TRUE ANAPHYLAXIS TO SUXAMETHONIUM CHLORIDE

A case report

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SUMMARY

A severe anaphylactic reaction to suxamethonium chloride is reported. The patient had received suxamethonium uneventfully on four previous occasions. Previous sensitization and immunological studies indicated that this was a classical type I hypersensitivity reaction.

During the past two decades there have been several case reports of adverse reactions to suxamethonium chloride attributed to excessive histamine release (Smith, 1957; Kepes and Haimorici, 1959; Fellini, Bernstein and Zauder, 1963; Eustace, 1967; Jerume, Whittingham and Wilson, 1967; Bele-Binda and Valerie, 1971; Katz and Mulligan, 1972; Fisher, 1975; Mandappa, Chandrasekhara and Nelvigi, 1975). Some of these reactions have been designated type I hypersensitivity (anaphylactic) reactions (Kepes and Haimorici, 1959; Jerume, Whittingham and Wilson, 1967; Mandappa, Chandrasekhara and Nelvigi, 1975), but evidence of a sensitizing exposure before the adverse reaction is lacking and indeed doubt has been expressed whether true anaphylaxis to suxamethonium occurs (Fisher, 1976).

We report classical anaphylaxis to suxamethonium chloride.

CASE HISTORY

In February 1975 a 19-yr-old previously healthy male weighing 75 kg was admitted to hospital following a crushing injury to his pelvis and lower abdomen. He required repeated general anaesthesia for manipulation of fractures, débridement of wounds, a suprapubic cystotomy and a descending colotomy. Sodium thiopentone was used for induction of anaesthesia on all occasions and, when muscle relaxation was required, alcuronium was given. Suxamethonium chloride was used on four occasions to facilitate tracheal intubation, twice in February and once each in March and April 1975. No adverse reaction occurred to any drug administered during any of these nine anaesthetics, each of which was documented fully.

In September 1976 the patient was readmitted to hospital for treatment of a traumatic urethral stricture by urethroplasty under general anaesthesia. He was a fit young man with no personal or family history of atopy. He had no symptoms or signs of cardiorespiratory disease and no neurological deficit. Diazepam 10 mg was given orally on the evening before operation and again 2 h before operation. Anaesthesia was induced with atropine 0.6 mg followed by sodium thiopentone 225 mg and, when the eyelash reflex was no longer present, suxamethonium chloride 50 mg was given to facilitate endotracheal intubation. After fasciculations had ceased, it was impossible to ventilate the lungs using a face-mask and an oropharyngeal airway. An endotracheal tube was inserted easily and ventilation with oxygen commenced with great difficulty despite excellent muscle relaxation. After checking the equipment, auscultation of the chest suggested severe bronchospasm. At this time the patient was deeply cyanosed, both peripherally and centrally, and about 3–4 min after induction of anaesthesia none of the major arterial pulses was palpable. External cardiac massage was commenced. An i.v. infusion was started and sodium bicarbonate 200 mmol was given. The e.c.g. showed an irregular ventricular tachycardia. Two litre of dextrose in saline was administered rapidly, a catheter was inserted into the right subclavian vein and this revealed a central venous pressure of −10 cm H₂O with reference to a zero at the level of the angle of Louis. The carotid pulse became palpable and external cardiac massage was stopped, but in spite of a steep head-down tilt and an e.c.g. showing sinus tachycardia, the patient remained cyanosed with extremely poor peripheral perfusion and he was developing generalized oedema which was present particularly in the face. The bronchospasm was relieved by aminophylline 250 mg and methyl prednisolone sodium succinate 1 g given i.v.

The patient was transferred to the intensive care unit approximately 1 h after the event, with a diagnosis...
Fig. 1. Results of monitoring and therapy during the first 24 h after induction of anaesthesia. c.v.p. = central venous pressure; p.a.w.p. = pulmonary artery wedge pressure; Hct. = haematocrit; B.P. = arterial pressure.
of anaphylactic or anaphylactoid reaction to one of the drugs used for induction of anaesthesia.

Figure 1 summarizes the results of investigations and details of therapy.

The pulmonary artery and pulmonary artery wedge pressures were measured with a 7-F. Swan-Ganz catheter inserted via the right subclavian vein to facilitate fluid therapy (Gilbertson, 1974). With restoration of effective plasma volume, the left atrial pressure (pulmonary wedge pressure) increased, and with it the systemic arterial pressure (fig. 1). The subsequent decrease in arterial pressure was associated with a diuresis induced by frusemide 40 mg given when the arterial pressure exceeded 80 mm Hg, the patient having remained anuric for more than 4 h since the reaction began.

Twenty-four hours after induction of anaesthesia, the patient was awake, alert and drinking fluids. Urine output was good, there were no neurological sequelae and his oedema had resolved.

Blood samples were taken according to the scheme of Watkins, Thornton and Clarke (1975) and sent to the Immunology Department at Sheffield University, where measurement of complement components C3 and C4, of the degree of C3 conversion and of the reagin antibody, IgE, were made (Watkins, Udnoon et al., 1976). The results of these investigations are shown in table I.

Six weeks later, a consultant allergist performed skin tests on the patient with the three drugs given i.v. during the induction of anaesthesia. The only reaction on prick testing was to suxamethonium chloride. This produced a weal 1 cm in diameter, with a large flare. Subsequently, suxamethonium chloride 50 µg was injected intradermally and this produced a weal 4 cm in diameter, and a larger flare. The patient then started to develop signs of anaphylaxis and was given promethazine hydrochloride 25 mg i.m.

