
Reactions to prick and intradermal skin tests

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Background: Allergy skin testing is a common procedure for the diagnosis of atopic diseases with a small risk of systemic reactions.

Objective: To determine the 12-month incidence of systemic reactions (SRs) to skin prick testing (SPT) and intradermal skin testing (ST) and the symptoms and response to immediate treatment with epinephrine intramuscularly.

Methods: A prospective study was conducted to evaluate SRs from ST in 1,456 patients. A standard form was used to record symptoms, signs, and treatment. The SRs are defined as any sign or symptom other than a local reaction thought to be secondary to ST. No vasovagal reactions were included. Nurses, as instructed by attending physicians, administered epinephrine (0.2 mL of a 1:1,000 dilution) intramuscularly in the deltoid as soon as any remote signs or symptoms occurred.

Results: Fifty-two patients (3.6%) had SRs (6 SPT and 46 intradermal): 43 (83%) were female, and 17 (33%) had asthma. Systemic symptoms included (SPT/intradermal) pruritic eyes, nose, or pharynx (0%/46%); worsening cough (50%/26%); sensation of difficulty swallowing (0%/20%); worsening nasal congestion (17%/15%); rhinorrhea (17%/13%); chest tightness or shortness of breath (33%/11%); generalized pruritus (17%/11%); sneezing (33%/9%); wheeze (0%/4%); and urticaria (17%/2%). No severe asthma, shock, hypotension, unconsciousness, or biphasic reactions occurred. All 52 patients received epinephrine intramuscularly, 48 (92%) oral prednisone, 9 (17%) oral prednisone to take 6 to 8 hours after a reaction, 50 (96%) oral antihistamine, and 6 (12%) nebulized β -agonist.

Conclusions: Of patients who underwent ST, SRs occurred in 3.6% (0.4% for SPT and 3.2% for intradermal ST), all of whom readily responded to epinephrine intramuscularly in the deltoid. This immediate administration of epinephrine seems to prevent more serious and biphasic reactions.

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INTRODUCTION

Allergy skin testing (ST) is a common procedure for the diagnosis of atopic diseases. There is a small risk of systemic reactions (SRs) associated with ST. Lin et al¹ described 2 patients who had SRs to ST (both skin prick testing [SPT] and intradermal ST) for respiratory allergies of 10,400 patients tested. They determined the overall risk of inducing systemic symptoms indicative of possible early anaphylaxis to be less than 0.02%. Other studies^{2,3} have produced similar results. Thompson et al⁴ reported a higher SR rate of 6%. The purpose of this study was to determine during 12 months (February 1, 2006, to January 31, 2007) the incidence and characteristics of SRs to SPT and intradermal ST and the response of the same to immediate intramuscular administration of epinephrine into the deltoid.

METHODS

Approved by the University of South Florida institutional review board, this was a prospective observational study of patients receiving ST for the diagnosis of allergic diseases. All ST devices and extracts were from Greer Laboratories (Lenoir, North Carolina). All the participants came from a

single allergy/immunology clinic associated with the University of South Florida College of Medicine. Written informed consent was obtained from all patients before ST. A form outlining the events that occurred after the first symptom was completed by either a nurse or the physician during and immediately after the reaction was terminated. The physicians in charge define an SR as any sign or symptom other than a local reaction thought to be secondary to ST. All patients received standard care, ie, they were taken to the clinic's emergency treatment room, were put in the recombinant position, and were given 0.2 mL of intramuscular epinephrine, 1:1,000 vol/vol, in their deltoid.

RESULTS

A total of 1,456 patients (58% female) underwent SPT, intradermal ST, or both in 1 year with 20 to 50 allergens (trees, grasses, weeds, animals, molds, foods, medications, and Hymenoptera). Fifty-two of the 1,456 patients (3.6%) who underwent ST experienced an SR, as previously defined. Forty-three patients (83%) were female, and the average patient age was 40.6 years (range, 13–70 years; median, 35.5 years). Seventeen of the 52 patients with SRs (33%) had asthma. Six patients (0.4%) had SRs during SPT. One of these 6 patients reacted to aeroallergens alone, whereas the other 5 reacted to aeroallergens and food. Forty-six patients (3.2%) had SRs during or after intradermal ST: 1 to Hymenoptera and 45 to aeroallergens.

For the 6 patients reacting to SPT, symptoms reported included cough (n = 3; 50%), dyspnea and chest tightness (n = 2; 33%), sneezing (n = 2; 33%), nasal congestion (n =

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1; 17%), rhinorrhea (n = 1; 17%), pruritus (n = 1; 17%), and urticaria (n = 1; 17%). For intradermal reactions, symptoms reported included pruritic eyes, nose, or pharynx (46%); worsening cough (26%); sensation of difficulty swallowing (20%); worsening nasal congestion (15%); rhinorrhea (13%); chest tightness or shortness of breath (11%); generalized pruritus (11%); sneezing (9%); wheeze (4%); and urticaria (2%). No severe asthma, shock, hypotension, unconsciousness, or biphasic reactions occurred.

