

# Ondansetron for Food Protein-Induced Enterocolitis Syndrome

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## Established Facts

- The symptoms of acute food protein-induced enterocolitis syndrome (FPIES) are projectile and profuse vomit, pallor and lethargy (and, in some cases, hypotension) starting 1–4 h after the ingestion of the culprit food.
- Current therapy is based on intravenous fluid replacement and steroid administration.
- Holbrook et al. [J Allergy Clin Immunol 2013;132:1219–1220] reported on the efficacy of intravenous ondansetron in 5 patients ( $\geq 3$  years old) with acute FPIES during an oral food challenge.

## Novel Insights

- We used intramuscular ondansetron treatment for 5 patients (4 were  $< 3$  years old) who had acute FPIES symptoms; our results are absolutely comparable with those of Holbrook et al. [J Allergy Clin Immunol 2013;132:1219–1220].
- Intramuscular administration of ondansetron is easy to perform and we believe that it could be important for the management of acute FPIES episodes at home.

## Key Words

Food allergy · Food protein-induced enterocolitis · Ondansetron · Oral food challenge

## Abstract

Recently, a study on 5 patients [Holbrook et al.: J Allergy Clin Immunol 2013;132:1219–1220] documented the efficacy of the intravenous administration of ondansetron in children with acute symptoms due to food protein-induced enterocolitis syndrome (FPIES). We report on the experience at our institution using ondansetron during oral food challenge

(OFC) in 5 children affected by FPIES. In all 5 cases, the use of intramuscular ondansetron led to a complete and rapid resolution of symptoms within 15 min. Intramuscular administration, without the need for intravenous access for an infusion or steroid administration, enables this therapy to be easily performed, even at home (i.e. out of a hospital setting). A home treatment with ondansetron cannot be considered as an alternative to a medical examination with eventual treatment in hospital, which is advised after any acute episode of FPIES. We consider ondansetron to be very useful in the management of acute FPIES. Further study is required to confirm its efficacy.

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## Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated food allergy, with the acute form being by far the most common. Acute episodes start 1–4 h after the ingestion of the culprit food and are characterized by projectile and profuse vomiting, pallor, lethargy and, in some cases, hypotension [1]. Current therapy is based on intravenous fluid replacement and steroid administration, while oral rehydration may be sufficient in mild cases. There are no randomized controlled trials that support this therapy for acute episodes of FPIES, and our own experience with this approach is not very convincing [2]. Holbrook et al. [3] have reported on the efficacy of ondansetron, an antiemetic drug with an antiserotonergic peripheral and central action, for acute episodes of FPIES during oral food challenge (OFC). Serotonin is, in fact, a major mediator in the gut, signaling via the afferent nerves to influence gut motility and secretion, and antiserotonergic drugs are already in common use for treating chemotherapy-induced nausea and vomiting in cancer patients. Holbrook et al. [3] treated 5 children ( $\geq 3$  years old) with intravenous ondansetron, and observed a rapid resolution of all acute symptoms (not only vomiting) within 15 min of administration of the drug. In 1 case, the ondansetron was first administered orally, but the response was not good.

We report on our own successful experience with intramuscular administration of ondansetron to 5 children in six episodes of acute FPIES during OFC.

## Case Reports

Patient No. 1 was a 13-month-old girl diagnosed at the age of 5 months with cow's milk (CM)-FPIES due to two typical clinical episodes [a skin prick test (SPT) was negative]. Her breast-feeding mother had always consumed CM without any problems for the infant. Eight months after diagnosis, we decided to verify the patient's tolerance by testing with parmesan that had been aged for 48 months; the SPT was positive (mean wheal diameter = 4 mm). She then ate 15 g of parmesan and vomited after 2 h. In the next 90 min, she vomited 4 times. The fifth episode was associated with the onset of pallor and lethargy; blood pressure levels remained acceptable. Intramuscular ondansetron (0.2 mg/kg) was administered with complete resolution of symptoms within 15 min.

Patient No. 2 was a 15-month-old girl diagnosed with CM-FPIES at the age of 7 months due to two typical clinical episodes, the second after eating a teaspoon of parmesan. Since the age of 7 months, the girl has drunk donkey's milk without any adverse reactions. Eight months after the last episode, we performed an OFC with 100 ml of CM. After 3 h, she presented with a vomiting episode, without other correlated symptoms. Ondansetron (0.2 mg/

kg) was administered intramuscularly, and there was a complete recovery within 15 min. One month later, the patient performed an OFC with baked milk in a wheat matrix and passed it.

