**Tonic water: A rare cause of exanthema**

*To the Editor,*

Tonic water (or Indian tonic water) is a carbonated soft drink in which quinine is dissolved. Quinine is an alkaloid extracted from cinchona's bark. Originally used as a prophylactic drink against malaria, nowadays it has significantly lower quinine content and is drunk for its distinctively bitter taste. In Europe, the European Food Safety Authority limits quinine's concentration in tonic water to 100 mg/L, 0.25–0.50% of the concentration used in original therapeutic tonic water. Quinine is also a flavour component of bitter lemon, carbonated chinotto beverages and some traditional flavoured wines. Nowadays, tonic water containing quinine is added to many jello shot recipes to make the shot fluorescent. Reported cases of exanthemas caused by quinine contained in tonic water are rare.

Suspected allergy to quinine has to be studied, especially if the patient is planning to travel to a malaria endemic region. This allergy confirmation is still so important because, even nowadays, quinine is a mainstay in the treatment of severe malaria. Other antimalarial medicines, used extensively in the treatment and prevention of malaria, such as chloroquine and mefloquine, share a common quinoline core with quinine which may explain the possibility of cross reactivity, although this process has not been clearly demonstrated. This evidence emphasises, even more, the importance of quinine allergy investigation.

We report the case of a 37-year-old man who was sent to our outpatient clinic by the traveller’s health clinic for suspicion of quinine allergy. The patient mentioned that more than 20 years ago he had a maculopapular exanthema hours after the ingestion of tonic water. At that time he was observed by a general practitioner who assumed that this reaction was a manifestation of quinine allergy. The doctor advised to keep quinine eviction, which the patient assumed rigorously, without accidental ingestions.

Due to the necessity of professional travel to Angola (a malaria endemic region) the patient was observed in a traveller’s health clinic and referred to our outpatient clinic in order to confirm this allergy that hindered the possible prescription of any anti-malaria drugs containing quinine. As the reaction had occurred a long time before and there was not a clear association with quinine, we decided to perform, after obtaining written informed consent, a drug provocation test (DPT) without previously performing skin prick tests and patch testing. Two hours after the last administration (cumulative dose: 300 mg quinine sulphate) the patient developed a purpurigus maculopapular exanthema (each lesion lasting more than 24 h) in the limbs, trunk and face. This exanthema persisted for five days despite therapies with oral corticosteroids and H1-antihistaminics. The patient did not present any other signals or symptoms.

Quinine-related hypersensitivity manifestations have been reported to include thrombocytopenia and haemolytic uremic syndrome, lupus-like syndrome, photosensitivity, cutaneous vasculitis and anaphylactic shock. Reported cases of exanthema due to quinine contained in tonic water are rare. In this case quinine hypersensitivity was confirmed by the DPT. The patient and the traveller’s health clinic were advised to do malaria prevention, and eventual treatment, with antimalarial drugs not sharing the quinoline core. Based on our clinical evaluation and after consulting the traveller’s health clinic, the patient, by his own personal initiative, refused to travel and, consequently, was not medicated with any antimalarial drugs. Tonic water is widely consumed worldwide and may be an unreported cause of maculopapular exanthema.

**References**

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Anaphylaxis during skin test with vecuronium

To the Editor,

During perioperative periods anaphylactic reactions are not uncommon events. Their prevalence is estimated to be 1 in every 10,000–20,000 anaesthetic cases.\(^1\) Neuromuscular blocking drugs (NMBD) are the most causative agents in such events, contributing to 69.2% of the cases.\(^2\) Natural rubber latex (NRL, or cis-1,4-polyisoprene) was the second most implicated agent. Antibiotics and anaesthesia induction drugs are the other drugs leading to anaphylaxis. The evaluation is based on serum tryptase levels, skin prick and intradermal tests, basophil activation assays and drug specific IgE levels. Although skin tests with anaesthetic agents are known to be safe and feasible, we have reported a boy with an anaphylactic reaction to vecuronium during the intradermal test.