All 52 patients experiencing SRs immediately received 0.2 mL of a 1:1,000 dilution of epinephrine in their deltoid muscle, as per study protocol. Two patients (4%) received a second dose of 0.1 mL of epinephrine. Forty-eight patients (92%) received oral prednisone, 9 (17%) oral prednisone to take 6 to 8 hours after a reaction, 50 (96%) oral antihistamine, and 6 (12%) nebulized β -agonist.

DISCUSSION

Although rare, fatalities have occurred from ST. Six fatalities were reported between 1945 and 1984 via a questionnaire mailed to 3,400 members and fellows of the American Academy of Allergy Asthma and Immunology, and its analysis was published in the *Journal of Allergy and Clinical Immunology* in 1987.⁵ A later survey on deaths in the United States from subcutaneous immunotherapy reported no deaths from ST between 1985 and 1989.⁶ There was 1 death associated with intradermal ST in a similar report covering events from January 1990 to June 1995.⁷ A fourth survey (1990–2001) reported 1 ST fatality associated with SPT to 90 food allergens.⁸

ST is associated with nonfatal SRs, and previous studies^{1–3} have determined the overall risk to be less than 0.02%. However, such reactions may be underreported since Thompson et al⁴ reported an SR rate of 6%. The present study and that by Thompson et al report higher SR rates than do most other studies in the literature. A major reason for this discrepancy could be how associated SRs are defined.

For example, there is disagreement in the medical literature about how to define anaphylaxis. The *Journal of Allergy and Clinical Immunology* anaphylaxis practice parameters indicate that there is no universally accepted clinical definition of anaphylaxis.⁹ Anaphylaxis can affect the level of consciousness (impairment might reflect hypoxia), the upper and lower airways (dysphonia, stridor, cough, wheezing, and shortness of breath), the cardiovascular system (hypotension with or without syncope and cardiac arrhythmias), the skin (diffuse or localized erythema, pruritus, urticaria, and angioedema), and the gastrointestinal system (nausea, vomiting, and diarrhea).⁹ Some authors believe that more than 1 organ system should be involved before the diagnosis of anaphylaxis is made. The Second National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network Symposium convened in 2005 and established a working definition of anaphylaxis. The group proposed that anaphylaxis is likely to be present clinically if there is involvement of at least 2 organ systems or hypotension.¹⁰ Delaying treatment

until the development of multiorgan symptoms carries an inherent risk of a sudden worsening of symptoms because the ultimate severity of anaphylaxis is difficult to predict at the onset of the episode. Therefore, some members of the World Allergy Organization Ad Hoc Committee on Epinephrine and Anaphylaxis recommend that any symptom of anaphylaxis be treated immediately with intramuscular epinephrine to prevent more severe anaphylaxis from occurring.¹¹ Anaphylaxis, for the purposes of this study, was defined as follows: an acute and potentially lethal multisystem allergic reaction in which some or all of the following signs and symptoms occur: diffuse erythema, pruritus, urticaria, and angioedema; bronchospasm; laryngeal edema; hypotension; cardiac arrhythmias; feeling of impending doom; unconsciousness; and shock. Other earlier or concomitant signs and symptoms can include itchy nose, eyes, pharynx, genitalia, palms, and soles; rhinorrhea; change in voice; metallic taste; nausea, vomiting, diarrhea, abdominal cramps, and bloating; lightheadedness; headache; uterine cramps; and generalized warmth.

In this study (and in the standard of care per this allergy clinic's protocol), only 1 systemic symptom is required to diagnose and treat anaphylaxis. By using this definition, patients having only 1 symptom, such as generalized pruritus, would qualify as having a systemic symptom and would be treated for such with intramuscular epinephrine in the deltoid.

Fatalities during anaphylaxis usually result from delayed administration of epinephrine. In a retrospective review¹² of anaphylaxis, all surviving individuals were given epinephrine, and none with fatal attacks received epinephrine before the onset of severe respiratory symptoms. The more rapidly anaphylaxis develops, the more likely the reaction is to be severe, and symptoms not immediately life-threatening might progress rapidly unless treated promptly and appropriately.⁹ All patients with SRs in this study were given intramuscular epinephrine in the deltoid. Epinephrine was given in the arm instead of in the lateral thigh because the arm is easily accessible and results in faster administration of the epinephrine by clinic personnel. During this study, there were no serious or biphasic reactions. In 2007, a case series¹³ of biphasic anaphylaxis revealed that in patients who received treatment with epinephrine within 30 minutes of symptom onset, the incidence of biphasic response was zero compared with the overall mean of 19%. It is important to recognize that the risk of SRs associated with ST may be more frequent than previously realized, especially when one expands the definition of SR to include only 1 nonlocal symptom. It is also imperative to recognize the treatments for these reactions to prevent progression. In this study, SRs occurred in 3.6% of patients who underwent ST, were more common in females, and readily responded to early intervention with epinephrine intramuscularly in the deltoid. In conclusion, it is important to recognize the risk of SRs associated with ST (0.4% for SPT and 3.2% for intradermal ST). Early administration of epinephrine seems to prevent progression of symptoms and biphasic reactions.

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