

suppressor T cells (2), reduction of CD4+ CD45RA+ T cells (1), decreased CD40 ligand expression (1), increase of CD8+ CD57+ lymphocytes (2), and increase of CD8+ CD28- lymphocytes (3).

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Hypersensitivity reaction to ioversol

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Key words: drug-induced anaphylaxis; IgE-mediated hypersensitivity; ioversol; radiographic contrast medium.

● IOVERSOL is a monomeric, noniodinated radiographic contrast medium. It has three iodine atoms and six hydroxyl groups, but no carboxyl groups. The first monomeric, noniodinated contrast medium known was metrizamide. Second-generation monomeric, noniodinated contrast media (iopamide, ioversol, and iohexol) have

intermediate viscosity and osmototoxicity; therefore, the incidence of adverse effects from them is low (1).

Adverse reactions occur in about 5% of contrast media examinations. The incidence of mild reactions (flushing, nausea, and headache) is high. More

severe side-effects, such as asthma or anaphylactoid reactions, are rare, but the problems are serious enough to be of concern (2). Side-effects induced by contrast media have a complex etiology, and several pathogenic mechanisms have been suggested. Immunologic mechanisms have been proposed by some authors (3).

We report the case of a 44-year-old woman who had suffered an adverse reaction to ioversol 4 months before. This patient underwent intravenous urography with ioversol; she immediately developed nausea, vomiting, dizziness, hypotension (80/40 mmHg), widespread pruriginous erythema, lip angioedema, and shortness of breath. She received 6-methyl-prednisolone (60 mg intravenous), dexchlorpheniramine (10 mg intramuscular), and epinephrine (0.3 mg subcutaneous). Her symptoms subsided in 4 h.

After the patient gave written consent, an allergy study was carried out. Skin prick tests were performed with sodium and meglumine amidetrizoate (Urografin 76%; 20 ml; Schering AG, Germany), iopromide (Clarograf 300; 100 ml, iopromide DCI 623 mg/ml), and iodinated polyvinylpyrrolidone (Betadine 7.5% and 10% solutions; 100 ml, Asta Médica, Spain). The results of all of them were negative in our patient. We then performed a skin prick test with ioversol (Optiray 320; 100 ml; ioversol DCI 678 mg/ml, Mallinckrodt Medical, Spain), and we obtained a positive result (wheal of 8×8 mm with pruritus and erythema). Skin prick tests with ioversol

were also performed in 50 control subjects (25 of whom were atopic subjects), with negative results. Positive (histamine; 10 mg/ml) and negative (saline serum 0.9%) controls were also carried out. Serum total IgE was 231 kU/l. The histamine-release test with ioversol was negative. To develop this test, we used the automated fluorometric method described by Siraganian (4) and Hook, with the Technicon Autoanalyzer II.

We present a patient who developed anaphylactic shock caused by ioversol. The symptoms suffered by the patient, the latency of the reaction, and the positivity of the skin prick test with ioversol strongly suggest an underlying type-I, IgE-mediated hypersensitivity mechanism. *In vitro* tests have a high potential utility in the diagnosis of adverse reactions to drugs. However, their sensitivity is low; the value of the *in vitro* histamine release for the diagnosis of drug-induced anaphylaxis appears to be poor. Therefore, this test is scarcely used for the diagnosis of drug allergy (5).

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Ultrarush SIT in venom allergy

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Key words: Hymenoptera venom allergy; immunotherapy; sting challenge test.

● **ALTHOUGH** most stings by Hymenoptera species lead only to local reactions, systemic hypersensitivity and often life-threatening reactions occur in up to 5% of the general population (1). Patients with a history of a

Highly effective treatment of allergy to honeybee sting confirmed by sting provocation.

severe allergic reaction to a field sting by either a honeybee or a yellow jacket receive specific immunotherapy (SIT) with highly purified Hymenoptera venom according to the WHO guidelines (2). This therapy is highly effective because up to 80–100% of patients who formerly had reacted systemically do not react in the same way when restung after SIT has been started (2).

Many treatment schedules aim for satisfactory protection, minimal side-effects, optimal convenience, and minimal cost (2). In this regard, the maintenance dose is reached within 4–7 days in rush protocols, which represent the most common schedule (3). Here we describe an ultrarush SIT protocol in two patients with honeybee allergy, Müller III reactions, at which the maintenance dose (100 µg) of honeybee

venom was reached within 2 days of admission to hospital (Table 1). The cumulative dose was 150 µg at day 1 and 200 µg at day 2 (Table 1). While local reactions such as erythema and swelling occurred in both patients, no systemic side-reactions during this treatment were observed. Interestingly, local reactions began at 10 µg and were comparable to patients treated by a 5-day schedule. Maintenance injections of 100 µg honeybee venom (ALK-depot SQ801[®], aluminum hydroxide-adsorbed venom) were given during outpatient clinic visits by increasing the application time in 1-week, 2-week, 3-week, and 4-week intervals. The 4-week interval was then continued over 3 years.

Although ultrarush protocols at which the maintenance dose is reached within 6 h have been published, there were no data until now about the efficacy because the Hymenoptera sting challenge test was not carried out (4). To investigate whether the ultrarush SIT protocol in this study was effective, we administered the honeybee sting challenge test in hospital 4 months (patient 1) and 6 weeks (patient 2) after ultrarush SIT treatment had been started, according to the guidelines of the European Academy of Allergology and Clinical Immunology (5). No systemic anaphylactic reaction occurred after sting challenge tests in either patient.

Therefore, this ultrarush SIT protocol was highly effective in the prevention of systemic reactions to another sting after treatment had been initiated. Moreover, beside satisfactory protection, this ultrarush SIT aimed at minimal side-effects, optimal convenience, and reduction of costs.

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Table 1. Ultrarush venom SIT protocol

Day	Injection ¹	Concentration (µg)	Type
1	1	0.01	lyo ²
1	2	0.1	lyo ²
1	3	1	lyo ²
1	4	10	lyo ²
1	5	20	lyo ²
1	6	40	lyo ²
1	7	80	lyo ²
2	8	100	lyo ²
2	9	100	Depot ³

1. The time interval between each application was 1 h at day 1 and 4 h at day 2.
2. Honeybee venom ALK-Lyophilisate SQ801[®].
3. Honeybee venom ALK-depot SQ801[®], aluminum hydroxide-adsorbed venom.