

Severe anaphylactic reactions outside hospital: etiology, symptoms and treatment

E. SØREIDE, T. BUXRUD and S. HARBOE

Norwegian Air Ambulance, Central Hospital of Akershus, Nordbyhagen and Department of Anaesthesiology, Central Hospital of Rogaland, Stavanger, Norway

Twenty-seven patients with severe anaphylactic reactions were treated by two anesthesiologist-staffed ambulance helicopters during a 5-year period. All patients had signs of respiratory and/or circulatory failure. Cutaneous symptoms were described in 70% of the patients, gastrointestinal symptoms in 30% and central nervous symptoms in 85%. Wasp sting and drugs were the most common causes. Other etiologies were bee sting, snakebite, nuts and exercise. All patients were provided with advanced pre-hospital medical care. Epinephrine was employed in 78% of the patients. I.v. fluid therapy was started in 77%. Three patients (11%) needed endotracheal intubation. The time-span from onset of symptoms to medical attendance exceeded 45 min in two patients; both died. Of the surviving patients, 23 were hospitalized. The majority had no signs of respiratory or circulatory failure on arrival in the emergency room and needed only observation in the hospital.

Received 14 August 1987, accepted for publication 22 January 1988

Key words: Anaphylaxis; emergencies; epinephrine; fluid therapy; insect bites and stings; snake bite.

In susceptible individuals various antigens may initiate a sudden release of endogenous mediators like histamine, leukotrienes and bradykinin (1, 2). The resulting clinical syndrome, anaphylaxis, is characterized by manifestations from the skin, the gastrointestinal and respiratory tract and the cardiovascular system (3).

To avoid a fatal outcome in severe anaphylaxis, rapid treatment is crucial (3, 4). Ideally, advanced life-support therapy should be provided at the site of the emergency. However, there are few data concerning the pre-hospital treatment of anaphylaxis. Most reports (5–8) deal with in-hospital treatment.

The purpose of the present study was to look at the etiology, symptoms and treatment of severe anaphylaxis outside hospital.

PATIENTS AND METHODS

The Norwegian Air Ambulance is a non-profit-making organization operating two hospital-based helicopter programs. Within a 45-min flight radius, the helicopters cover an area of 133 000 square-kilometers with a population of 2.1 million. Beside the pilot, the crew consists of a paramedic and an anesthesiologist. The ambulance helicopters respond to surgical, pediatric and medical emergencies (9, 10).

From 1981 to 1985, a total of 7114 missions were carried out. We identified 27 missions (0.4%) as being due to severe anaphylaxis. The diagnosis of anaphylaxis was solely based on history and clinical presentation (2, 3). When signs of respiratory failure (stridor, wheezing, insufficient respiration) and/or circulatory failure (systolic

blood pressure < 13.3 kPa (100 mmHg), shock symptoms) were present, the anaphylactic reaction was defined as severe.

Data were obtained from the anesthesiologist's report and the medical record for each patient.

RESULTS

A total of 27 patients were treated; 13 women and 14 men. The mean age was 41 years (5–74 years).

Table 1 shows the etiology. In Table 2 the clinical manifestations are summarized. The symptoms developed within 10 min in all patients stung by a wasp or a bee. In the others the time-interval between exposure and anaphylactic reaction varied from a few minutes to more than 1 h.

The time from the emergency call to medical attendance was less than 30 min in 19 patients. Two patients waited more than 45 min before adequate therapy was provided; both died. The fatal cases were women, 37 and 62 years old, and both had suffered anaphylactic reaction to previous stings. Lay people started cardiopulmonary resuscitation in both cases. One patient was declared dead after advanced resuscitation was tried. The other arrived at the hospital in coma, deep shock and apnea (intubated/ventilated) despite epinephrine and fluid therapy. Dopamine- and dextran infusion together with a shock dose of methylprednisolone raised the blood pressure, but it soon became clear that the patient was brain dead. The mortality thus reached 7%.

Table 1

Etiology of 27 severe anaphylactic reactions outside hospital.

	Number
Wasp sting	10
Bee sting	2
Snake bite (<i>Vipera berus</i>)	2
Drugs and vaccines	8
Nuts (food allergy)	2
Others*	3

* Exercise, cold and idiopathic urticaria.

Besides the two patients who died, one patient was endotracheally intubated by the anesthesiologist. The patient was mechanically ventilated till the next day. No patient was intubated after hospitalization.

Eighteen patients were attended by both local doctor and anesthesiologist. Table 3 shows the parenteral drug therapy. The local doctors used epinephrine subcutaneously in 12 patients, the anesthesiologist in none. The local doctors used i.m. and i.v. injections in seven patients, the anesthesiologists in four. In four patients the route of injection was not noted. Two patients given epinephrine subcutaneously needed additional vasopressor i.v. One patient received a total of 2 mg epinephrine; in the others the doses were 0.2–1.0 mg.

Pre-hospital fluid therapy with crystalloids (0.5–2.0 l) was initiated in 20 patients. In 16 patients the anesthesiologist started the fluid therapy.

All 25 patients who survived were transported to hospital. In the emergency room 24 had normalized respiration and 19 had normalized circulation. Central nervous symptoms were absent in all but four patients.

