CASE REPORT

Allergy to Ondansetron: The Other Side of the Coin

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Port J Pediatr 2019;50:184-6
DOI: https://doi.org/10.25754/pjp.2019.14746

Abstract

Ondansetron, a 5-hydroxytryptamine 3 receptor antagonist, has been increasingly used off-label in the pediatric population for the treatment of vomiting in the context of acute gastroenteritis. The authors describe the case of a 10-year-old girl with an immediate reaction of generalized urticaria after the oral intake of ondansetron. Allergology work-up, by performing skin tests, confirmed the diagnosis of immunoglobulin E mediated hypersensitivity. Five months earlier, she had taken the first dose of this drug in an earlier episode of acute gastroenteritis, which probably led to her sensitization. Although ondansetron is usually safe, its increased use will probably lead to more frequent adverse reactions, including allergic reactions. This case stands out for its rarity and emphasizes the need to use ondansetron judiciously and in the case of the absence of any therapeutic alternative.

Keywords: Anaphylaxis; Child; Drug Eruptions; Drug Hypersensitivity; Ondansetron/adverse effects

Introduction

Ondansetron is a powerful antiemetic, usually well tolerated, of the category of 5- hydroxytryptamine 3 receptor antagonists (5-HT3).[1]

Ondansetron, like other drugs from this category, such as granisetron, is a drug that by its power and safety is used for vomiting prevention in cases of chemotherapy or surgical anesthesia.[2-4]

However, this drug can be associated with side effects, usually mild, such as headache (17%), diarrhea (16%), and fever (8%).[5] Nevertheless, it is known that this drug can also be related to electrocardiographic alterations and coronary vasospasm,[6] seizures and allergic reactions, which can be fatal.[2-9]

The hypersensitivity to ondansetron is rare, but in recent years some cases have been reported, typically in patients with repeated intravenous treatments, during chemotherapy.[3,5,9]

The easy accessibility to ondansetron allowed its increased off-label use in different clinical contexts related to vomiting, such as headaches or acute gastroenteritis.[1]

Off-label use, which is outside the indications authorized by the drug regulatory authorities, is usual in pediatric patients due to a lack of clinical trials in this population, due to practical considerations and ethical implications. However, such use is often necessary and appropriate and should be evaluated according to the indications, therapeutic alternatives, and risk-benefit considerations. Its off-label use might implicate that parents/caregivers should be informed, and informed consent should be obtained.

Being acute gastroenteritis one of the main reasons for observation in the pediatric emergency department, and since ondansetron is an effective and usually safe drug, it is expected to observe its increasing use, in this case out of indication by age group.[10] However, physicians must be aware of the possibility of the occurrence of adverse reactions, particularly allergic reactions, predictable by the frequent general use of this drug.

Although the hypersensitivity to ondansetron might be related to hypersensitivity to other drugs from the same group of drugs,[11] there are some cases where there is no crossed reactivity with granisetron by its different chemical structure.[2,3,5,9,12] Granisetron may then be used as an alternative, especially in cases requiring frequent anti-emetic therapy, after performing an allergy study to exclude sensitization (by skin tests and, if they are negative, by provocative tests).[12]

Case Report

We describe the case of a 10-year-old girl, with a personal background of atopic eczema, asthma, allergic rhinitis, and no other relevant medical history. In February 2017, the child was admitted to the pediatric emergency department with a clinical condition of vomiting,

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Received: 03/07/2018 | Accepted: 06/02/2019

matching the diagnosis of acute gastroenteritis. She was prescribed 4 mg oral ondansetron and was discharged. About one hour after taking the drug, she presented generalized urticaria, oropharyngeal tightening, with no respiratory distress or other respiratory or cardiovascular complaints. The child returned to the pediatric emergency department again, where she was given adrenaline intramuscularly as well as intravenous clemastine, with the resolution of symptoms. Since then, she has had medical indications for the eviction of ondansetron and other 5HT3 antagonists. Five months before, she had taken ondansetron for the first time. It was taken orally as a therapeutic treatment for acute gastroenteritis, with no adverse reaction. On the course of the allergic testing, a prick skin test was performed with ondansetron (2 mg/mL concentration) that resulted negative. An intradermal skin test was then performed, with a positive result, which was found on the dilution of 1/100 (0.02 mg/mL concentration), with the emergence of a papule with 10 mm, erythema and pruritus, in the immediate reading of the test after 20 minutes (Fig. 1). The concentration levels used on the intradermal tests were supported by the consulted bibliography that showed no irritable reaction with these concentrations in a healthy control.[7,9]

In patients with clinical symptoms suggestive of anaphylaxis and positive skin tests, there is no need of any oral provocative test to confirm the diagnosis.[13,14] Therefore, the diagnosis of immunoglobulin (Ig) E mediated allergy to ondansetron was confirmed, with an indication for drug eviction. No cutaneous tests were made with other 5HT3 antagonists since there is no need for frequent antiemetic therapy for this child.

