

reactions are severe, it is important that clinicians address marijuana exposure when assessing a patient's exposure history.

Ayla Tessmer, BA*
Noam Berlin, BSc*
Gordon Sussman, MD†
Nathan Leader, BSc*
Eddie Chu Chung, BSc*
Donald Beezhold, PhD‡

*Gordon Sussman Clinical Allergy Research Inc
Toronto, Ontario, Canada

†Division of Allergy and Clinical Immunology
Department of Medicine
University of Toronto
Toronto, Ontario, Canada

‡Allergy and Clinical Immunology Branch
Health Effects Laboratory Division
National Institute for Occupational Safety and Health
Morgantown, West Virginia
gsussman@rogers.com

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Anaphylaxis caused by tetrazepam without cross-reactivity with other benzodiazepines

Benzodiazepines are sedative hypnotic agents that have been in clinical use since the 1960s for sedation and to treat anxiety, seizures, withdrawal states, insomnia, and drug-associated agitation. Adverse reactions are mostly related to overdosing. Allergic reactions are rare, with only a few cases reported in the literature.

A 33-year-old man presented with systemic urticaria after the intake of 50 mg of tetrazepam. Shortly thereafter, he received treatment in the emergency department with steroids and antihistamines. Afterward, he was referred to our unit for study.

Six months after the presentation in the emergency department, skin prick testing with tetrazepam (diluted 1% water) produced a negative result. A positive control test with 100 mg/mL of histamine was performed. Then, we proceeded to a single-blind, placebo-controlled challenge oral test with 5, 5, and 15 mg of tetrazepam. The interval between doses was 30 minutes. Fifty minutes after the intake of 25 mg of tetrazepam, our patient presented with generalized pruritus, urticaria, dyspnea without wheezing, and tachycardia (heart rate, 120/min). Blood pressure and oxygen saturation were normal. We administered treatment with adrenaline, methylprednisolone, and dexchlorpheniramine with resolution ad integrum. Blood samples for tryptase determination were taken. The basal tryptase level was 6.5 $\mu\text{g/L}$, reaching a peak of 17.5 $\mu\text{g/L}$ at 90 minutes and decreasing to 4 $\mu\text{g/L}$ 4 hours later. A hive appeared on the area of the forearm where the cutaneous test had been performed.

We performed prick (full strength) and intradermal tests (1/100) with midazolam, flunitrazepam, diazepam, and clorazepate, which produced negative results. Single blind placebo control challenges oral challenges with diazepam and clorazepate were performed according to the following protocol: 30 minutes between doses until a therapeutic dose of 5 mg (1, 2, and 2 mg) of diazepam and 10 mg (1, 4, and 5 mg-) of clorazepate. Both oral challenge results were negative.

Benzodiazepines are a rare cause of immediate allergic reactions, more of them in the context of general anesthesia. There

are some reports of anaphylactic reactions due to endovenous diazepam^{1,2} and midazolam³, but to the date, there are no reports of such reactions induced by tetrazepam.

Tetrazepam has been described as an inductor of delayed type IV reactions, such as maculopapular exantema⁴, Stevens-Johnson syndrome, toxic epidermal necrolysis, hypersensitivity syndrome⁴, and contact dermatitis⁵. The study of these patients usually did not show cross-reactivity among different benzodiazepines.⁴

Our patient presented with a clinical picture of anaphylaxis, which was reproduced after oral challenge. Interestingly, skin prick test results were negative initially but later turned positive after the development of a systemic reaction. This finding could be due to the local release of mediators from skin mast cells or the action of drug metabolites. Serum tryptase levels showed a progressive elevation and later a decrease, consistent with mast cell activation. These data strongly suggest a type I (IgE-mediated) mechanism.

Previous reports of type I reactions to benzodiazepines have not included studies to evaluate potential cross-reactivity. In our patient, skin testing and oral challenge performed with other benzodiazepines failed to show cross-reactivity, suggesting a selective pattern of sensitization.

Tetrazepam is similar chemically to diazepam, and this selective pattern of sensitization could be due to different metabolites.

In summary, we present a case of anaphylaxis to tetrazepam supported by serologic data. No evidence of cross-reactivity was found with other benzodiazepines, suggesting a selective IgE-mediated mechanism.

Juan Antonio Martínez-Tadeo, MD*

Eva Pérez-Rodríguez, MD*

Guacimara Hernández-Santana, MD*

José Carlos García-Robaina, MD, PhD*

Fernando de la Torre-Morín, MD, PhD*

*Hospital Universitario Ntra. Sra. De Candelaria
Allergy Service, Drug Allergy Unit
Santa Cruz de Tenerife, Canary Islands, Spain
arkanum78@hotmail.com

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Blood pressure monitoring in children undergoing food challenge: association with anaphylaxis

The diagnosis of food allergy is based mainly on oral food challenge (OFC).¹ Anaphylaxis represents the most serious outcome of OFC. Anaphylaxis has been proposed to be highly likely when exposure to known allergens elicits a 30% or greater decrease in systolic blood pressure (SBP) or a low SBP for age either isolated or accompanied by gastrointestinal, skin, or respiratory symptoms.² However, studies addressing the validity of these diagnostic criteria for anaphylaxis are needed.^{2,3} Data on blood pressure measurements during OFC are missing. We sought to determine whether suggested SBP values are helpful for diagnosing anaphylaxis in children who undergo OFC.

