

Original Article



Prevalence of β_2 -agonist inhalation for outpatients in a pediatric emergency center during enterovirus D68 epidemic

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ABSTRACT

Background: Enterovirus D68 (EV-D68) has been reported to have caused severe bronchial asthma attacks and hospitalization epidemics in Japan in September 2015.

Objective: To investigate the prevalence of β_2 -agonist inhalation in a pediatric emergency center during a period of increased hospitalization for bronchial asthma, which was suggested to be associated with EV-D68.

Methods: We investigated the prevalence of β_2 -agonist inhalation in a pediatric emergency center in Saga city, Japan, from April 2013 to October 2015, and also clarified the trends in bronchial asthma hospitalization in the same area during that time.

Results: The prevalence of β_2 -agonist inhalation in the pediatric emergency center, September 2015 was highest when EV-D68 became widespread. The monthly average for β_2 -agonist inhalation during the study period was 91 cases, but the count in September 2015 was 255 cases. Hospitalized cases of bronchial asthma in September 2015 were increased for age ≥ 3 years and not increased for age < 3 years, but the prevalence of β_2 -agonist inhalation at the pediatric emergency center was increased even under the age of 3 years.

Conclusion: During the epidemic period for EV-D68, cases requiring β_2 -agonist inhalation were increased. The EV-D68 epidemic may be related to not only severe cases requiring hospitalization, but also exacerbation of relatively mild symptoms of bronchial asthma.

Keywords: Enterovirus D68; Bronchial asthma; β_2 -agonist inhalation

INTRODUCTION

Enterovirus D68 (EV-D68) is a member of the Picornaviridae genus of enteroviruses, and infection can result in various respiratory diseases including nasal discharge, cough, wheeze, and severe pneumonia [1]. In the United States, an outbreak of EV-D68 infection occurred from August 2014 to January 2015, and severe respiratory failure due to infection was reported [1, 2]. In addition, EV-D68 was detected from a case of acute flaccid paralysis, and an association with EV-D68 infection was thus suspected [3]. In Japan, numbers of reported EV-D68 cases were large

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in 2010, 2013, and 2015, and in those epidemic years, the number of reports increased from summer to autumn, with a notable peak in September 2015 [4]. The Japanese Pediatric Allergy Society conducted a nationwide survey on childhood bronchial asthma cases and reported EV-D68 as an important virus causing severe bronchial asthma attacks and hospitalization epidemics, especially in September 2015 [5]. This study therefore investigated the prevalence of β_2 -agonist inhalation therapy for outpatients with wheeze in a pediatric emergency center in Saga city, Japan, including in September 2015 when EV-D68 was prevalent.

MATERIALS AND METHODS

To examine the prevalence of β_2 -agonist inhalation therapy for outpatients in a pediatric emergency center, we enrolled 2,814 cases of children who visited Saga City Holiday and Night Time Child Clinic in Saga city (Saga area of Western Kyushu, Japan) and inhaled β_2 agonists during the period from April 2013 to October 2015. Saga City Holiday and Night Time Child Clinic is a facility established by Saga city to ensure early emergency medical care for children during holidays and the night time for the entire Saga city area. In the 2015 census, Saga city had 32,324 residents under 15 years old. Saga City Holiday and Night Time Child Clinic provided aggregate numbers. We investigated the number of patients who inhaled β_2 agonists by month, sex, and age group (0–2, 3–6, 7–12, or 13–15 years). To clarify the prevalence of hospitalizations for bronchial asthma from April 2013 to October 2015, we enrolled 657 cases of children hospitalized for bronchial asthma exacerbation at Saga University Medical School Hospital, Saga-Ken Medical Centre Koseikan, and the National Hospital Organization Saga Hospital. Admissions to these 3 medical institutions generally correspond to child hospitalizations in the Saga city area.

This study protocols were approved by the clinical research ethics review board at Ureshino Medical Center (approval number: 16-46).

