

Severely Food-Allergic Children Die not Having Epinephrine at Hand

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Received Date: 20th February 2015

Accepted Date: 12th March 2015

Published Date: 25th March 2015

Citation: Cantani A (2015) Severely Food-Allergic Children Die not Having Epinephrine at Hand. Enliven: *Pediatr Neonatol Biol* 1(1): 006.

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Abstract

Despite careful contributions, food allergic children have a significant risk of anaphylactic episodes. Especially at risk are children not accompanied by parents or caregivers in public places, or restaurants, or not provided with injectable epinephrine. We shortly report two children and conclude that parents should be provided with medication for emergency treatment.

Keywords: Children; Anaphylaxis; Epinephrine; Public places; Restaurants

Two Fatal Cases

Two fatal cases of food induced anaphylaxis were triggered by inadvertent food ingestion. Both cases were reported by the Italian press during last summer. Nobody had epinephrine ready, so both were rushed to a local emergency department (ED), but there apparently was a delay before they received epinephrine, and both died.

In a city of Northern Italy, during a dance exhibition as part of a flower celebration, a severely nut-allergic 12-year-old girl as soon as she ate a home-made cake perceived a nut-taste and soon systemic symptoms were triggered. Nobody had epinephrine at hand, and the girl, despite the hospital cures died of anaphylactic shock.

In Rome, an exquisitely CM allergic 9-year-old boy went to a pizza-parlor with his mates. Some adults were also present. He may have touched some mozzarella cheese on the pizza-maker counter, or when mozzarella is sliced, fresh cow's milk (CM) gushes out and the child may have touched some drops of CM spilling from a pizza. Also in this case nobody had epinephrine ready, and the anaphylactic shock was so severe that no hospital cure saved him.

In these cases, in addition to the lacking epinephrine, the allergic history of both children was rich of similar, less severe manifestations. Obviously, both were subjected to skin-prick tests, clearly highly positive to the incriminated foods. Of such children the allergy world is very rich, but strangely enough, some parents do not perceive that their allergic children should always be accompanied by a parent or a caregiver expert on the use of Epi-Pen.

Epidemiology

Anaphylaxis is frequent in children: 27 out of 544 (4.9%) investigated children with food allergy (FA) had anaphylaxis as part of their clinical

presentation [1]. In 76 children occurred 95 cases of anaphylaxis, 62 of them (82%) had a personal history of atopic symptoms; foods were identified as causative agents in 57% of the episodes of anaphylaxis [2]. Instead, the parents of 4,173 children aged 3-17 reported a food-induced anaphylaxis rate of 0.59% [3]. Anaphylactic shock was triggered in 17 children and adolescents [4,5]. In 13 cases of anaphylaxis, all were due to masked allergens, peanut in three cases, cashew in two, and egg in one, and of the six patients who died only two received epinephrine in the first hour [4] as in the two reported cases: no child soon recognized the impending danger. However, in one fatality in France not even a quick injection of epinephrine saved the child's life [6], as 2 children who died despite receiving epinephrine before admission to hospital [7]. Unfortunately, no reliable data exist on the epidemiology of lethal food-induced anaphylaxis in children (Table 1) [4].

In a meta-analysis we have summarized 70 cases [8], 23 (32.4%) to peanuts, 17 (23.9%) to nuts, 13 (18.3%) to CM, and 5 to eggs (7.0%), but in the 17 children, peanut and nuts accounted for 15 (88.2%) deaths [4,5]. Bock reported several cases also in 3- to 4-year-old children due to peanut, walnut, shrimp, spices, and to sulfite containing foods, such as catchup and vinegar.

Table 1: Epidemiology of lethal food-induced anaphylaxis in children

No reliable data on	Incidence
	Prevalence
	Mortality

Adapted from reference [4]

Cow's Milk-Induced Anaphylaxis in Children

In addition to peanut and tree-nuts, another allergen as much potent is CM, responsible for cases of anaphylaxis in up to 11% [9] and 12.6% of cases [2] and severe reactions triggered by 1-2 drops put upon the inner border of the lower lip [10], up to anaphylactic death as 5 victims aged 2-16 who died at home or at a friend's home because they received no epinephrine, or received it late [11]. In England, there were 8 deaths over a 11-year period in 3-month- to 15-year-old children, and 4 were caused by CM (50%) [7]. Four babies aged 6 weeks to 6 months experienced severe life-threatening reactions, all related to unsupervised self-challenge with either a CM-based formula or a dairy product [12]. We have reported 3 cases of shock and 15 of anaphylaxis to CM-based formulas in children aged 1 month-7 years [13] and in 41 children aged 7 days-15 months worsening of atopic dermatitis, urticaria, vomiting, wheezing, shock (1 case), bronchospasm requiring epinephrine to a CM-based formula [14]. A CM-sensitive infant was hospitalized with systemic anaphylaxis that developed immediately after the application of a diaper rash ointment that contained 5% Ca caseinate [15]. A child aged 12 developed systemic anaphylaxis after eating a cheese-free pizza. It was shown that a small amount of CM was added to the pizza dough. The boy was treated with emergency medication [17].