The study group consisted of 80 children (male-female ratio, 53:27; age range, 18 months to 16 years; median age, 5 years 4 months) with a history of reaction to foods and/or positive food specific IgE tests. Exclusion criteria included a history of anaphylaxis or intake of small food amounts with clinical symptoms in the past 2 years. All children underwent an open OFC. When open challenge resulted in subjective or unclear symptoms, a double-blind, placebo-controlled OFC was performed.⁴ Before OFC, children were not given antihistamines for 7 days and corticosteroids, theophylline, leukotriene modifiers, or chromoglycates for 24 hours. The test consisted of the administration of increasing doses

of food every 20 minutes until it reached a daily mean amount. Before OFC and every 10 minutes during OFC, brachial blood pressures were measured with an automated oscillometric device (Dinamap pro200v2; GE Healthcare, Milan, Italy), using a cuff with an inflatable bladder width that was 40% of the arm circumference and length covering 80% of the arm. Children were seated with the arm supported horizontally to keep the cuff at heart level⁵ and controlled to avoid sudden movements. The supervising investigator was masked to the blood pressure values until a reaction severe enough to terminate OFC occurred.

The most common foods challenged were hen's egg ($n = 45$), cow milk ($n = 25$), wheat ($n = 3$), and soy ($n = 2$). The OFC results were positive in 26 of 80 children (32%): 19 children (73%) tested positive to egg, 5 (19%) to cow milk, and 2 (7%) to wheat. In 26 children, OFC elicited skin symptoms (12 urticaria-angioedema, 11 rash, and 3 pruritus), in 11 children gastrointestinal reactions (3 oral allergy syndrome, 2 vomiting, 1 diarrhea, 1 nausea, and 1 abdominal pain), in 1 child bronchospasm, wheezing, and coughing. Three of the 26 children with positive OFC results had symptoms consistent with anaphylaxis.² Age, height, weight, and sex did not differ between reactive and tolerant children. The mean (SD) SBP was 99.5 (14) mm Hg (coefficient of variation, 14.1%). During OFC, a SBP decrease greater than 30% was recorded in 6 children

Disclosures: Authors have nothing to disclose.

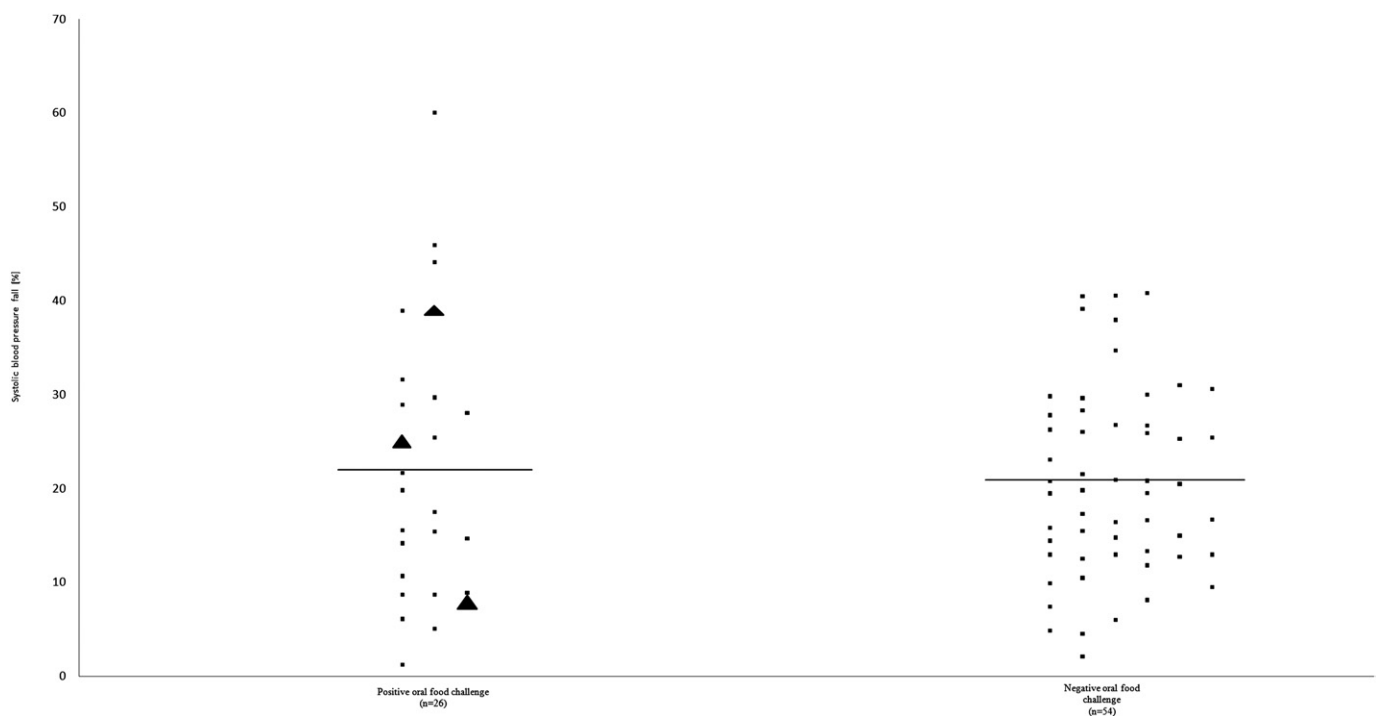


Fig. 1. Percentage of systolic blood pressure decrease in children with positive or negative oral food challenge results. Horizontal line indicates the mean percentage of systolic blood pressure and black triangle indicates children who had anaphylaxis.