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Peranaesthetic anaphylactoid shock due to mannitol

Allergic and pseudoallergic reactions due to anaesthetics, especially muscle relaxants, are well known. We investigated a case of severe anaphylactoid shock during general anaesthesia, in which mannitol appears to have been the causative agent.

A 40-year-old man had to undergo retromaxillary tumour resection. Two general anaesthesias had previously been done without any complications. There was no history of asthma or atopy. Anaesthesia was realized with thiopental, suxamethonium, fentanyl, alcuronium and an ethrane-inhalation-mixture. The induction period passed uneventfully. About 90 min after intubation, before surgical intervention, an infusion of 20% mannitol (100 ml) was given. Minutes later, hypotension and tachycardia suddenly appeared, followed by ventricular fibrillation. No cutaneous changes or bronchospasm were observed. Immediate cardiopulmonary resuscitation with catecholamines and repeated defibrillation were successfully initiated; the patient recovered the same day without any sequelae.

An allergological study was carried out 8 weeks later. Routine skin tests and RAST determinations (Phadebas, Pharmacia) with common inhalant allergens as well as with latex, thiopental and suxamethonium were negative. Prick tests with thiopental (50 mg/ml), suxamethonium (10 mg/ml), alcuronium (5 mg/ml), fentanyl (0.05 mg/ml) and mannitol (200 mg/ml equal 1.1 M) – all tested in their commercial forms – were negative. Intradermal testing at a 1:100 dilution revealed a clear positive reaction (wheal of 7 mm diameter with flare) only to mannitol. Control testing in 10 voluntary persons at the same mannitol concentration resulted in all negative. Consecutively, the *in vitro* leukocyte histamine release (HR) induced by the drugs in serial 10-fold dilutions was studied; histamine was measured by a RIA-method (5) using a commercial assay (Immunotech). Mannitol induced 20% HR of total leukocyte histamine in the 1.1 molar solution and 9% in the 0.1 molar dilution. Controls ($n = 14$) with normal donor cells showed higher HR in 8 cases (57%) to nondilute mannitol (18.6% ± 10.6, mean ± SD), but there was practically no HR to the 0.1 molar dilution (1.0% ± 1.3). Only thiopental also induced HR: 40% in the nondilute and 7% in the 10-fold dilute solution. Here controls revealed similar results to both concentrations (32.9 ± 21.9 and 6.2% ± 6.5) (Table 1).

From the clinical development, the positive specific skin test, and the higher tendency to release histamine in a 0.1 molar concentration, we concluded hypersensitivity to mannitol as the cause of this life-threatening anaphylactoid reaction. In spite of the widespread use of mannitol, only 5 cases of hypersensitivity have been reported (1–4, 6). The induced HR by hyperosmolar (1.1 M) mannitol also in normal controls demonstrates its potency to liberate histamine as previously reported by Findlay et al. (2). Thus the incident might be aggravated by the foregoing use of other histamine releasing drugs as thiopental and suxamethonium. Further studies will be necessary to elucidate the mechanism of – probably IgE-mediated – hypersensitivity in this pa-

Table 1. Percent histamine release induced by mannitol and thiopental

	Patient	Controls	
		Atopic ($n=7$)	Nonatopic ($n=7$)
Mannitol:			
20 mg/ml	9	0.6±0.8	1.4±1.6
200 mg/ml	20	17.7±9.9	19.6±12.1
Thiopental			
5 mg/ml	7	6.6±6.3	5.9±7.2
50 mg/ml	40	39.0±26.5	26.7±15.9

All values are given after deduction of spontaneous histamine release (mean±SD).
Atopic: mean age 32.6 years (21–55y); nonatopic: mean age 32.6 y (19–51y).

tient. Clinicians should be aware of this potential side effect of mannitol.

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