HISTAMINE-LIKE REACTION TO TUBOCURARINE

Case Report

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SUMMARY

In preparation for an appendicectomy the anaesthesia was started with thiopentone 350 mg followed by a dose of 24 mg of tubocurarine, intravenously, in a patient with 39°C (102°F) temperature and a history of sensitivity to detergents; an anaphylactoid reaction resulted. The intradermal sensitivity tests to tubocurarine, performed with the skin at room temperature 30°C (85°F) and at 39°C (102°F), were positive and at higher skin temperature the responses were stronger. It was concluded that tubocurarine may induce anaphylactoid reactions in susceptible individuals and that an increase in body temperature acts as a contributory factor.

If an amount of 0.3 mg/kg of tubocurarine is injected fast intravenously the concentration of the drug in plasma at its first circulation through the tissues may reach the threshold of histamine release (Paton, 1959). A case suggesting such an occurrence is presented.

CASE REPORT

This was the first exposure to anaesthesia and surgery of an 18-year-old male of muscular build, weight 70 kg, admitted to the hospital with a diagnosis of acute appendicitis. This was the first exposure to anaesthesia and surgery of an 18-year-old male of muscular build, weight 70 kg, admitted to the hospital with a diagnosis of acute appendicitis. The other abnormal findings, from the available data, were: tachycardia (150 beats/min) and fever of 101°F. Appendix was acutely inflamed on examination. In preparation for an appendicectomy the anaesthesia was started with thiopentone 350 mg followed by a dose of 24 mg of tubocurarine, intravenously, in a patient with 39°C (102°F) temperature and a history of sensitivity to detergents; an anaphylactoid reaction resulted. The intradermal sensitivity tests to tubocurarine, performed with the skin at room temperature 30°C (85°F) and at 39°C (102°F), were positive and at higher skin temperature the responses were stronger. It was concluded that tubocurarine may induce anaphylactoid reactions in susceptible individuals and that an increase in body temperature acts as a contributory factor.

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Skin tests.

Skin tests were performed several weeks after the patient left the hospital. Four individuals acting as controls. When injected intradermally, tubocurarine in a concentration of a little less than 0.1 mg/ml produces histamine release (Paton, 1957). The tests were done on both forearms, one exposed to room temperature, the skin temperature being 30°C (85°F) ± 3°C and the other forearm kept at 39°C (102°F) with a thermal blanket, the temperature at the time of surgery when tubocurarine was injected intravenously. Intradermal weals of about 1 mm diameter were raised with solutions of tubocurarine chloride in 0.9% NaCl in concentrations of 0.1, 0.067 and 0.05 mg/ml, and plain 0.9% NaCl as control. At room temperature three of the controls had positive reactions, papulae of 1.2-0.75 cm in diameter, at concentrations of 0.1 and 0.067 mg/ml, surrounded by a faint erythematous area of about 3 cm, but no reactions at 0.05 mg/ml or 0.9% NaCl. Under the same conditions the patient had positive reactions at all three concentrations, with papulae of similar magnitude but with marked erythema. At 39°C (102°F) skin temperature the same three controls reacted positively, this time at all three concentrations, the papulae being of about the same size as previously but the erythema being more marked. In the patient similar papulae developed and the reaction progressed to a large confluent erythema covering the entire forearm and half of the arm.

DISCUSSION

Two drugs were injected intravenously in close succession and both were able, each through a different mechanism, to release histamine from the tissues.

The release of histamine by thiopentone is mediated through an immunological mechanism. Normally, the organism does not produce antibodies against its own proteins. If a drug or some of its degradation products combines with a protein of the recipient, the complex so formed may act as an antigen able to stimulate specific antibody formation and
The reaction takes place on the surface of the cells, where the antibody is fixed and initiates the process of histamine release from these cells. The responses of "target organs" to histamine acting as a chemical mediator are manifested clinically as anaphylactic reactions (Carr, 1954). Starting from 1966, seven such cases were reported in the literature, all with a common history of repeated (average eight) exposures to thiopentone (Clark and Cockburn, 1971).

