

Current Situation of Treatment for Anaphylaxis in a Japanese Pediatric Emergency Center

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Objective: Anaphylaxis is a systemic allergic reaction that sometimes requires prompt treatment with intramuscular adrenaline. The aim of the study was to investigate the current situation regarding anaphylaxis treatment in a representative pediatric primary emergency facility in Japan.

Methods: We retrospectively examined the medical records dating from April 2011 through March 2014 from Kobe Children's Primary Emergency Medical Center, where general pediatricians work on a part-time basis. Clinical characteristics and current treatments for patients with anaphylaxis who presented to the facility were investigated. Furthermore, we compared the clinical characteristics between anaphylaxis patients given intramuscular adrenaline and those not given it.

Results: During the study period, 217 patients were diagnosed with anaphylaxis. The median Sampson grade at the time of visit was 2, and 90 patients (41%) were grade 4 or higher. No patients received self-intramuscular injected adrenaline before arrival at our emergency medical center because none of the patients had been prescribed it. Further treatment during the visit was provided to 128 patients (59%), with only 17 (8%) receiving intramuscular adrenaline. Patients given intramuscular adrenaline had significantly lower peripheral saturation of oxygen at the visit ($P = 0.025$) and more frequent transfer to a referral hospital ($P < 0.001$) than those not given intramuscular adrenaline.

Conclusions: Education for Japanese pediatric practitioners and patients is warranted, because no patients used self-intramuscular injected adrenaline as a prehospital treatment for anaphylaxis, and only severely affected patients who needed oxygen therapy or hospitalization received intramuscular adrenaline in a pediatric primary emergency setting.

Key Words: anaphylaxis, intramuscular adrenaline, Japan, general pediatrician, primary pediatric facility

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Anaphylaxis is a serious systemic allergic reaction that requires prompt treatment.¹ In 2011, the World Allergy Organization (WAO) published guidelines and created a consensus document regarding worldwide diagnostic criteria and management.² These guidelines specify intramuscular adrenaline as the drug of first choice for treating anaphylaxis and state that delayed administration can affect patient prognosis. Although a standard timing for intramuscular adrenaline administration still remains to be established, it is generally recommended for patients with respiratory and cardiovascular symptoms such as stridor, wheezing, respiratory distress, and shock (Sampson grade [SG] ≥ 4). However, adrenaline is an inotropic agent, and Japanese general pediatricians have no opportunities to use it outside of resuscitation.

Although awareness of intramuscular adrenaline use has increased in recent years, particularly among allergy specialists,³ the realities of its use in a pediatric emergency facility that employs nonallergy specialists remain unknown. Therefore, we retrospectively investigated the clinical characteristics and treatments for pediatric patients with anaphylaxis at a representative Japanese pediatric primary emergency facility to clarify the current status of the treatment of anaphylaxis.

METHODS

Setting

Kobe Children's Primary Emergency Medical Center (KCPEMC) provides medical services for pediatric patients without trauma during holidays and outside of working hours. Approximately 30,000 pediatric patients per year visit the center to receive medication. More than 140 pediatricians work there on a part-time basis, most of whom are nonallergy specialists.

Study Design

For this retrospective study, we picked the patient charts up from the medical records between April 2011 and March 2014 on the basis of the *International Classification of Diseases, Tenth Revision*, as anaphylaxis and anaphylactic shock (code numbers: T78.0 and T78.2), food allergy reactions (T78.1), unspecified allergy (T78.4), and generalized skin eruption due to drugs (L27.0). Then, the clinical profiles of patients diagnosed with anaphylaxis were examined using their chart reviews. Clinical characteristics and current treatments for anaphylaxis patients were investigated. Furthermore, we compared the clinical characteristics between anaphylaxis patients given intramuscular adrenaline and those not given it. The institutional review board approved this study (#57–6), and informed consent was obtained from guardians.

Diagnostic Criteria

The diagnostic criteria for anaphylaxis were based on the WAO guidelines,² shown in Appendix 1 (Supplemental Digital Content 1, <http://links.lww.com/PEC/A107>).

TABLE 1. Patients' Characteristics (N = 217)

	n (%)
Males	90 (41)
Age, y	
<1	29 (13)
1–6	117 (54)
6–12	63 (29)
>12	8 (4)
Antigen	
Food	193 (89)
Drug	3 (1)
Others	2 (1)
Unknown	19 (9)
Allergen that the patient reacted to before	
Yes	78 (36)
No	65 (30)
Unclear	74 (34)
History	
Anaphylaxis	17 (8)
Asthma	38 (18)
Others	9 (4)

Evaluation of Severity

Symptom severity for anaphylaxis patients was evaluated using the SG,⁴ shown in Appendix 2 (Supplemental Digital Content 2, <http://links.lww.com/PEC/A108>).