Two patients were dismissed after consultation in the emergency room; the rest were hospitalized. Drug therapy after hospitalization is shown in Table 3. Recurrence of anaphylactic symptoms was not described. Six patients with wasp stings and one patient with food allergy were provided with epinephrine for self-injection. Cerebral sequelae were not noted in any patient. The mean hospital stay was 2.0 days (1–7 days).

Table 2

Clinical manifestations of severe anaphylactic reaction in 27 patients.

	No.	(%)
Respiratory (dyspnea, stridor, insufficient respiration)	18	(66.6)
Cardiovascular (hypotension, shock, cardiac arrest*)	24	(88.8)
Cutaneous (urticaria, itching, erythema)	17	(70.0)
Gastrointestinal (nausea, vomiting, pain)	8	(29.6)
Central nervous (impaired consciousness, seizures, spasms, involuntary voiding and defecating)	23	(85.2)

* In three patients no signs of heart activity were present at the start of resuscitation.

Table 3

Parenteral drug therapy in 27 patients with severe anaphylactic reaction.

Drug	Local doctor	Anesthe-siologist	Hospital
Epinephrine	18	6	1
Hydrocortisone	6	8	5
Antihistamine (H ₁ -blockers)	4	4	4
Calcium gluconate	1	4	4
Teofyllamine	1	1	1
Others	0	10*	9**

* Metaraminol (n = 1), atropine (n = 1), diazepam (n = 3), metoclopramide (n = 1), NaHCO₃ (n = 4). ** Dopamine (n = 1), diazepam (n = 2), methylprednisolone (n = 1), dexamethasone (n = 1), antibiotics (n = 2), pethidine (n = 1), Zagreb-serum (n = 1).

DISCUSSION

To our knowledge, no similar study has previously been presented. In the present study insect stings and drugs, both well known causes of anaphylaxis, were the most frequent etiology.

Adder bites are an uncommon cause of anaphylaxis. The adder (*Vipera berus*) is the only venomous snake in Scandinavia. Life-threatening symptoms may develop after some hours, but as shown in our two patients anaphylactic symptoms may dominate the clinical picture (11, 12).

Another unusual cause found in our study was exercise. Anaphylactic symptoms may develop after vigorous exercise, particularly running (13).

As shown in our study circulatory and respiratory symptoms may develop independently of each other (5). Cutaneous manifestations are not always present. We found central nervous symptoms in as many as 85%. In most cases central nervous symptoms are secondary to hypotension and hypoxia, but they may occur without signs of respiratory and circulatory failure (14).

Epinephrine is the drug of choice in anaphylaxis (1–3). It was the most frequently employed drug in our study. Local doctors often injected epinephrine subcutaneously. We think that subcutaneous injections should be avoided in patients with circulatory failure. Instead, 0.3–0.5 mg epinephrine i.m. as standard dosage in adults can be recommended if the i.v. route is not available.

The potential hazard of inducing cardiac arrhythmias and coronary ischemia through the use of i.v. epinephrine (1:10 000 dilution) has been stressed by several authors (1, 2). However, arrhythmias and myocardial ischemia may develop because of the anaphylactic reaction (15). Therefore, the correct approach seems to be rapid treatment of the circulatory and respiratory failure, adjusting the doses of epineph-

rine to the severity of the cardiovascular collapse. ECG-monitoring is necessary (1, 15). In the present study ECG-monitoring was possible in all cases, and severe ventricular arrhythmias were not described after epinephrine.

Six patients (22%) were not given epinephrine outside hospital. One of them needed epinephrine in the emergency room. Two patients experienced spontaneous recovery. Three patients were treated with i.v. crystalloids and drugs like atropine, antihistamines and calcium gluconate. They had no signs of respiratory or circulatory failure on arrival in the hospital.

Waldhausen et al. (8) have questioned the central role of epinephrine in anaphylaxis. They suggest i.v. fluid therapy as standard treatment. Rapid plasma loss up to 35% of blood volume has been found in anaphylaxis (5, 7, 8). This emphasizes a high priority of lines for rapid infusions. The anesthesiologist started volume therapy four times as often as the local doctors in our study. Only crystalloids (up to 2 l) were used. Many authors (2, 5, 7, 8) recommend colloids. Our data indicate that plasma expanders are not necessary.

Endotracheal intubation may be essential in cases of respiratory arrest, and also when pharmacological therapy does not reverse laryngeal edema and bronchospasm. One hundred per cent O₂ is usually given in cases of severe anaphylaxis (2, 3, 5). Only three patients in our study received teofyllamine. In most cases epinephrine alone seemed to be enough.

Both metabolic and respiratory acidosis may develop in anaphylaxis (5). A pre-hospital infusion of sodium bicarbonate should always be considered, and was given to four of our patients. Sodium bicarbonate was used either because of cardiac and respiratory arrest or for long-standing circulatory failure, and merely as an adjunct to correction of acidosis through reversing of hypotension and hypoxia.

Antihistamines have been recommended as adjuvant therapy (2, 3). Recently, promising results concerning the combined use of H₁- and H₂-blockers have been published (7, 16). In our study only H₁-blockers were given.