In our case there is nothing to suggest the possibility of a previous sensitization to thiopentone or to a chemically related drug, the past history of the patient being well documented in the files of the hospital's outpatient department where he was registered since childhood. However, one year previously he had an episode of itching erythematous rash on the body and facelike rash on the extremities, traced to the use of a laundry detergent, which responded favourably to antihistaminic drugs.

Tubocurarine acts by displacing the histamine, a dibasic substance, from mast cell granules where it is stored bound to heparin and to other substances possessing acid groups. The stability of heparin-histamine complex is enhanced by lowering the temperature or the pH. Basic substances with cationic groups suitably spaced within their molecules, if in sufficient concentrations, may displace and liberate histamine. Among the substances sharing these properties are the opium alkaloids, belladonna alkaloids, trimetaphan camsylate (Arfonad), some detergents and the muscle-relaxant drugs, in order of decreasing histamine-liberating activity, tubocurarine, laudexium, benzquinonium, decamethonium, suxamethonium and gallamine. The release of histamine by "liberators" may occur on the first exposure to the drug and the responses of histamine-sensitive organs are classified as anaphylactoid reactions (Paton, 1957).

There is parallelism in the susceptibility of various organs to respond to chemical liberators or to the specific antigens and also quantitative correlation in the percentage of the amounts of histamine released, respectively (Mongar and Schild, 1952). Although most of the body tissues contain histamine, its release by chemicals or antigens is not equally successful: almost impossible from the intestinal mucosa, which does not contain mast cells, it is difficult from the mast cells located beneath the mucosal tissue of the respiratory system and relatively easy from granulocytes, the basophils containing half of the blood histamine, or from the mast cells distributed in the skin or in the connective tissue along the vessels of the peripheral vascular system. These readily available stores are responsible for most of the reactions attributable to histamine and in this respect the anaphylactic and anaphylactoid reactions share a common symptomatology systematized around the pharmacology of histamine (Mongar and Schild, 1962; Lichtenstein and Norman, 1969).

In humans, pruritus, urticaria, angioedema, tachycardia and moderate hypotension are the most common manifestations of anaphylactic reaction, the bronchospasm being uncommon except in individuals with a history of asthma or urticaria. Antihistaminic drugs, while not preventing the release of histamine, are effective antagonists of anaphylactoid reactions but poor antagonists of anaphylactic reactions (Douglas, 1970).

It is concluded that under clinical conditions of administration tubocurarine can cause anaphylactoid reactions in susceptible individuals and a rise in body temperature may act as a contributory factor.

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REFERENCES


REACTION GENRE HISTAMINE A LA TUBOCURARINE: DESCRIPTION D'UN CAS

SOMMAIRE

En préparation à une appendicтомie, on débuta l'anesthésie avec 350mg de thiopentone suivi d'une dose de 24mg de tubocurarine par voie intraveineuse chez un patient avec une température de 39°C et une anamnèse de sensibilité aux détergents; une réaction anaphylactoïde se produisit. Les tests intradermiques de sensibilité à la tubocurarine, faits sur la peau à température de chambre 30°C et à 39°C, étaient positifs et les réactions étaient plus prononcées lorsque la température cutanée était plus élevée. On conclut que tubocurarine peut produire des réactions anaphylactoïdes chez des sujets suspects et qu'une élévation de la temperature corporelle agit comme facteur contribuant.
ZUSAMMENFASSUNG

RESUMEN
Durante la preparación para una appendicectomía la anestesia fue iniciada con 350 mg de tiopentona seguidos por una dosis de 24 mg de tubocurarin por vía intravenosa en un paciente con 39°C (102°F) de temperatura y una anamnesis de sensibilidad a los detergentes: Se desarrolló una reacción anafiláctica. Las pruebas de sensibilidad intradérmica a tubocurarin, llevadas a cabo con la piel a la temperatura del cuarto a 30°C (85°F) y 39°C (102°F) fueron positivas y a temperaturas cutáneas más elevadas las respuestas eran más intensas. Se concluyó que la tubocurarin puede inducir reacciones anafilactoides en individuos susceptibles y que un incremento en la temperatura corporal actúa como factor contribuyente.

SOCIETY OF ANAESTHETIC LABORATORY TECHNICIANS
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