Definitions

Patients who visited our center for recurrent anaphylactic symptoms within 24 hours after the first anaphylaxis treatment were considered revisits. When a pediatrician decided that further treatment was needed, patients were sent to a referral medical center and the case was defined as a transferal. Anaphylaxis treatment policies and transfer decisions were at the discretion of the attending pediatrician.

Statistical Analysis

Data are expressed as the median (range) or n (%). Statistical analysis was performed using JMP Version 10.0 (SAS Institute, Cary, NC). In univariate analyses, a Fisher exact test was used for categorical variables and a Mann-Whitney *U* test for noncategorical variables. In all analyses, a *P* value of less than 0.05 was regarded as significant.

RESULTS

Patients' Characteristics

Table 1 shows the clinical characteristics of the 217 anaphylaxis cases ultimately subjected to analysis. The age of patients was 3.7 (0.4–16.9) years. The suspected antigen was most commonly food. Medical history mainly included asthma and anaphylaxis. Sixty-five patients (30%) developed allergic symptoms for the first time in their life, and some of them determined the allergen.

Status Before Visit

Table 2 shows the prehospital symptoms and treatments in our cohort. Time from antigen exposure to symptom onset was 0.05 (0–4.5) hours, with skin symptoms being the most common.

Sampson Grade at onset was 3 (1–5), and 101 patients (47%) were SG 4 or higher. Forty-four patients (20%) had been treated with obtainable drugs before their visit, but no patients had been administered self-injected intramuscular adrenaline via an EpiPen (Mylan, Canonsburg, PA).

Course and Outcome After Visit

Table 3 shows the symptoms and treatments of our cohort, and their outcomes after visiting to KCPEMC. Time from symptom onset to the visit was 1.5 (0.1–7.0) hours, SG at the visit was 2 (0–5), and 90 patients (41%) were SG 4 or higher. Additional treatment during the visit was provided to 128 patients (59%). Such treatment most commonly took the form of inhaled β -agonist or adrenaline (42%), followed by intravenous steroids (32%) and intravenous antihistamines (19%). Seventeen patients (8%) were given adrenaline intramuscularly. Of the 17 patients who were given intramuscular epinephrine, 8 patients (47%) were given other medications first and then received intramuscular epinephrine. Intramuscular adrenaline was given to only 15 of the 90 patients with SG 4 or higher and only 1 of the 17 patients with a history of anaphylaxis. The observational period after treatments was 1 to 3 hours.

Despite these treatments, 13 patients were transferred to a referral hospital because patients experienced exacerbation or showed no improvement and 5 patients revisited because of recurrent anaphylactic symptoms. Ten (77%) of the 13 transferred patients had SG 4 or higher and low peripheral saturation of oxygen (SpO₂). Eleven of the 13 referrals required hospitalization to continue the treatments; however, no patients needed intubations, intravenous epinephrine infusions, or intensive care unit stays.

Comparison of the patients given or not given intramuscular adrenaline revealed no significant difference in SG at onset between the groups, but SG at the visit was significantly higher and SpO₂ was significantly lower in the patients given adrenaline intramuscularly. In comparison with the nonadrenaline group, patients given intramuscular adrenaline had higher rates of additional treatment and transfer to referral facilities (Table 4).

TABLE 2. Prehospital Symptoms and Treatment (N = 217)

	n (%)
Initial symptom*	
Cutaneous	197 (91)
Gastrointestinal	85 (39)
Respiratory	172 (79)
Circulatory	0 (0)
SG at onset	
1	6 (3)
2	81 (37)
3	29 (13)
4	100 (46)
5	1 (1)
Prehospital treatment (n = 44) [†]	
Oral antihistamine	24 (11)
Oral corticosteroid	21 (10)
Inhaled β -stimulant	9 (4)
Self-intramuscular injected epinephrine (EpiPen)	0 (0)
Others	3 (1)

*Some patients had multiple clinical symptoms at onset.

[†]Some patients had multiple treatments.