Hydrocortisone (100–250 mg) was the only steroid used outside hospital in the present study. High doses of methylprednisolone and dexamethasone were utilized in the hospital treatment. The effect of steroids in anaphylaxis is still under debate (16).

Sympathomimetic drugs like metaraminol, dopamine, norepinephrine and isoprenaline should not replace epinephrine as the first line of therapy (2, 7). They can be employed as second-line inotropes. In our study metaraminol and dopamine were each used in one patient.

Calcium gluconate was given to almost 1/3 of our

patients. No recent data support the use of calcium in anaphylaxis. Asystole and cardiovascular collapse are possible side-effects (17). Although such side-effects were not noted in our study, we do not recommend the use of calcium gluconate in anaphylaxis.

The MAST-suit (2, 18) has shown an excellent vasopressor effect in anaphylactic shock. It was not applied in any case in our study. This mechanical vasopressor is particularly helpful in cases where venous access is a problem or if epinephrine is unavailable (18).

Although the majority of our patients were stabilized on arrival in hospital, 23 of the 25 surviving patients were hospitalized. We consider hospitalization for at least 24 h to be the rule in cases of severe anaphylaxis. Although not found in our relatively small series, biphasic anaphylaxis has been described (16).

Specific therapy, such as antivenom, which was given to one of our cases of snakebite, may be necessary at the hospital. Prevention of new anaphylactic episodes should be discussed with the patients. In some cases epinephrine for self-injection and immunotherapy are indicated (19). Seven patients were offered such therapy in our study.

In summary, we found wasp stings and drugs to be the most common causes of severe anaphylactic reactions outside hospital. The importance of rapid medical attendance is stressed. In all our patients advanced life-support therapy was started at the site of the emergency. This included epinephrine, infusion of crystalloids and endotracheal intubation. Two patients died, both were stung by wasps and had suffered severe anaphylactic reactions to previous stings. Treatment should be continued in the hospital, and most patients observed for at least 24 hours.

REFERENCES

1. Barach E M, Nowak R M, Tennyson G L, Tomlanovich M C. Epinephrine for treatment of anaphylactic shock. *JAMA* 1984; **251**: 2118–2122.
2. Perkin R M, Anas N G. Mechanism and management of anaphylactic shock not responding to traditional therapy. *Ann Allergy* 1985; **54**: 202–208.
3. Kelly J F, Patterson R. Anaphylaxis. *JAMA* 1974; **227**: 1431–1436.
4. Barnard J H. Studies of 400 *Hymenoptera* sting deaths in the United States. *J Allergy Clin Immunol* 1973; **52**: 259–264.
5. Pavsek K, Wegmann A. Pathophysiology of anaphylactic and anaphylactoid shock. *Fortschr Med* 1981; **99**: 1994–1999.
6. Smith P L, Kagey-Sobotka A, Bleecker E R. Physiological manifestations of human anaphylaxis. *J Clin Invest* 1980; **66**: 1072–1080.
7. Fisher M. Clinical observations on the pathophysiology and treatment of anaphylactic cardiovascular collapse. *Anaesth Intensive Care* 1986; **14**: 17–21.

8. Waldhausen E, Keser G, Marquardt B. Anaphylactic shock. *Anaesthesist* 1987; **36**: 150–158.
9. Harboe S, Veum Eielsen O, Hapnes S A, Søreide E, Mikkelsen H. The use of ambulance helicopters in Western Norway. *Tidsskr Nor Lægeforen* 1985; **105**: 1863–1866.
10. Søreide E, Sandstad O, Buxrud T, Home J A. Critically ill and injured patients. *Tidsskr Nor Lægeforen* 1985; **105**: 1216–1219.
11. Wahlberg P. Viper bite. *Nord Med* 1986; **101**: 200.
12. Reid H A. Adder bites in Britain. *Br Med J* 1976; **ii**: 153–156.
13. Sheffer A L, Austen K F. Exercise-induced anaphylaxis. *J Allergy Clin Immunol* 1980; **66**: 106–111.
14. Meszaros I. Transient cerebral ischemic attack by *Hymenoptera* stings: the brain as an anaphylactic shock organ. *Eur Neurol* 1986; **25**: 248–252.
15. Levine H D. Acute myocardial infarction following wasp sting. *Am J Med* 1976; **91**: 365–374.
16. Stark B J, Sullivan T J. Biphasic and protracted anaphylaxis. *J Allergy Clin Immunol* 1986; **78**: 76–83.
17. Tanz R D, Kettelkamp N, Hirshman C A. The effect of calcium on cardiac anaphylaxis in guinea-pig Langendorff heart preparations. *Agents Actions* 1985; **16**: 415–424.
18. Oertel T, Loehr M M, Vista C. Bee sting anaphylaxis: the use of medical antishock trousers. *Ann Emerg Med* 1984; **13**: 459–461.
19. Golden D B, Valantine M D. Insect sting allergy. *Ann Allergy* 1984; **53**: 444–449.

Address:
Eldar Søreide, M. D.
Ammerudgrenda 281
0960 Oslo 9
Norway