We were consulted at the paediatric surgery about an 18-month-old boy with Hirschsprung disease for oxygen desaturation (90%) just a few minutes after induction of anaesthesia. This was the second operation that he had undergone for his disease and propofol 20 mg iv, vecuronium 1 mg iv and sevoflurane were administered. Amoxicillin had been administered intravenously, 20 min before the operation. There was no other reason for considering anaphylaxis such as hypotension (his blood pressure was 95/60 mmHg), skin eruption, angio-oedema or gastrointestinal symptoms. He had no family or personal history of allergy. Serum tryptase levels were within normal ranges (8.4 μg/L) (normal range: 3.5–11.4 μg/L). The specific IgE of latex, penicillin, and egg white were negative. Six weeks later he was referred to our allergy department in order to detect the possible causes of intraoperative anaphylaxis and to determine potentially safe alternative drugs (for anaesthetics) for future surgery. The child underwent skin prick tests with common allergens then prick and intradermal tests for penicillin and ampicillin. Skin tests were interpreted as being positive if a wheal larger than 3 mm in diameter accompanied by erythema was present 20 min later. Histamine hydrochloride was used as the positive control and 0.9% sodium chloride as the negative control. Skin prick testing only gave negative results. Then, we performed an oral provocation test with amoxicillin, giving a total dose of 500 mg by gradually increasing the dose (5–250 mg). There was no reaction. One week later we performed a prick test with vecuronium. Again this proved to be negative. Following this, an intradermal test by 1/10 concentration (400 μg/mL) of vecuronium was performed on the forearm. After 5 min, he became agitated; he had angio-oedema around his eyes and also hoarseness. Then, he had respiratory failure with an oxygen saturation of 88%. His blood pressure was 60/30 mmHg. The patient responded positively to an intradermal test resulting in doubling of the size of the injection wheal. Epinephrine 0.01 mg/kg was administered intra-muscularly. Intravenous steroid 1 mg/kg and 100% oxygen were administered. Intravenous fluid was infused continuously to maintain his blood pressure. His blood pressure increased to 80/40 mmHg and his oxygen saturation to 99% but his respiratory distress continued. Beta-2 agonist was administered via a nebuliser. His serum tryptase level was at the upper limit of normal (11.5 μg/L). After 1 h his symptoms reduced and resolved completely in 2 h. After 24 h he was discharged.

Anaphylaxis is an acute systemic hypersensitivity reaction involving several organ systems, particularly the skin, respiratory tract, gastrointestinal tract and the cardiovascular system. During surgery, early cutaneous signs of anaphylaxis are often recognised because patients are unconscious and they are under drapes. Therefore, bronchospasm and cardiovascular collapse are the first recognisable signs of anaphylaxis. A survey of anaphylaxis when under anaesthesia demonstrated that cardiovascular symptoms (73.6%), cutaneous symptoms (69.6%), and bronchospasm (44.2%) were the most common clinical features.\(^2\) During this operation only oxygen desaturation occurred. There were no cardiovascular or cutaneous symptoms. However, during prick testing he had angio-oedema and although there were no signs of bronchospasm he had symptoms of laryngeal obstruction and hypotension.

Serum tryptase is a mast cell protease that is increased in cases of anaphylaxis and can be measured in serum and plasma 30 min after the first signs of anaphylaxis and correlate with the presence of hypotension. The half-life of tryptase is 2 h and the levels gradually decrease over time. Tryptase may not be increased in the absence of hypotension.\(^3\) In our case, during anaesthesia serum tryptase levels did not increase as he had no hypotension and also during prick testing his serum tryptase level was at the upper limit. The absence of serum tryptase does not eliminate an anaphylactic reaction since there have been reports of anaphylaxis with positive tests for IgE antibodies in the setting of an absence of serum tryptase.

The evaluation of anaphylaxis is based on serum tryptase levels, skin prick and intradermal tests, basophil activation assays and drug specific IgE levels. The specificity and sensitivity of the skin tests to muscle relaxants is greater than...