

Correspondence

Intraoperative anaphylaxis after intravenous atropine

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EDITOR:

Although it is commonly used in clinical practice, there is not much awareness of the allergic potential of atropine since there are some reports of adverse reactions but rarely with clinical significance [1]. In the current literature on allergic reactions during anaesthesia, atropine appears in a very small number of patients, unlike the more frequent causative agents such as neuromuscular blocking drugs, antibiotics, latex and colloid solutions [2–7]. We report a case of intraoperative anaphylaxis after administration of intravenous (i.v.) atropine and following immunological investigation in a reference centre.

A 65-yr-old man was scheduled for elective lumbar spine surgery. He had been submitted to two recent spinal surgeries for treatment of herniated intervertebral discs uneventfully. Past medical history included hypertension, obesity, dyslipidaemia and coronary artery disease. He had undergone recent cardiologic evaluation and was currently medicated with isosorbide mononitrate 60 mg day⁻¹, bisoprolol 5 mg day⁻¹, amlodipine 5 mg day⁻¹, simvastatin 20 mg day⁻¹, aspirin 100 mg day⁻¹ and ezetimibe 10 mg day⁻¹. There was no history of allergies or atopy. He was premedicated with diazepam 10 mg the night before surgery.

General anaesthesia was induced with fentanyl, propofol and vecuronium and maintained with sevoflurane and fentanyl boluses. A nitroglycerin infusion 0.5 mg h⁻¹ was started. One hour before the end of the procedure paracetamol 1 g i.v., tramadol 100 mg i.v. and diclofenac 75 mg intramuscularly were administered. At the end of the procedure neostigmine 2.5 mg and atropine 1 mg i.v. were given for reversal of neuromuscular

blockade and immediately a sudden drop of the arterial pressure (systolic pressure fell from 140 to 60 mmHg) was noticed. An increase in heart rate and ST–T segment depression (–2 mV) were also seen. No error was detected in the monitoring and infusion systems. No surgical event was observed. There were no changes in cardiac rhythm, end-tidal CO₂, oximetry and heart or breath sounds. I.v. fluids and dopamine infusion were started producing no change in haemodynamics. Generalized erythema was then noticed. A norepinephrine infusion targeted to maintain systolic pressure around 100 mmHg was started and hydrocortisone 200 mg, clemastine 2 mg and ranitidine 50 mg i.v. were administered. The clinical picture resolved almost completely in approximately 10 min. There were no changes in the 12-lead ECG and there were no laboratory changes compatible with ischaemia. Tryptase values in blood drawn 60 min after the event were 70 mcg L⁻¹. He was admitted to the intensive care unit and discharged to the ward 14 h later. There were no incidents during the rest of his hospital stay.

Contact with a centre specialized in drug allergy was established. Seven weeks after the event (having stopped bisoprolol), the patient was submitted to further immunologic investigation consisting of skin prick and intradermal tests to all drugs used during anaesthesia and also to latex. Positive intradermal reactions were observed to tramadol (1/100 dilution) and atropine (1/10 dilution). In order to exclude the possibility of a false positive intradermal test to atropine due to an irritant effect, we also performed this test in 13 controls using the same dilution. All controls (eight females and five males) had negative test results.

In this case, severe hypotension and generalized erythema occurred shortly after administration of an i.v. drug, which highly suggests a severe allergic reaction.

Allergic reactions demand immediate and aggressive treatment. Standard treatment recommendations

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consist of provision of oxygen and airway support, vigorous fluid loading and parenteral epinephrine (as a vasopressor and inotrope) [8]. However, these recommendations are based on clinical observation and studies in animal models but there are no clinical trials providing evidence for treatment of acute anaphylaxis [9,10].

Norepinephrine was used as a vasopressor trying to avoid excessive tachycardia in a patient with known severe coronary artery disease. Several recent articles support the use of norepinephrine and pure alpha-agonist in the setting of anaphylaxis, arguing that systemic vascular resistance more than inotropism are compromised – there is good contraction in an underfilled heart [11].

After initial assessment and treatment, it is essential to proceed with laboratory confirmation and identification of the causative agent. High tryptase serum values (which result from mast cells degranulation) collected in the first 2 h after the event confirm the clinical diagnosis of an anaphylactoid reaction. Additionally, levels greater than $25 \mu\text{g L}^{-1}$ (in our case $70 \mu\text{g L}^{-1}$) are highly suggestive of anaphylaxis [12].

Intradermal tests raised the possibility of tramadol and/or atropine as the causative agent(s). The temporal coincidence between the administration of atropine and anaphylaxis and the fact that tramadol was administered without incident in the postoperative period strongly indicated that atropine was the causative drug. The sensitization process can easily be explained by the use of atropine in both previous anaesthesias. Detection of specific IgE atropine antibodies in serum was not performed because there are no tests available commercially to date. Provocative tests would give definitive diagnostic evidence as to the identification of the causative drug but the severity of the reaction in question contraindicates its use.

The patient was informed regarding this event and future implications. Glycopyrrolate was tested as an alternative to atropine and the intradermal skin test was negative.

The diagnosis of anaphylaxis and the identification of its cause in the perioperative period can be challenging to the anaesthesiologist. The close contact between institutions involved was essential to the care of this patient. Being aware that this can be a time consuming effort and to avoid 'loss' of patients/patient data in the process, we think there should be an institutional protocol to follow up these cases, preferably in cooperation

with a centre dedicated to pharmacologic allergy investigation.

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