Ondansetron is a 5-hydroxytryptamine (5-HT₃) receptor antagonist with antiemetic properties used extensively in the treatment of nausea and vomiting, especially postoperatively and in patients receiving chemotherapy. It decreases vagal activity and inhibits the vomiting center in the medulla oblongata. It is also known to decrease activity of the chemoreceptor trigger zone by blocking the serotonin receptors in the brain. Ondansetron does not affect dopaminergic, histaminergic, adrenergic, or cholinergic receptor activity and it has few neurologic adverse effects.¹

It is used widely as an antiemetic in gastroenteritis in children.²⁻⁹ Unlike other antiemetic drugs, it rarely produces extrapyramidal symptoms or seizures, although a few cases of extrapyramidal adverse effects¹⁰⁻¹⁸ and isolated cases of seizures¹⁹⁻²⁰ have been reported. 5-HT₃ receptors have been found to mediate stress-induced secretion of arginine vasopressin.²¹⁻³²

We describe a 4-year-old boy who developed dystonia, seizures, and hypoglycemia soon after receiving an intravenous dose of ondansetron. We speculate on the mechanism underlying these reactions.

Case Report

A 4-year-old boy weighing 15 kg presented to our emergency department following an episode of dystonia.

OBJECTIVE: To document ondansetron-induced dystonia, hypoglycemia, and seizures in a child.

CASE SUMMARY: A 4-year-old boy was admitted with dystonia following an intravenous dose of ondansetron 2 mg (0.13 mg/kg) that he had received for vomiting that day. In the emergency department, he developed generalized tonic-clonic seizures lasting for a few minutes. He was administered lorazepam 1.5 mg (0.1 mg/kg) to control the seizures. His blood glucose level was 10 mg/dL; the hypoglycemia responded promptly to intravenous dextrose 10% (7 mL/kg). Serum electrolytes, renal profile, capillary blood gas, and results of a computed tomography scan of the brain were normal. Subsequent blood glucose values were within normal range. On follow-up after 7 days, the child was healthy with no recurrences of the symptoms. A provisional diagnosis of ondansetron-induced acute dystonia with seizures and hypoglycemia was made.

DISCUSSION: Ondansetron is an antiemetic known for its safety profile. There have been a few case reports of extrapyramidal adverse effects and seizures from this drug but none of ondansetron-associated hypoglycemia. 5-Hydroxytryptamine (5-HT₃) receptors are involved in arginine vasopressin–mediated release of adrenocorticotropin hormone and cortisol in response to stress. Blunting of this stress response by ondansetron, a 5-HT₃ receptor antagonist, could have caused the hypoglycemia in this patient. According to the Naranjo scale, ondansetron was probably the cause of the dystonia and seizures, and possibly the cause of the hypoglycemia. Other potential explanations for hypoglycemia were considered but were thought to be less likely.

CONCLUSIONS: Dystonia and seizures have been associated with ondansetron in a few case reports. In addition, clinicians need to consider hypoglycemia as a possible adverse effect of ondansetron.

KEY WORDS: 5-hydroxytryptamine (5-HT₃) receptor, dystonia, hypoglycemia, ondansetron, seizures.

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Earlier that day, he had pain in his abdomen and 2 episodes of non-bilious, non-projectile vomiting and an episode of passing loose stools for which a physician had administered ondansetron 2 mg (0.13 mg/kg) intravenously. Within half an hour, he developed dystonic posturing of both upper limbs and clenching of teeth while still at the physi-
Very few cases of seizures have been reported. Ondansetron, a 5-HT3 receptor antagonist, may lead to hypoglycemia by inhibiting the release of adrenocorticotropic hormone (ACTH) and cortisol. It is postulated that ondansetron may inhibit or reduce mesolimbic dopaminergic activity and antagonize the locomotor activity caused by mesolimbic dopamine. Very few cases of seizures have been reported with ondansetron. 5-HT3 receptor antagonists are known to have a role in epileptogenesis and seizure propagation.

Hypoglycemia associated with dystonia and seizures on receiving an intravenous dose of a 5-HT3 receptor antagonist has not been reported previously. In various studies, 5-HT3 receptors have been found to mediate stress-induced release of adrenocorticotropic hormone (ACTH) and cortisol. It is postulated that in response to stress, arginine vasopressin (AVP) is secreted from the hypothalamus into the hypophysial pituitary portal system and it is through this that ACTH is stimulated. The stress of hypoglycemia and the resulting stimulation of AVP have been examined in various human and animal studies. Plotsky et al. reported that insulin-induced hypoglycemia in rats resulted in no change in hypophysial portal venous corticotropin-releasing factor levels, but caused significant increases in AVP levels. When hypoglycemia is moderate, corticotropin-releasing factor is the main factor responsible for the release of ACTH, which normalizes blood glucose. In severe hypoglycemia, AVP is dramatically increased and this regulates ACTH response. 5-HT3 receptors have also been studied in exercise-induced vasopressin secretion and it has been shown that ondansetron significantly reduced the AVP increase induced by physical exercise.

Serotoninergic receptors act asafferent pathways that stimulate AVP-induced release of ACTH and cortisol in response to stress. Ondansetron, a 5-HT3 receptor antagonist, may lead to hypoglycemia by inhibiting the release of ACTH and cortisol.

Our patient had dystonia and seizures, as well as low blood glucose, in close proximity to an intravenous dose of ondansetron. Hypoglycemia per se can produce seizures. Symptomatic hypoglycemia in a child who was completely well before the episode seems unlikely to be due to a storage disorder. It is postulated that the glucose stores were low in this child who was vomiting and that on-
Ondansetron mediated both the dystonic reaction and blunted the steroid response to hypoglycemia through antagonism of serotoninergic receptors. This is, however, speculative and more studies are warranted to establish this association. According to the Naranjo scale, ondansetron was a possible cause of our patient’s hypoglycemia.  

The dramatic onset of dystonia and seizures in our patient, an otherwise developmentally and neurologically healthy child, could be related to ondansetron. The associated hypoglycemia also seems to be related to the 5-HT₃ receptor antagonist ondansetron. The child recovered completely and has had no recurrence of dystonia or seizures and no neurologic sequelae subsequently. In conclusion, ondansetron is a relatively safe antiemetic but in rare instances it may result in adverse effects such as hypoglycemia, seizures, and dystonia.  

Aneet Patel, MBBS Student, Department of Pediatrics, St. Stephen’s Hospital, Tis Hazari, New Delhi, India  
Shweta Mittal MD, Registrar, Department of Pediatrics, St. Stephen’s Hospital  
Samiksha Manchanda MBBS, House Officer, Department of Pediatrics, St. Stephen’s Hospital  
Jacob Mammen Puliyel MD MRCP M Phil, Head of Department, Department of Pediatrics, St. Stephen’s Hospital  
Correspondence: Dr. Mittal, dr_shveta07@rediffmail.com  
Reprints/Online Access: www.theannals.com/cgi/reprint/aph.1P332  
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