, along with stiffness in the neck. The extra-pyramidal side effects of metoclopramide were immediately thought and metoclopramide was stopped. In the indoor file, notes were documented that she is having rare extra-pyramidal side effects due to metoclopramide, hence not to be used in future.

## DISCUSSION

Metoclopramide is commonly prescribed antiemetic because of its antiemetic and prokinetic properties. Metoclopramide promotes muscular contractions in the upper digestive tract, leading to increased gastric emptying and motility. Metoclopramide acts by blocking dopamine D2 and serotonin 5-HT3 receptors in the chemoreceptor trigger zone (CTZ), which is located in the area of the postrema of the brain. It leads to prokinetic effects which are mediated by inhibitory actions on presynaptic and postsynaptic D2 receptors, agonism of serotonin 5-HT4 receptors, and antagonism of muscarinic receptor blockage. This action increases acetylcholine release, resulting in enhanced LES and gastric tone, which speeds up gastric emptying. [5]

Extrapyramidal reactions are the most common acute side effect of metoclopramide, with a reported frequency of 0.2%, but this incidence can rise to as high as 25% in the elderly and young. In the developing world, despite high rates of prescription, very little research has been done on metoclopramide-induced acute dystonic reaction or extrapyramidal side effects. The incidence is underreported due to lack of data collection and less reporting of cases.

Long-term use, female sex, older age, diabetes mellitus, and polypharmacy are risk factors for developing a metoclopramide-induced dystonic reaction [6].

The symptoms of metoclopramide-induced dystonic reaction include involuntary limb movement, generalized body stiffness, slurred speech, trismus, torticollis, and oculogyric crises, which can occur hours to days after the medication is delivered. [7]

The treatment of a metoclopramide-induced acute dystonic reaction involves stopping the offending drug immediately and administering medications for reversal of the condition which include anticholinergics or antihistamines intravenously or intramuscularly, most commonly biperiden, benztropine, or diphenhydramine. [8]

Our case had well defined risk factors like old age and there was no confusion in diagnosis because extra-pyramidal symptoms occurred twice due to use of metoclopramide in same stay. Moreover, symptoms improved immediately after stopping metoclopramide. The main aim of reporting this case report is that one should be very cautious in using metoclopramide in old age and especially those who have underlying cirrhosis or other neurological problems which can lead to diagnostic dilemma. In cirrhotic, single episode of hepatic encephalopathy is indication for liver transplantation and thus EPS due to metoclopramide can cause false listing of patient for liver transplantation.

**CONFLICT OF INTEREST**- None and no funding was taken for this case report.

## CONCLUSION

Every drug has well documented common side effects but treating doctor should be aware of rare and atypical side effects of every drug being prescribed by him or her. The extra-pyramidal side effects of metoclopramide are rare and older age group are at more risk for it, and in cirrhotic patients, they can mimic hepatic encephalopathy which is an indication for liver transplantation. Hence, a cautious approach of using metoclopramide in them is need of time.

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