LETTER TO THE EDITOR

Acute Akathisia Following Intravenous Push of Metoclopramide

A 79-year-old male (height 168 cm; weight 75 kg) was noted fever with chills by his family and sent to our emergency department. Abdomen X-ray showed gas-filled bowel loops, and the chest X-ray showed left pleural effusion with bilateral infiltration. His serum creatinine level was 0.95 mg/dL, and the glutamate oxaloacetate transaminase (GOT) level was 17 IU/L. Under the impression of pneumonia, he was admitted for further treatment. The patient’s past medical history included hypertension, benign prostate hypertrophy, sinusitis, and asthma for years. He had a surgical history of left total hip replacement. The patient had quit smoking 10 years ago, and he denied the any drinking habit. The patient had no known allergies. During admission, the patient was diagnosed with gastroesophageal reflux disease, grade A, and metoclopramide 10 mg (intravenous) i.v. drip over 15 minutes was prescribed by the attending physician to relieve his symptoms. However, the patient was administered with an i.v. bolus of metoclopramide over 1 minute. The symptoms did not improve the next day, and he was administered with metoclopramide 10 mg by i.v. push every eight hours. Soon after the third dose of metoclopramide was administered, the patient exhibited involuntary movement and restlessness. The physician suspected akathisia induced by metoclopramide. The patient was treated with diphenhydramine 30-mg i.v. drip. The symptoms did not relieve, and a second dose of 30-mg diphenhydramine was administered. The symptoms of akathisia gradually improved and subsided finally.

Metoclopramide is a substituted benzamide that affects both peripheral gastrointestinal and central nervous systems. The peripheral prokinetic effects of metoclopramide are owing to the improvement of acetylcholine release from the gastric myenteric neurons and therefore ameliorate the upper gastrointestinal motility and contraction of the gastric smooth muscle. Besides, it augments the lower esophageal sphincter tone, but loosens the pyloric sphincter. These effects of metoclopramide result in accelerated gastric emptying. In addition, metoclopramide possesses antiemetic effect via the blockade of dopamine receptors in the chemoreceptor trigger zone of the central nervous system. Metoclopramide also blocks 5-HT3 in lower case receptors and therefore may help relieve headache.1

Metoclopramide is widely used to treat various upper gastrointestinal motility disorders such as gastroesophageal reflux disease and diabetic gastroparesis. It is also approved to prevent chemotherapy and postoperation-induced nausea and vomiting. Other FDA-labeled indications include the assistance of small bowel intubation and gastrointestinal tract radiography.1 Metoclopramide may cause some central nervous system adverse reactions, such as sedation, drowsiness, restlessness, and movement disorders. It has been reported that the central dopaminergic receptor antagonism of metoclopramide causes extrapyramidal side effects such as akathisia, asthenia, dystonia, parkinsonism, tardive dyskinesia, and neuroleptic malignant syndrome.2-6 Akathisia and dystonia appear at the early course of metoclopramide treatment. In contrast, parkinsonism and tardive dyskinesia showed delayed onset following weeks of treatment with metoclopramide.1

The syndrome of akathisia involves various involuntary actions such as foot or hand movements, inability to keep still while sitting or standing. Furthermore, patient may feel restless and urge to move.7 It has been reported that the incidence and severity of akathisia is related to the infusion rate of metoclopramide. Three prospective, double blind, and randomized studies have demonstrated that the slow intravenous infusion of metoclopramide over 15 minutes significantly reduces incidence and severity of akathisia compared with fast intravenous bolus over two minutes.8-10 Furthermore, the infusion rate of metoclopramide does not affect its therapeutic effect on alleviation of nausea.10 The present case was an elderly patient who received metoclopramide three times with fast intravenous bolus over 1 minute that lead to the incidence of akathisia within 24 hours.

The first step in managing akathisia induced by metoclopramide is to discontinue the drug immediately. Diphenhydramine, a centrally-acting anticholinergic, is effective to reverse drug-induced akathisia by normalizing acetylcholine and dopamine balance. Midazolam, a rapid-acting benzodiazepine, is also useful to treat symptoms of akathisia.8 A clinical study has shown that midazolam relieves metoclopramide-induced akathisia more rapidly than diphenhydramine. However, midazolam leads to more sedation in comparison to diphenhydramine.11

Akathisia appeared after three doses of 10 mg metoclopramide administered by a rapid intravenous bolus infusion in 1 minute, which apparently did not follow the prescription issued by the attending physician (metoclopramide 10 mg i.v. dripping for 15 minutes). After discontinuing metoclopramide and then administering two doses of diphenhydramine, the symptoms of akathisia resolved. This adverse drug reaction can be prevented by slowing down the rate of intravenous infusion by following the instruction of the attending physician.

References


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