RESULTS

Cases of β_2 -agonist inhalation therapy at the pediatric emergency center in the Saga city area during EV-D68 epidemic

A total of 2,814 cases of β_2 -agonist inhalation therapy were performed at Saga City Holiday and Night Time Child Clinic between April 2013 and October 2015, in 1,731 males and 1,083 females. The monthly average for this period was 91 cases. The greatest monthly number of cases was 255 cases, seen in September 2015, when EV-D68 was prevalent (**Fig. 1A**). By age group, 1,291 cases were at 0–2 years old, 1,081 cases at 3–6 years old, 415 cases at 7–12 years old, and 27 cases at 13–15 years old. The monthly average for each age class was 42 cases for 0–2 years old, 35 cases for 3–6 years old, 13 cases for 7–12 years old, and 0.9 cases for 13–15 years old. For 0–2 years old, 3–6 years old and 7–12 years old, but not 13–15 years old, cases of β_2 -agonist inhalation peaked in September 2015 when EV-D68 was prevalent (101 cases for 0–2 years old, 101 for 3–6 years old, and 51 cases for 7–12 years old) (**Fig. 1B**).

Number of hospitalizations for bronchial asthma in the Saga city area during EV-D68 epidemic

A total of 657 children (422 males, 235 females) were admitted for bronchial asthma in Saga city from April 2013 to October 2015, with an average of 21 cases per month. The greatest