The patient has received subsequently four further general anaesthetics using sodium thiopentone, alcuronium hydrochloride, nitrous oxide and oxygen, and no difficulty has been encountered. He has been discharged from hospital with a "Medic-Alert" disc stating his extreme sensitivity to suxamethonium.

DISCUSSION

Most adverse reactions to suxamethonium probably result from the direct release of histamine without involving immune mechanisms. There is evidence that cholinergic agents liberate histamine via a guanosine monophosphate pathway (Kaliner, Orange and Austen, 1972), so that it is not surprising that a drug comprising 2 molecules of acetylcholine should occasionally produce severe histaminic reactions.

However, our patient received suxamethonium on four occasions in a 10-week period without any adverse effects, but on the fifth occasion, 18 months later, suffered a reaction so severe as to be potentially lethal. This, with positive skin tests and the measured plasma IgE consumption, strongly suggests a classical type I hypersensitivity reaction to suxamethonium. There is a tendency to dismiss skin testing as a means of distinguishing between pharmacological and immune-mediated drug reactions, but a positive result to a prick as distinct from an intradermal test is highly sensitive and specific for a reaginic or type I reaction.

The decrease in IgE concentrations in the plasma following anaphylactic reactions requires explanation, since very little of the circulating IgE is likely to be specific antibody to the drug or drug–protein complex. One theory is that the initial antigen–antibody reaction takes place on the mast cells which are later swept clean, possibly by macrophages, of all the surface-bound immunoglobulin, whether this is bound to antigen or not. Repopulation of the surface

![Table I. Results of the measurement of consumption and conversion of complement component C3 and of immunoglobulin IgE concentrations in sequential blood samples taken after the adverse reaction to suxamethonium chloride](https://academic.oup.com/bja/article-abstract/50/6/611/308761)
of viable cells occurs from the plasma pool with IgE molecules after the adverse reaction (J. Watkins, personal communication). The degree of C3 consumption and conversion (table I) is significant but insufficient to cause the severe clinical signs encountered, making it very unlikely that this is a direct comple ment-mediated response as has been reported for some reactions to Althesin (Watkins, Clarke et al., 1976).

Severe anaphylactoid and anaphylactic reactions to i.v. drug administration are rare but life threatening. The anaesthetist should have a plan of treatment if deaths are to be avoided.

Several pharmacological mediators are probably responsible for each reaction, but histamine appears to be the most important in man, and therapy should be directed towards reversal of the end-organ responses to histamine—bronchospasm, vasodilatation and increased permeability of the microvasculature.

Adrenaline has the virtue of both suppressing the release of histamine and also reversing the end-organ responses. Administration of the drug i.v. is recommended as the prime treatment for severe drug reactions (Kelly and Patterson, 1974; Fisher, 1975).

However, in reactions following i.v. drug administration, maximal histamine release will have occurred before any drug treatment can be instituted. The considerable hazards associated with i.v. adrenaline therapy, especially in situations of severe hypoxaemia, do not seem to us to be justified when other less dangerous drugs are available. We consider aminophylline to be the initial agent of choice to treat bronchospasm in these circumstances.

One of the most important aspects of therapy is the administration of i.v. fluids. This case report demonstrates clearly that reduction in effective plasma volume is a major cause of circulatory insufficiency in severe anaphylactoid-type reactions. Calculations from the haematocrit changes indicate that 2 litre or 50% of the patient’s plasma volume was lost. Restoration of the haematocrit to the values observed before operation and the establishment of a satisfactory urine output required more than 5 litre of i.v. fluids. Monitoring of the intravascular volume is essential and for this a c.v.p. line is desirable, but a Swan–Ganz catheter is preferable in patients with previous heart disease.

The use of steroids in large doses is difficult to justify on theoretical grounds for a type I hypersensitivity reaction, since these drugs do not block allergin–IgE binding or prevent the release of histamine from cells, but they have been shown largely to prevent the pharmacological effects of a massive release of histamine (Rocha e Silva, 1966; Loremy et al., 1972). They are safe given in large doses over short periods and may have some value in the treatment of shock (Lillehei et al., 1974).

Antihistamine drugs are surprisingly ineffective in the treatment of severe histaminic reactions (Loremy et al., 1972). Although it would be illogical not to use these drugs, their use should not detract from the more important aspects of treatment.

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REFERENCES


VERITABLE ANAPHYLAXIE AU SUXAMETHONIUM

RESUME
On décrit dans cet article une grave réaction anaphylactique au chlorure de suxaméthonium. Le malade avait pourtant déjà reçu du suxaméthonium à quatre reprises sans qu'il n'y ait jamais eu d'incident. La sensibilisation antérieure et les études immunologiques ont fait ressortir qu'il s'agissait là d'une réaction classique d'hypersensibilité du type I.

ECHTE ANAPHYLAXE AUF SUXAMETHONIUM

ZUSAMMENFASSUNG

ANAFILAXIA REAL ANTE SUXAMETONIO

SUMARIO
Se informa sobre una severa reacción anafiláctica ante el cloruro de suxametonio. El paciente había recibido suxametonio sin novedad en cuatro ocasiones anteriores. Los estudios previos de sensitización e inmunológicos indicaron que ésta fue una reacción de hipersensitividad clásica de tipo I.