DISCUSSION

This retrospective study reveals for the first time the course and treatment of anaphylaxis in a Japanese primary emergency medical facility. In our cohort, the proportion of boys, age distribution, and frequency of organ-specific onset as an initial symptom were consistent with previously reported data.^{5–8} However, food allergies were identified in approximately 90% of patients, a slightly larger percentage than in most previous reports.^{9–11} The general epidemiological characteristics of our cohort, therefore, were found not to be ostensibly different from those of previous reports, although KCPEMC provides treatment primarily for pediatric patients during holidays and outside of working hours.

Despite the fact that anaphylaxis patients with SG 4 or higher accounted for more than 40% of presenting patients, the most common treatment was inhaled β -agonists or adrenaline. Intravenous antihistamines, which have been considered ineffective in alleviating respiratory symptoms, were given to approximately 20% of patients. Similarly, intravenous steroids are slow to show an effect but were given to more than 30% of patients. By contrast, intramuscular adrenaline was administered to only 8% of patients, representing a much lower frequency of use than in other reports published to date.^{3,6,8,12} Reasons for this discrepancy may include the large number of nonallergy specialists employed at KCPEMC, who do not necessarily have knowledge about intramuscular adrenaline administration, and the lack of a unified treatment protocol for anaphylaxis.

The comparison data between the intramuscular adrenaline and nonadrenaline patients indicate a situation whereby adrenaline is inevitably used in severe cases, such as patients who needed oxygen therapy or hospitalization. The WAO guidelines stipulate

TABLE 3. Symptoms, Treatment, and Outcomes After Visit (N = 217)

	n (%)
SG at visit	
Asymptomatic	18 (8)
1	29 (13)
2	64 (30)
3	16 (7)
4	88 (41)
5	2 (1)
Treatment in our facility*	
None	89 (41)
β -Agonist or adrenaline inhalation	91 (42)
β -Agonist	63 (29)
Adrenaline	24 (11)
Both	4 (2)
Intravenous antihistamine	41 (19)
Intravenous corticosteroid	69 (32)
Intramuscular epinephrine	17 (8)
Outcome	
Improved	206 (95)
No change	8 (4)
Worsened	3 (1)
Transferal	13 (6)
Revisit	5 (2)

*Some patients received multiple treatments.

TABLE 4. Comparison of Patients Given Intramuscular Adrenaline With Those Not

	Ad (+) (n = 17)	Ad (–) (n = 200)	P
Age, y	4.2 (0.7–14.8)	3.6 (0.4–16.9)	0.51
Males	12 (71)	115 (58)	0.29
SG at onset	4 (2–4)	3 (1–5)	0.39
Time from onset to visit, h	1.9 (0.5–4)	1.4 (0.1–7)	0.24
Prehospital treatment	3 (18)	41 (21)	0.78
SG at visit	4 (2–5)	2 (0–5)	<0.001
SpO ₂ (%) at visit	97 (89–100)	98 (88–100)	0.025
Any treatment in our facility	17 (100)	111 (56)	<0.001
Transfer to a referral facility	5 (29)	8 (4)	<0.001

Values in parentheses are range or percentage.

Ad (+) indicates given intramuscular adrenaline; Ad (–), not given adrenaline.

that intramuscular injection of adrenaline is indicated for patients with a serious medical history or relatively serious reactions, such as SG 4 or higher.² Despite adrenaline being given to only a small number of patients in our cohort, fortunately, few hospitalizations and revisits were necessary. Moreover, no deaths and no cases that needed intubations, intravenous epinephrine infusions, or intensive care unit stays were documented.

Approximately 20% of patients had used household medicines, including oral steroids and antihistamines prescribed for past medical conditions. Remarkably, however, none of the patients in this study had been given adrenaline by EpiPen as treatment before their visit, because EpiPen was not prescribed by their primary care physician although it is available in Japan. As the use of the EpiPen has been emphasized in various studies as an early treatment option for anaphylaxis,^{13,14} in Japan, therefore, both pediatricians not specializing in allergy and their patients need to be educated about the importance of prehospital treatment using the EpiPen.

As a limitation of this study, we could not find any risk factors for the revisit due to recurrent anaphylactic symptoms because of a small number of patients with the revisit (there were only 5 revisited patients). Further studies are needed to reveal risk factors using a large number of patients with revisits.

In conclusion, this study is the first to elucidate the clinical and treatment circumstances for anaphylaxis at a primary pediatric emergency facility in Japan. Education for Japanese pediatricians and patients is warranted because none of the patients in this study used intramuscular adrenaline as a prehospital treatment, and only those who needed oxygen therapy or hospitalization were treated with intramuscular adrenaline.

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