

from the same centre with its own selection bias. Thirdly, some patients with severe AD did not have enough dermatitis-free body areas to patch test and chronic immunosuppressant therapies were directly indicated. Considering the limitations of our work, prospective and multicentre studies would be necessary to evaluate the true scope of patch testing in patients with therapy-resistant atopic dermatitis. In this respect, our work increases the recommendation grade of patch test patients with therapy-resistant AD from recommendation grade D (expert opinions) to recommendation grade C (the present cohort retrospective study).⁸ In the event that our results would be confirmed, patch testing should be recommended, where feasible, prior to the use of long-term systemic immunosuppressive therapy.

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DOI: 10.1111/jdv.15672

A case of hypersensitivity reaction to alcohol confirmed by oral provocation test

Editor

Alcoholic beverages may lead to adverse reactions of high variability. Impaired alcohol metabolism, mainly seen in individuals

of Asian descent, is known as 'oriental flushing syndrome'.¹ When reactions exclusively occur after selected alcoholic beverages, food additives, i.e. preservatives and dyes, should be considered as possible elicitors.² Few reports exist about anaphylactoid reactions to ethanol, the first one dating back to 1983.³

We report on a 20-year-old non-atopic Caucasian woman with no comorbidities who presented to our university allergy department with recent history of facial flushing, prickling of palms, generalized urticaria, angioedema, globus sensation and dyspnoea shortly after ingestion of passion fruit liqueur (containing azorubin and tartrazine amongst others). She also reported on rhinitis, globus sensation and prickling of the palms after drinking prosecco, and on another occasion, she had experienced facial flushing, anxiety, prickling in the throat and dizziness, after ingestion of panna cotta with raspberries and egg liqueur. After ingestion of vinegar, she reported on prickling of the oral mucosa.

In addition, she reported on angioedema, abdominal pain, vomiting and collapse 20 min after ingestion of metamizole taken for symptomatic treatment of a common cold.

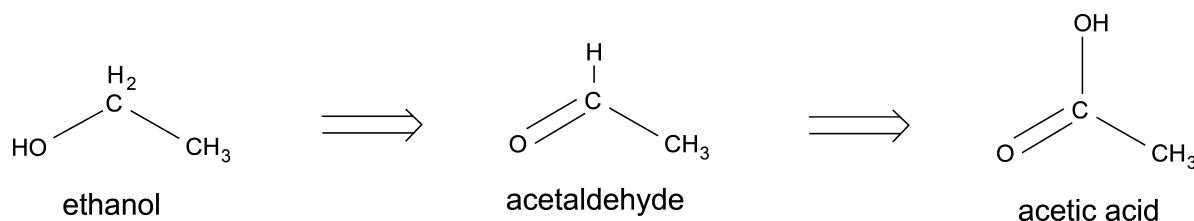
Skin prick test (ALK-Abelló, Hamburg, Germany) was negative for common inhalative allergens, common food allergens and for native strawberry, raspberry, blackcurrant, passion fruit, passion fruit liqueur, tartrazine, ethanol 96% diluted 1 : 10, ethanol 96% undiluted as well as for acetic acid 0.6%, 1.2% and 9.6%. Intradermal test was positive for metamizole. There was no specific IgE (CAP FEIA; Thermo Fischer, Waltham, USA) detectable for passion fruit, Pru p 3, Bet v 1, ragweed, lactoprotein, guar, tragant or carmine red. Total IgE (38.5 kU/L) and serum tryptase (8.0 µg/L) were within normal range. Cutaneous mastocytosis was ruled out by clinical examination. CD63 expression (Flow-CAST Basophil Activation Test/BAT; Bühlmann Inc, Schönenbuch, Switzerland) was negative for metamizole and tartrazine.

Titration, single-blind, placebo-controlled oral provocation test (OPT) was performed (Table 1) on two separate occasions and was repeatedly positive for ethanol but not for food additives. The patient was on a potato-rice diet during provocation. The tryptase was within normal range one hour after the first positive reaction to ethanol (9.3 µg/L).

In conclusion, we diagnosed an alcohol-induced hypersensitivity reaction. Even though there are some reports about alcohol/ethanol causing urticaria and anaphylaxis, the exact mechanism remains unknown. Most studies attributed the reaction to the metabolites of ethanol, namely acetic acid and acetaldehyde (Fig. 1).⁴ They detected positive prick test to acetaldehyde or/and acetic acid, so an IgE-mediated mechanism was suspected. It also has been shown that acetaldehyde functions as a hapten and specific IgE against acetaldehyde protein complex was detected in the serum of non-patients of Asian descent with severe hypersensitivity reaction to

Table 1 Oral provocation tests in our patient were repeatedly positive for ethanol

	Oral provocation test	Provocation meal	Dose	Results	Rescue medication
First	Day 1	Azorubin	Single dose of 5 mg	Negative	–
	Day 2	Tartrazin	Maximum single dose of 20 mg, cumulative dose of 35 mg	Negative	–
	Day 2 (3 h after tartrazin application)	95% ethanol in blackcurrant juice	Single dose 20 mL in 200 mL	Angio-oedema of the lips, urticaria and prickling of the palms	Intravenous prednisolone and dimetindene
Second	Day 1	Blackcurrant juice	Single dose 200 mL	Negative	–
	Day 1 (3 h after blackcurrant juice)	95% ethanol in water	Single dose 20 mL in 200 mL	Inner unrest, globus sensation and prickling of palms	–
	Day 2	95% ethanol in blackcurrant juice	Single dose 20 mL in 200 mL	Generalized urticaria, prickling, erythema and angio-oedema of the palms as well as globus sensation	Intravenous prednisolone and dimetindene

**Figure 1** Oxidation products of ethanol. From: CC BY-SA 3.0, Richtom80 at English Wikipedia, https://commons.wikimedia.org/wiki/File:Oxidation_of_ethanol.svg

alcohol.⁵ But also non-IgE-mediated reactions are discussed.⁶ In the study of Worm *et al.*, none of 12 patients with a history of immediate type reaction after consumption of alcoholic beverages had positive skin prick test to ethanol, acetic acid or acetaldehyde. The authors suspected ethanol itself as elicitor and not the metabolites. In our patient, the pathophysiological mechanism also remains unknown but due to negative skin prick tests and missing increase in tryptase after ethanol challenge, a non-IgE-mediated mechanism is likely. Symptoms also might be provoked by alcohol intolerance, which is more prevalent in individuals with asthma, nasal polyps, chronic sinusitis or aspirin intolerance.⁷ Despite the hypersensitivity to metamizole, none of those symptoms was prevalent in our patient.

With regard to our patient's concomitant hypersensitivity to metamizole, we recommended to avoid this drug; COX-2-inhibitors, meloxicam and tramadol were well tolerated.

In summary, we report on a patient with hypersensitivity reaction to ethanol. We did not suspect an IgE-mediated mechanism. Alcohol should not be overlooked as rare inducer of hypersensitivity and may not only act as a cofactor.

The authors declare that no funding was received for the present study.

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DOI: 10.1111/jdv.15673