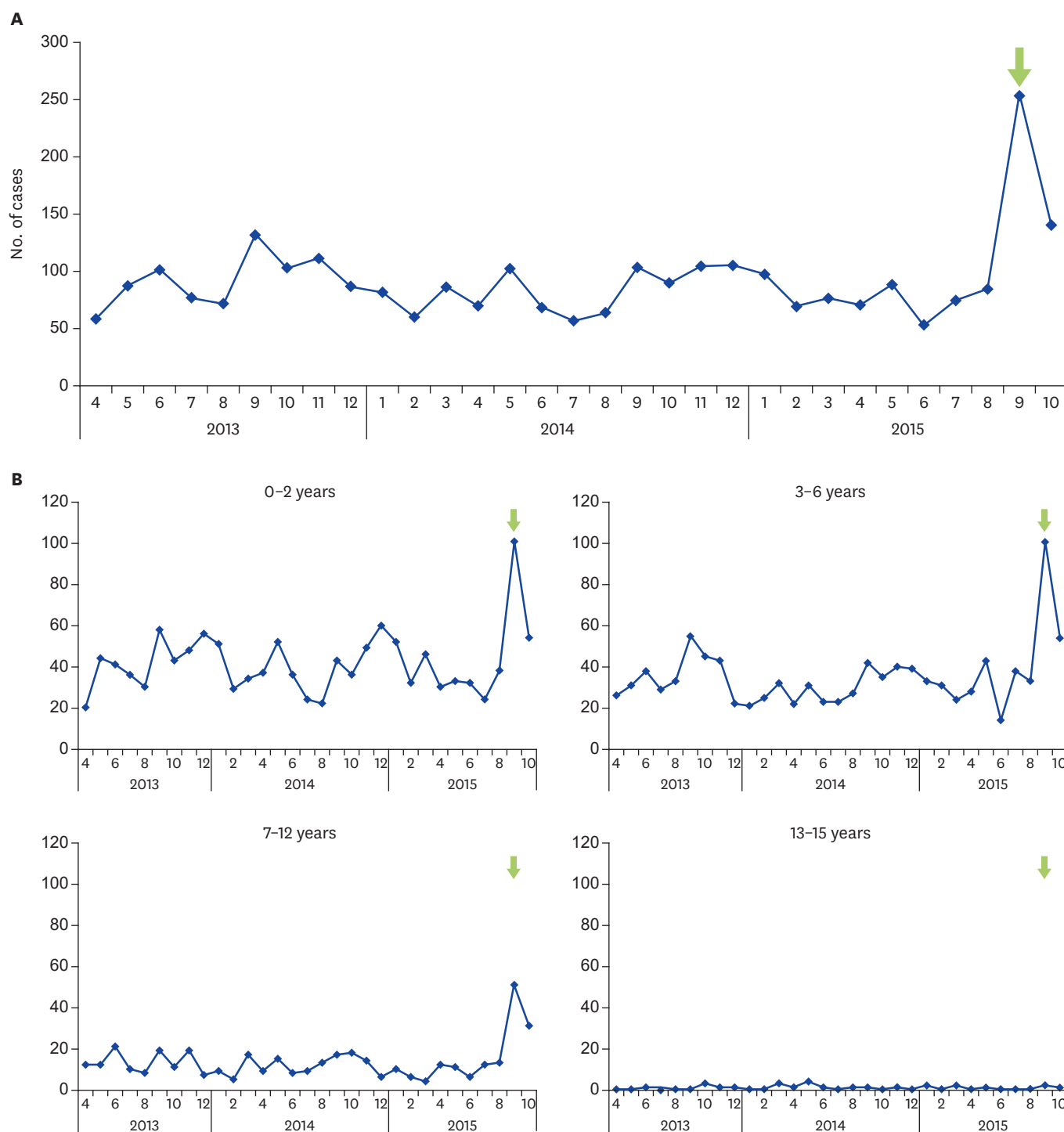


Fig. 1. (A) Time-trend in cases of β_2 -agonist inhalation therapy at the pediatric emergency center from April 2013 to October 2015. Arrow indicates September 2015. (B) Time-trend in cases of β_2 -agonist inhalation therapy at the pediatric emergency center by age group (0–2, 3–6, 7–12, and 13–15 years). Arrows indicate September 2015.

number of admissions was seen in September 2015 when EV-D68 was prevalent, with 56 cases. By age group, 311 cases were 0–2 years old, 228 cases were 3–6 years old, 112 cases were 7–12 years old, and 6 cases were 13–15 years old. Monthly averages for each age class were 10 cases at 0–2 years old, 7.4 cases at 3–6 years old, 3.6 cases at 7–12 years old, and 0.2 cases at

13–15 years old. The number of cases of bronchial asthma peaked in September 2015 at 3–6 years old and 7–12 years old, but not 0–2 years old and 13–15 years old. We had no patient with mechanical ventilation and/or intensive care unit (ICU) admission for severe asthma exacerbation from April 2013 to October 2015.

DISCUSSION

According to a survey conducted by the Japan Pediatric Allergy Society to investigate the relationship between EV-D68 and bronchial asthma, Korematsu et al. [5] reported that the number of children hospitalized and mechanical ventilated for bronchial asthma in Japan was highest in September 2015 when EV-D68 was prevalent. They concluded that the EV-D68 epidemic was likely involved in the increase in bronchial asthma hospital cases among children at 3–6 years old and 7–12 years old, but not 0–2 years old. In our area (Saga city, Western Kyushu, Japan), a child case was reported in which EV-D68 was detected in September 2015, when EV-D68 was prevalent [6]. We thought in September 2015 that EV-D68 was supposed to be also epidemic in Saga city, same as the nationwide survey. In our study, in September 2015, the number of hospitalized patients with bronchial asthma markedly increased in three hospitals in Saga City. By age group, the marked increase in the number of hospitalized patients in September 2015 was found at 3–6 years old, and this tendency was also recognized at 7–12 years old. The result of increased hospitalizations over 3 years old was similar to the findings of a nationwide survey [5]. However, we had no patient with mechanical ventilation and/or ICU admission during that.

Additionally, we reported in this study, in cases of β_2 -agonist inhalation therapy in the pediatric emergency center, a marked increase was observed in September 2015 along with the increase in hospitalizations. And, for cases of β_2 -agonist inhalation at the pediatric emergency center, in addition to an increase at 3–6 years old and 7–12 years old, an increase was also seen for 0–2 years old. A relationship between EV-D68 outbreak and exacerbation of bronchial asthma symptoms was also suggested in children under 3 years of age, whereas this was not clarified in the nationwide hospital surveys. Then, we could not completely explain why the numbers of cases of β_2 -agonist inhalation and also hospitalization in the patients over the age of 13 tended not to increase in September 2015. Similarly in the nationwide hospital survey, the “spike” in September 2015 does not appear in patients over the age of 13, suggesting the possibility of a difference in susceptibility and severity depending on age.

The EV-D68 epidemic might be suggested to be related not only to severe cases requiring hospitalization, but also to exacerbation of relatively mild bronchial asthma symptoms. Recently, Itagaki et al. [7] reported the detection rate of EV-D68 during the epidemic period (in August–October 2015, in Yamagata, Japan), and demonstrated that the most cases with EV-D68 infection were managed as outpatients. Bronchial asthma is a disease frequently encountered in pediatric outpatient clinics and pediatric emergency centers. When the outpatient visits for bronchial asthma attack and/or wheeze increase at all ages around autumn, earlier than usual, consideration of exacerbation of bronchial asthma symptoms accompanying an EV-D68 epidemic may be warranted. However, we had no direct evidence for exacerbation of asthma due to EV-D68 in September 2015, the circumstantial evidence was only present. Then, surveillances of infectious diseases and asthma in pediatric emergency centers might be beneficial for better control of asthma and early response to exacerbation associated with infection, and further studies are necessary.

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