Patient No. 3 was a 20-month-old girl diagnosed with CM-FPIES at the age of 9 months after four acute episodes, all characterized by repetitive profuse vomiting, pallor and lethargy but no diarrhea, starting about 2 h after the ingestion of CM (3 times) and parmesan (the final episode). At the age of diagnosis, an SPT with CM had been positive, but at OFC, it was found to be negative. At the age of 20 months, we performed an OFC with CM yogurt and ice-cream (just a few spoons) and 2 h after the beginning of the test, she presented with a vomiting episode. We immediately administered 0.2 mg/kg of intramuscular ondansetron. She has not presented with another vomiting episode, pallor or lethargy, and her blood pressure levels have remained good. Also worthy of note is that her breast-feeding mother has always eaten CM without any problem for the baby.

Patient No. 4 was an 18-month-old girl diagnosed with egg FPIES due to three episodes characterized by vomiting and mild lethargy after the ingestion of a small quantity of cooked egg. At the age of 16 months, we performed an OFC with boiled egg. After 2.5 h, she presented with two vomiting episodes associated with mild lethargy; there was no hypotension or diarrhea. Ondansetron (0.2 mg/kg) was administered intramuscularly with an immediate resolution of symptoms. One month later, we performed another OFC with baked egg in a wheat matrix; 3 h after the ingestion, she presented with a profuse vomiting episode. The same dose of ondansetron was administered and, again, there was a rapid resolution of symptoms.

Patient No. 5 was a 4-year-old boy diagnosed with egg FPIES. His SPT have always been negative. He had already undergone two OFCs at the age of 1 and 3 years, presenting with profuse vomiting episodes, lethargy and pallor on both occasions. At the age of 4 years, we performed another OFC with baked egg in a wheat matrix; 3 h after the beginning of the test, he presented with two profuse vomiting episodes associated with pallor and lethargy. Intramuscular ondansetron (0.2 mg/kg) was administered with a prompt resolution of symptoms.

## Discussion

Although our experience with the use of ondansetron in patients with FPIES is not extensive, it is nonetheless absolutely consistent with Holbrook et al.'s results [3]. The younger age of our patients also enabled us to demonstrate the efficacy of ondansetron in infants: intramuscular administration of ondansetron brought a rapid resolution of symptoms (within 15 min), and the effect on both vomiting and lethargy was positive. Before starting an OFC, we do not usually set a venous access in a patient, so we administered ondansetron intramuscularly. The efficacy was comparable to that reported by Holbrook et al. [3] for intravenous administration (whereas oral administration did not give the same results). Moreover, ondansetron has been shown to be effective even if administered

far from the onset of symptoms (patient No. 1) or in the case of severe symptoms (patient Nos. 1 and 5).

The efficacy of intramuscular ondansetron in cases of acute FPIES, without the need for intravenous fluid replacement or corticosteroids, could be important for the management of episodes at home. Indeed, most FPIES episodes occur far from a hospital setting. At present, no pharmacological therapy is recommended that enables the parents to deal with such situations. Given that intramuscular administration is easy to perform, this technique may represent an excellent chance to solve this problem. However, in the case of new acute episodes, infants with a history of severe FPIES (characterized by severe vomiting and/or lethargy and pallor) should always be referred for medical examination, even if the vomiting stops after administering the ondansetron. It is also important to highlight that it is still suggested that a venous access be set before starting an OFC in children with suspected/certain FPIES.

Our 5 cases provide us with the opportunity to make some other observations on the management of children with FPIES. First, patient Nos. 1 and 3 had breast-fed without any problems even though their mothers had followed a free diet which included CM and dairy products. This point is in agreement with the suggestion made by Järvinen and Nowak-Węgrzyn [4]: '... the causative food should only be removed from the maternal diet if reactions occur after breast-feeding or if the infant is failing

to thrive'. However, in the case of severe FPIES episodes, some authors [5] recommend also eliminating the culprit food from the maternal diet even when symptoms have only been caused by direct ingestion by the child. Second, patient No. 2 passed the OFC with baked milk in a wheat matrix without problems, as we already noted in another study on 4 children with CM-FPIES and 1 child affected by egg FPIES [6]. However, in this study, the 2 patients with egg FPIES did not tolerate the baked egg. So it might be possible to assume that tolerance to baked food is not certain, but is, rather, limited to only some (as of yet unknown) FPIES phenotypes. It has been reported how different ways of cooking may also influence the reduction of the allergenic properties of egg [7]. Finally, it was found that patient No. 2 tolerated donkey's milk. To our knowledge, this tolerance has not yet been reported in children with CM-FPIES, although it has been described in children with IgE-mediated CM allergy [8].

In conclusion, our case reports, together with the report of Holbrook et al. [3], suggest that ondansetron may be a valid therapeutic option for the management of acute FPIES in the future.

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