Figure 1. Positive intradermal skin test with ondansetron (at 1/100 dilution), on a reading performed at 20 minutes.

Discussion

In this article, we present a rare case of a girl with an IgE mediated hypersensitivity to the 5HT3 antagonist ondansetron, after oral administration, with highly probable hypersensitivity due to taking the oral drug previously, both in the context of acute gastroenteritis.

Anaphylaxis is a clinical diagnosis that can be supported by laboratorial tests, particularly by the increase of serum tryptase. It is recommended to measure serum tryptase in the first six hours after the onset of symptoms (ideally between 30 and 90 minutes).[13,15] If there is a follow-up evaluation, with increases followed by a regression in less than 24 to 48 hours to baseline values, it indicates a mastocytary activation and supports the diagnosis of anaphylaxis. In this case, in the emergency department, serum tryptase could have been measured.

The published ondansetron hypersensitivity cases in pediatric ages are rare[5,8] and, according to the indexed literature, this is the first case reported in Portugal. Most published cases of allergic reaction were described in adults frequently after taking this antiemetic drug by intravenously during chemotherapy treatments.[3,9,11,12] or after surgery.[2,7,16] In 2010,[5] a case of a 1-year-old child was published. This child was on chemotherapy treatment for neuroblastoma and had a serious allergic reaction that resulted in a cardiorespiratory arrest, immediately after intravenous ondansetron administration (in the 56th dose of the drug). For this child, there was a need to find a therapeutic alternative because of frequent antiemetic necessity, and some cutaneous tests were made with granisetron that came back negative, being well tolerated later on.

Posteriorly, another case report of an Australian adolescent girl was published with an immediate anaphylactic reaction after an oral dosage of 4 mg of ondansetron, showing effects of mucocutaneous and respiratory difficulties that regressed after intramuscular adrenaline but with biphasic anaphylaxis and the necessity of another dosage of intramuscular adrenaline.[8] Similar to the current published case, this adolescent had this treatment in the context of acute gastroenteritis and had no need of frequent antiemetic treatment. Therefore, she was told to avoid the use of all 5HT3 antagonist drugs, and no testing was conducted, including to granisetron. Although ondansetron is considered a safe drug, it could be associated with potential serious effects that should be taken into consideration when it concerns the prescription of the drug.[2,5] The possibility of serious reactions is especially important when the drug is prescribed for outpatient context where a fast and proper treatment may not be possible.[4] This case emphasizes the need to rationalize the prescription of ondansetron to prevent cases of children who present hypersensitivity to this drug.

WHAT THIS CASE REPORT ADDS

- Despite the safe profile, ondansetron can cause hypersensitivity reactions, particularly after several administrations that may cause sensitization to the drug.
- After sensitization to a drug, any new exposure can cause a reaction that can be slight or serious, and in some cases potentially fatal.
- Hypersensitivity reactions to ondansetron have been described, being the first case in the national literature, to the best of our knowledge. This case emphasizes that the use of ondansetron should be rationalized to avoid a possible increase in the incidence of hypersensitivity reactions.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

There were no external funding sources for the realization of this paper.

Provenance and peer review

Not commissioned; externally peer reviewed.

Consent for publication

Consent for publication was obtained.

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Alergia ao Ondansetron: O Reverso da Medalha num Caso Clínico

Resumo:

O ondansetrom, antagonista do recetor da 5-hidroxitriptamina 3, tem sido cada vez mais utilizado fora da indicação ("off-label") na população pediátrica, no tratamento de vómitos em contexto de gastroenterite aguda. Os autores descrevem o caso clínico de uma adolescente de 10 anos do género feminino com uma reação imediata de urticária generalizada após toma oral de ondansetrom. A avaliação alergológica, pela realização de testes cutâneos, confirmou o diagnóstico de hipersensibilidade mediada por IgE. Cinco meses antes a criança tinha feito uma primeira toma deste fármaco, num episódio anterior de gastroenterite aguda, que terá induzido a sensibilização. Embora o ondansetrom seja habitualmente seguro, a sua utilização cada vez mais frequente poderá levar ao aparecimento de reações adversas, nomeadamente alérgicas. Este caso destaca-se pela sua raridade e vem enfatizar a necessidade de utilizar o ondansetrom racionalmente e caso não haja alternativas terapêuticas indicadas.

Palavras-Chave: Anafilaxia; Criança; Erupção por Droga; Hipersensibilidade a Drogas; Ondansetron/efeitos adversos