

## Suspected Oseltamivir-induced bradycardia in a pediatric patient: A case report from King Abdullah Specialist Children's Hospital, Riyadh, Saudi Arabia

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### Abstract

In recent years, influenza infection in the pediatric population has been a wide-scale issue that physicians face during the winter season. Medications used to treat and prevent such infections include Oseltamivir, an anti-viral neuraminidase inhibitor developed for both influenzas A and B. The most commonly well-known and manifesting adverse effects are nausea, vomiting and gastrointestinal upset. There is paucity of reports on other potential serious side effects of Oseltamivir in the pediatric population. One of the rarely reported adverse reactions in adult population is sinus bradycardia. This case reports the development of sinus bradycardia in a pediatric patient after administration of Oseltamivir. The previously healthy five-year-old patient was started on Oseltamivir after a positive polymerase chain reaction for influenza. The patient developed sinus bradycardia but remained hemodynamically stable. This finding led to consultations and investigations to determine the cause of bradycardia. It is pivotal to increase the awareness of the potential link between Oseltamivir and bradycardia in pediatric and adult populations to avoid unnecessary clinical investigations and to enhance physician decision-making. A prospective cohort study on Oseltamivir is needed for better understanding of its adverse effects in the pediatric population.

### Introduction

Following the last influenza season, the Center of Disease Control (CDC) reported 183 children have died from flu. Almost 11.5 million cases of influenza in children have been estimated, with a reported hospi-

talization of 48,000 children this last season. The 2017-2018 season showed the highest peak of flu-associated deaths in children since the 2009 H1N1 pandemic.<sup>1,2</sup> The reported numbers must be taken as a reminder that seasonal influenza can be very unpredictable and severe.

In the new version of American Academy of Pediatrics recommendations (2017-2018), Oseltamivir and Zanamivir (another neuraminidase inhibitor) are specified as the only antiviral medications recommended for chemoprophylaxis and treatment of influenza in children during the current flu season.<sup>3</sup>

Oseltamivir carboxylate is an inhibitor of influenza virus neuraminidase; it works through the inhibition of viral particle release.<sup>4</sup> This antiviral is used for prophylaxis and treatment of Influenza A and Influenza B in adults, adolescents, and pediatric populations.<sup>5</sup>

Although the CDC has addressed recent reports of several side effects caused by antiviral drugs, it has also affirmed that antivirals are still recommended in the treatment of hospitalized flu patients. On review of the literature, only a few reports are available on the Oseltamivir induced side effects. The most commonly observed and manifesting adverse effects caused by Oseltamivir, were nausea, vomiting and gastrointestinal upset.<sup>6</sup> There is paucity of reports on potential serious side effect of Oseltamivir in pediatric population. A few sporadic adult case reports are available.<sup>7</sup> In this report, we present one case with suspected Oseltamivir-induced bradycardia in a pediatric patient.

### Case Report

A five-year-old previously healthy patient who is a known case of bronchial asthma was admitted for viral pneumonia following a week of upper respiratory tract infection symptoms: fever, hypoactivity and decreased oral intake. Viral multiplex polymerase chain reaction was positive for influenza A, and Oseltamivir was administered shortly after on the first day of admission. However, there was a concern from the treating team of a newly recorded bradycardia post Oseltamivir administration. The notion that Oseltamivir might be the cause of this was not considered, which prompted further investigation as to why the patient was experiencing bradycardia. The lowest heart rate was 66 beat per minute; however, the patient was hemodynamically stable. The cardiology and pediatric intensive care were consulted for identifying the cause of bradycardia, and they

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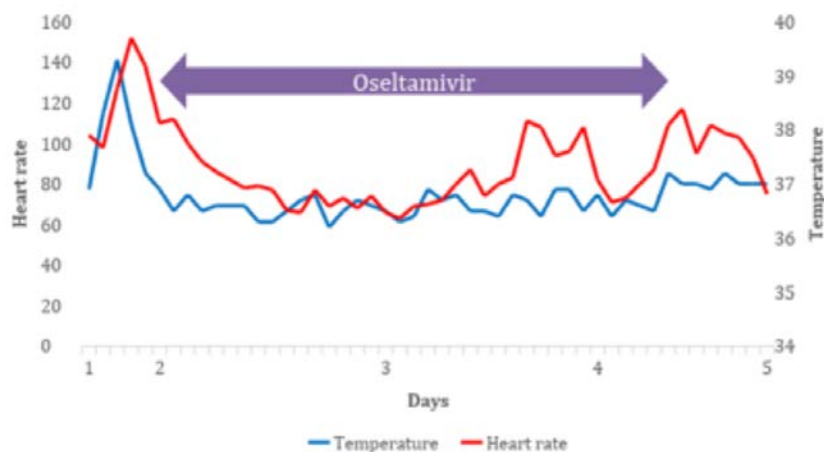
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concluded that electrolytes, thyroid function testing and cardiac function were normal, other than the present sinus bradycardia, which was recorded while the patient was awake. After discontinuation of Oseltamivir, the patient's heart rate went back to baseline. Oxygen saturation was at 97% throughout the hospital course. This patient's heart rate and temperature is shown in Figure 1, as was recorded on BESTCare, the health information system used by King Abdullah Specialist Children's Hospital.

### Discussion

The use of Oseltamivir for the pediatric population is favorable among pediatric physicians; however, the controversy may be due to the lack of solid data examining the character and incidence of its possible adverse effects. The majority of physicians would justify their use of Oseltamivir for children suffering from influenza as the benefits may outweigh the risks.<sup>8</sup> It has been reported in the literature of a possible link between Oseltamivir and bradycardia among the adult and neonatal population, that may be because of Oseltamivir's interference of human endogenous neuraminidase.<sup>7,9</sup> In a systematic review that aimed to define clear centiles for resting



**Figure 1. Heart rate and temperature for the pediatric patient on Oseltamivir.**

pulse rates (RPRs) in children of all ages, the 50th percentile RPR for a 5 year old female is estimated at 95 beats per minute (bpm), and the lowest (1st percentile) for the same age/gender is estimated at 65 bpm.<sup>10</sup>

In this case, the patient presented with acute signs and symptoms of viral pneumonia that were treated accordingly with antiviral medication; specifically, Oseltamivir. The patient, to the medical teams' surprise, presented with sinus bradycardia the day of administration.

Oseltamivir is relatively newly introduced antiviral agent in pediatric use for seasonal flu. Due to the unfamiliarity with and the lack of awareness of potential side effect, it can cause significant concern of the treating teams leading to unnecessary extensive investigations and involvement of different pediatric subspecialties. While the occurrence of Oseltamivir-induced bradycardia is considered rare, it is crucial to determine the hidden and silent side effect and to consider all the potential risks and outcomes upon prescribing Oseltamivir.

This case report shows the importance of considering all documented adverse effects when it comes to using Oseltamivir, and other antiviral medications, in a pedi-

atric population. A prospective cohort study is needed in the pediatric population to document Oseltamivir-induced sinus bradycardia. Such a study will minimize time consuming and financial efforts in investigating bradycardia as a clinical sign, as it seems that this drug's adverse effect is reversible with no effect on patients' hemodynamics.

## Conclusions

The case presented demonstrates a potential link between Oseltamivir and bradycardia in the pediatric population. In order to help physicians make decisions and prevent uncalled clinical investigations, a prospective cohort study focusing on observing pediatric patients' heart rate and rhythm after Oseltamivir administration is needed.

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