Contact with minute doses of CM may trigger severe symptoms. Drops of CM inadvertently spilled on the leg of a CM-allergic boy seen by us and on the head of a girl [16] caused severe reactions. Systemic symptoms were triggered by accidental skin contact with a drop of CM dripped from a sandwich containing fresh cheese [17]. Critical risk situations may be induced by an unexpected means of CM activity. Several incredible cases due to CM-inhalation occurred, when the so exquisitely CM-allergic 4-year-old child developed urticaria and wheals whenever he entered a place where CM was stored (personal case), a young woman allergic to long-term eliminated CM walked into a grocery store where unknowingly to her CM was also sold, and she was dead after anaphylaxis by inhalation of CM protein, as reported in 1992 by the Italian daily press, an 18-year old girl severely allergic to CM inadvertently entered a dairy shop where she inhaled CM proteins and experienced a fatal reaction [18], and a child with repeated episodes of acute bronchospasm, also by CM inhalation, that was so severe that his younger nonallergic brother had to follow the soy-based diet of his elder brother [19]. Barbi et al. [18] suggest that the death of the 18-year old girl was possibly caused by the long-term CM elimination diet but a surprising reason is that casein may remain active for 2,500 years [20]. This may explain singular cases.

Where are the Children Safe?

More than the home, the school appears to be safer. In a cohort of 100 subjects, teachers in 55% of the cases, school nurse in 10% of the cases, and even school secretary or cafeteria worker took charge of the situation. In 60% of cases the parents were notified about the emergency [21]. On the contrary, in a school setting two-thirds of children with anaphylaxis did not have emergency medication available, an emergency action plan, or a teacher on site able to administer epinephrine for first aid use [3]. In another report, 77% had the medication available in school, and 81% stated that the school knew the indications for administration [22]. Otherwise, the medications were kept in the health room in 71%, the classroom in 26% [23], the nurse's office in 46%, with the teacher in 23%, in the child's bag in 18%, and in

the front office in 15% of cases, however no protocol or medications was available for 9% and 7% of all children respectively [24]. The emergency kit was stored in the classroom (51.3%), in the infirmary of the junior high school (23%), or in the director's office (25.7%) [25]. Notably, in 32% of cases, the reaction was not appreciated by school personnel, and a singular fraction of reactions (64%) occurred in preschool or day care, and the school reaction represented the first reaction for 25% of the children (especially those aged <4 years) [21].

The allergic child is no more secure at home. The anaphylactic event occurs at home in 25% [26], 57% [2], or 78% of cases, sometimes due to a lack of parental surveillance [25], or unsatisfactory (50%) understanding of anaphylaxis management [28] and prevention (Table 2) [4,27].

Then, where is secure the allergic child? According to a recent study parents provided schools with protocols and medications for treatment of acute allergic reactions in 91% and 93% of children respectively [24]. Moreover, a single multidisciplinary evaluation within a specialist pediatric allergy clinic considerably improves (58.4%) parental knowledge on how to manage anaphylaxis [28]. The first treatment was self-administered or given by a parent (57.1%) or a physician or an emergency team, or by a teacher or a caregiver in 91.8% of cases. A total of 64.0% of the entrants received epinephrine with a median time from 1min to 4.5h. The parents felt that the instructions were followed correctly by the staff in 87.5% of cases [26]. So the sound prevention of severe episodes (Table 3) [29,30] and the presence of a parent/caregiver provided with Epi-pen would have saved the two reported children and who says how many other children in different location (Table 4) [2,26,27]. Comprehensive evidence-based guidelines for first-aid self-management of anaphylaxis in the community consensus definition [31] as well as a diagnostic description of anaphylaxis are also necessary [32].

Table 2: Prevention of lethal food-induced anaphylaxis in children

Prevention of lethal food-induced anaphylaxis in children	Accurate identification of the offending food(s)
	Education of the child, parents, day-care providers, school personnel, and restaurant personnel about lethal food-induced anaphylaxis
	Education of pediatricians, GP and nurses on the unsafe partly hydrolysate formulas in children with CMA
	Education of pediatricians, GP and nurses on cross-reactivity

Adapted from references [4,7]

Table 3: Conclusion

Provide emergency kits containing epinephrine in spring-loaded self injectable syringes to:	The parents and the care givers
	The child > 7 years of age
	The dairy-care and school personnel

Adapted from references [29,30]

Table 4: Location of the anaphylactic events

	Novembre	Eigenmann	Dibs
In the home	(57%)	(25.5%)	(45%)
Outdoors	(12%)		
Relative or friend's home		(13.7%)	
In restaurants	(5%)	(17.6%)	
In the doctor's office	(5%)		
In hospitals	(3%)		
On football fields	(3%)		
On the beach	(2%)		
In the church	(3.9%)		
In the gym	(1%)		
At school	(1%)	(15.7%)*	(4%)
In the operating room	(1%)		(15%)
In an hospital ward	(3.9%)	(27%)	

* or daycare or kindergarten

In the Novembre et al. paper [2] the children ranged in age from 1 month to 16 years (mean age \pm SD = 6.1 \pm 4.6 years).

In the Eigenmann et al. paper [26] the median age of the subjects was 7 years (range 0.5–61), with 33/51 (64.7%) being less than 16 years of age.

In the Dibs et al. papers [27] there were 50 children 1 to 19 years of age. Latex (27%) and drugs (16%) may explain the high rate of hospital events.

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