A case of anaphylaxis occurring during a general anesthesia is presented. The reaction was severe with bronchospasm and hypotension (grade 2 in the severity of peri-operative anaphylactic shock). The responsibility of hydroxyzine, administered for premedication was suspected by intradermal testing with the molecule, which was twice positive at a 10⁻² dilution of the commercial solution. The same test remained negative in 5 control subjects. All the other drugs received during anesthesia gave negative results. Using the same protocol excepted for the use of hydroxyzine a new general anesthesia could be performed under a premedication with dexchlorpheniramine without any allergic reaction. Anaphylactic reactions are very rare with hydroxyzine used in premedication for anesthesia in regard to the large prescription of the drug. Only two previous cases were reported but attention of the allergist must be also pointed towards the medications received in the perioperative period as for the anesthetic drugs.
Anaphylactic reaction to hydroxyzine in an anesthetized patient

Anaphylactic reaction to hydroxyzine in an anesthetized patient

In order to propose an alternative premedication for further anesthesia, a new screening by cutaneous tests and provocative reintroduction tests was performed several months later. The skin tests were identical, with a wheal of 15 mm after hydroxyzine (at 10^{-1}), contraindicating a reintroduction challenge test with hydroxyzine. The skin tests (SPTs in native form for all drugs, IDTs from 10^{-3} to 10^{-1} of the commercial solution for disposable soluble forms) with several antihistaminic agents (cetirizine, dexchlorpheniramine, ebastine, loratadine and desloratadine, mequitazine) were negative. So we choose to perform an oral reintroduction test with dexchlorpheniramine. Finally, a total dose of 6.6 mg of dexchlorpheniramine (step by step 4.1 mg orally and 2.5 mg intramuscularly) was given without any immediate or delayed adverse reaction. Under 2 mg of dexchlorpheniramine and 0.25 mg of alprazolam premedications given orally before thyroidectomy, general anesthesia with propofol, sufentanil and sevoflurane was uneventfully performed. The follow-up of our patient during 3 days was simple without any allergic reaction.

Discussion

There are only few case reports quoted in the Medline database, and hypersensitivity reactions with histamine receptor antagonists are mostly of delayed type (2–8). The signs reported with hydroxyzine are skin rashes, urticaria or photosensibilisation, erythema multiform with positive patch tests, fixed drug eruption or systemic eczema. There are only 2 case reports of hypersensitivity reactions to hydroxyzine during anesthesia (10,11). In the first case hypoxemia and skin eruption were noticed during an orthopedic procedure (10), and in the second a generalized urticaria occurred 30 minutes after hydroxyzine premedication during cardiac surgery (11). In the former case skin tests were positive to hydroxyzine, in the second case
an immunological mechanism has been evoked because lymphocyte stimulation test turned positive to hydroxyzine. In our patient, a severe bronchospasm associated to an arterial hypotension occurred after induction of anesthesia. The high concentrations of tryptase and histamine after the reaction and the positivity of intradermal tests (positive twice) supported the diagnosis of an immediate hypersensitivity reaction to hydroxyzine.

As positive skin tests with hydroxyzine have not been yet reported, we performed the same tests to 5 control subjects. They remained all negative in IDTs up to a 10⁻¹ concentration of the commercial solution. In order to rule out the responsibility of compounds found in hydroxyzine tablets, which are also contained in surgical antiseptic distemper, we tested povidone in SPTs, which were all negative in our patient.

This is the first case of a well documented immediate hypersensitivity reaction to hydroxyzine. Mostly curares, latex and antibiotics are responsible for such events during an anesthesia (12). The anaphylactic reaction to hydroxyzine was annoying because such agent is often given to prepare the patient before an anesthesia. Mostly curares, latex and antibiotics are responsible for such events during an anesthesia.

As our patient must be again anesthetized, it was necessary to find an alternative to hydroxyzine as premedication. Among the histamine receptor antagonists, cetirizine and hydroxyzine share a common core, the piperazine core. We speculated that epitope for hypersensitivity reaction in our patient was perhaps the piperazine core (3,5,6,13) because the patient reported previous rashes with cetirizine. However, SPT remained negative with cetirizine but also with hydroxyzine certainly due to a lower sensitivity of SPT compared to IDTs (9).

Cetirizine was not suitable for IDTs so we could not conclude about a sensitization to the drug without a provocative test which was not performed for ethical reasons. Nevertheless, to find an alternative to hydroxyzine as premedication before an anesthesia, we decided to perform provocative test with an other compound family rather than with cetirizine in such indication. In regard to its sedative properties and considering a possible iv administration, we test dexchlorpheniramine by using IDTs and oral and systemic reintroduction tests. As skin tests and provocative reintroduction challenge were negative we proposed it as premedication before the new anesthesia, which was uneventful.

In conclusion, we report a peri-operative anaphylaxis to hydroxyzine used in premedication before an anesthesia. The allergological investigation supports the hypothesis that it may be considered as a potential allergen for immediate hypersensitivity reaction. By using screening tests and provocative reintroduction test we found an alternative to hydroxyzine to prepare the patient before the new anesthesia. Moreover, our case report underlines that it is important to test also the molecules used for premedication in the diagnosis of immediate hypersensitivity reactions occurring during an anesthesia.

References