Extrapyramidal Side Effects of Metoclopramide in a Child-A Case Report

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Abstract

Metoclopramide is an antiemetic, antinauseant and gastric prokinetic. European medicines agency (EMA) in July 2013 has officially recommended a very restricted use of metoclopramide in children, because of serious and common neurological side effects. A 3 years old boy was admitted to our pediatric department due to altered consciousness, nausea, vomiting and dehydration. Immediately after admission he developed dramatic neurological symptoms with face and extremity muscles spasms, trismus, ophistotonus and extreme agitation. Neurological symptoms were present for about 3 hours, with periodically withdrawal and worsening. He received only symptomatic therapy and after 6 hours child was fully recovered and without complaints. Despite repeated warnings about the possible neurological side effects, metoclopramide continues to be used in children for the treatment of nausea and vomiting. If the physician is not familiar with these side effects of metoclopramide physician can easily incorrectly interpret these symptoms and diagnose it as tetany, convulsions, encephalitis, food poisoning, intoxication etc. Physicians need to follow the recommendations about indications, dosage, drug forms and way of administration of metoclopramide in children. Detailed previous medical history and drug use history is necessary for avoiding misdiagnosis, and for timely recognition and adequate treatment of metoclopramide side effects in children.

Keywords: Metoclopramide; Extrapyramidal; Side Effects; Children

Introduction

Metoclopramide (chemical name: 4-amino-5-chloro-N-2-diethylaminoethyl-2-methoxybenzamide hydrochloride monohydrate) is antiemetic, antinauseant and gastric prokinetic. By blocking dopamine (D2) receptors, and affecting 5HT3 receptors as antagonist and 5HT4 receptors as agonist, metoclopramide inhibits brain vomiting center, accelerates gastric emptying and increases the resting tone of the lower esophageal sphincter. Metoclopramid administered intravenously expresses its effects after 1-3 minutes. The effect occurs 10-15 minutes after intramuscular administration, and 15-20 minutes after oral dose. Metabolism takes place in the liver, and about 80% of the drug is excreted in the urine in the first 24 hours after intake. Half-life varies from 2.5 to 6 hours. Dose of metoclopramide in children, if it must be given, should not exceed 0.10-1.15 mg/kg/8h; or 0.5 mg/kg/day.

European medicines agency (EMA) in July 2013 has officially recommended a changes to the use of metoclopramide in children. The use of metoclopramide in children now is very restricted because of serious and common neurological side effects, especially extrapyramidal disorders (acute dystonia, rigidity, hypokinesia/akinesia, dyskinesia, akathisia, tremor and paraesthesias, neuroleptic malignant syndrome). Acute dystonia is most frequent side effect in children. It includes tonic muscular contractions (face and extremity muscles), trismus, oculogyric crisis, torticollis, opisthotonus and extreme agitation. Rigidity is increased muscle tone and steady resistance to passive movements of the limbs. Tardive dyskinesia is characterized by involuntary choreiform movements of the tongue, face, mouth and extremities. It is side effect that appears more often in the elderly and can be permanent.

Akathisia is a subjective feeling of objective sign of muscle unrest, particularly in the lower extremities. Patient has difficulty to remain lying and stay calm, and it can be misdiagnosed as psychiatric disorder or encephalitis. Neuroleptic malignant syndrome is rare but fatal complication. It is presented with hypertermia, skeletal muscles hypertonicity, mental changes and autonomic instability. The incidence of some of these side effects in children is 6 times higher than in adults, and it can be up to 25%. Extrapyramidal disorders can occur even at minimal dosage level, usually within 24-72 hours after taking this medicine. Typical medical history and clinical signs are sufficient for diagnosis. Other less frequent side effects of metoclopramide are elevated prolactine levels, transient hypertension, cardiac conduction disturbances, altered hepatic function test results, methaemoglobinemia,
A 3 years old boy was admitted to our pediatric department due to altered consciousness, nausea, vomiting and dehydration. One day before admission started diarrhea and vomiting. A morning before he received a single adequate therapeutic oral dose of Reglan (metoclopramide), and night before in the emergency service with intravenous crystalloids he received one adequate therapeutic intravenous dose of Reglan. At the admission child was exhausted, somnolent, and had signs of mild to moderate dehydration. His vital signs were as following: arterial blood pressure 90/60 mmHg, pulse 100/min, respiratory rate 20/min, axillary temperature 37,5°C, capillary rellifes 2-3 sec. Immediately after admission he developed dramatic neurological symptoms with face and extremity muscles spasms, trismus, ophistotonus and extreme agitation. Child periodically complained of pain in the arms and stomach. Laboratory testing was done and intravenous rehydration with crystalloids was administered. In laboratory results we found mild metabolic acidosis and mild hypokalaemia which were not present in control laboratory testing after one hour of rehydration and potassium substitution. Stool testing has shown a positive result for Rota virus. Neurological symptoms were present for about 3 hours, with periodically withdrawal and worsening. Intravenous rehydration and electrolyte substitution were continued and after 6 hours child was fully recovered and without complaints. Control examination was performed after two days, and finding was completely normal.

**Discussion**

Despite repeated warnings about the possible neurological and other side effects, metoclopramide continues to be used in children for the treatment of nausea and vomiting. Metoclopramide is prescribed to the children most often by the general practitioners and doctors in the emergency services. It is the duty of pediatricians to inform these colleagues with whom they cooperate about possible side effects of metoclopramide in children. Neurological adverse effects of metoclopramide are idiosyncratic and do not depend on dosage. They can appear even at standard treatment dose, but they are more likely to appear in overdoses and have cumulative effect with repeated use. Possible explanation is that metoclopramide by blocking a specific postsynaptic dopamine receptors in basal ganglia can produce acute extrapyramidal reactions. Children, particularly females are more susceptible. Fortunately, acute reactions are usually self limited, respond well to the treatment and do not need any further evaluation and follow-up. In children most frequent neurological reactions are face and extremity muscle contractions, torticollis, ophistotonus, oculogyric crises.

Patient and parents experience these sudden and rapidly accelerated symptoms very dramatically and should be, in case of prescribing metoclopramide, warned in advance about the possibility of developing these symptoms. If he is not familiar with these side effects of metoclopramide physician can easily incorrectly interpret these symptoms and diagnose it as tetany, convulsions, encephalitis, food poisoning, intoxication etc. Physicians in the first place need to take good previous medical history, and history about drug use, and then recognize these side effects of metoclopramide. Physicians in the first place need to take good previous medical history, and history about drug use, and then recognize these side effects of metoclopramide. Physicians in the first place need to take good previous medical history, and history about drug use, and then recognize these side effects of metoclopramide.

**Case Report**

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Conclusion

Use of metoclopramide in the pediatric population should be restricted to some specific conditions such as small bowel intubation procedures, radiotherapy, chemotherapy and postoperative period associated nausea and vomiting, and only as a second line medication. Metoclopramide is contraindicated in children under one year of age. Physicians need to follow the recommendations about dosage, drug forms and way of administration of metoclopramide in children. Detail previous medical history and drug use history is necessary for avoiding misdiagnosis, and for timely recognition and adequate treatment of metoclopramide side effects in children.

References

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