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Pre skin prick testing: A curfew required on herbals too

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ABSTRACT

Background: Allergic diseases are hypersensitivity disorders induced by an allergen specific immunoglobulin E (IgE) mediated response; Skin PrickTest (SPT) remains the gold standard for the in vivo assessment of IgEs. Many drugs are known to have anti histaminic effects and as such need to be stopped prior to the testing. However, the role of alternative system of medicine and other herbal remedies remains controversial in this regard.
Objectives: To study the effect of alternative system of medicine and other herbal remedies on the results of SPT.
Methods: The patients having a strong history and clinical symptoms of allergic diseases like allergic rhinitis, bronchial asthma and chronic urticaria were subjected to skin prick testing.
Results: There were six patients whose SPT results were negative although history and clinical symptoms suggested otherwise. On probing the drug intake of the patients prior to the testing, it was observed that the patients had taken certain herbal medications which interfered with the allergy testing and gave false negatives.
Conclusion: It is for the first time that a study has reported the significant effect of alternative medicine and other herbal supplements in suppression of skin prick test results. Therefore it is extremely important to ask properly the history of intake of alternative medicine and other dietary herbal ingredients and then insist on its abstinence for 10 days before SPT. A protocol wherein the allergist recommends to stop the use of any regional herbs prior to allergy testing will be the right step in improving the results of allergy testing and preventing false positives.

1. Introduction

Allergic diseases are hypersensitivity disorders of the immune system which occur through allergic inflammation induced by an allergen specific immunoglobulin E (IgE) mediated response and food allergies [1,2]. The various allergic disorders include Allergic rhinitis, Bronchial asthma Chronic urticaria which are diagnosed by having the proper history of patients, physical examination and some paraclinical tests to find out about specific IgE. Skin prick test (SPT) continues to be the most appropriate and gold standard diagnostic in vivo test for the identification of the allergen responsible for the allergic disorder [1].

Before scheduling a patient for Skin Prick Testing, it's important to know the drug history of the patient as some drugs are known to interfere with the histamine response during SPT. Antihistamines suppress the histamine response for a variable period of time, ranging from 72 h to 11 days [3,4]. Topical glucocorticosteroids can also block the histamine response [5]. Application of potent topical steroids have been shown to stop the histamine response for up to three weeks [6]. Tricyclic antidepressants can suppress the antihistamine response from 7 to 14 days depending upon the type [7,8].H2 blockers have the potential to suppress histamine skin reactions for up to two days and include cimetidine, ranitidine, and famotidine [9,10].

Given the widespread use of herbal supplements, it would be important to know the effects of herbal supplements on allergy skin testing. While the use of herbal supplements is common, little is known about their pharmacological properties [11,12]. Many herbs are presumed to possess diverse properties such as anti-inflammatory or antiallergy effects [13–19] yet their effect on the histamine skin response is unknown. Presently, the effect of herbal supplements on the skin prick tests, for the diagnosis of allergy to various allergen molecules is controversial; with some studies showing no effect of these supplements on skin prick testing [20]. In the most comprehensive study [20] using

Abbreviations: SPT, Skin Prick Testing; ISM, Indian System of Medicine

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a single– dose crossover study, it was felt that common herbal products did not significantly affect the histamine skin response.

The purpose of this study was to focus on the effects of various ayurvedic and unani supplements on skin prick testing (SPT), importance of history taking to rule out the use of any of these medications prior to skin prick testing and identification of frequently used herbs in the diet which can interfere with the test.

2. Methods

This study was carried out in the Allergy Unit of Department of Immunology & Molecular Medicine, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India. The patients undertaking the skin prick test were strictly instructed to discontinue the use of certain allopathic medications that could interfere with the skin prick testing. An informed written consent was taken from all the patients undertaking the skin prick test for aero and food allergens. The skin prick testing is a routine diagnostic allergy test carried out in the Dept. of Immunology & Molecular Medicine and as such is not a part of any research study on patients. Hence, Institutional Review Board (IRB) approval is not required for reporting of our observations.

3. Results

All the patients undergoing the skin prick test were asked to discontinue all the medications ten days prior to the testing. However, we had six patients from time to time attending our allergy unit for atopic diathesis presenting in various forms of organ system involvement spanning from allergic rhinitis to bronchial asthma to chronic urticaria with most of them having strong family history of atopy and classical history of worsening of symptoms on exposure to dust, some pollens and ingestion of some foods. The patients after being kept off routine antihistaminic medication for 7–10 days were subjected to skin prick test for aero and food allergens which gave unexpectedly negative or weakly positive results. Since the results were unexpected and paradoxical, these patients were further reviewed and digging history deeper down revealed that they were taking various Ayurvedic and Unani medications (Table 1), which they had not discontinued before skin prick testing. The patients were using these herbs for some unrelated comorbidities like diabetes mellitus, gyneocological disorders and general weakness. They were further asked to strictly avoid these drugs for 7–10 days and then skin prick testing was redone which thankfully revealed positivity to the expected allergens as was expected with their clinical history.

4. Discussion

The allergy testing requires a patient to stop the use of any anti histamines, β blockers, tricyclic anti depressants, anti inflammatory drugs, decongestants and H2 antagonists at least one week prior to testing as these can interfere with the test, giving false negatives. However, we observed that herbal medication {Indian system medicine (ISM)} can remarkably affect the results of allergy testing. Ours is the first reported study showing a significant relationship between the use of herbals and suppression of positive skin prick test results.

From our first hand experience, six patients showed a negative allergy test despite the history suggesting otherwise. On digging the history deeper, patients admitted using certain herbal remedies for other comorbidities than allergies which they had not stopped before undergoing SPT. The composition of these remedies pointed to a few ingredients which could be responsible for inhibiting the test. These included *Curcumae rhizome, Adhota vasica, Glycyrrhiza glabra, Cyperus rotundus, Mentha piperita, Ocemium tenoflorium and nigella sativa.*

Table 1
Details of the herbal drugs taken by the patients and their effect on skin prick testing.

Patient ID	Clinical Presentation of patient	Active contents of ISM drug used	SPT results before avoiding the herbal drug	SPT results after avoiding the drug
01	Allergic rhinitis, Bronchial Asthma	Glycyrhiza glabra, Adhota vasica	Positive control = 5 × 4mm, other allergens (-)	Positive control = 10 × 9mm, Dust mite (+ + + +), pollens (+ + +)
02	Allergic Rhinitis, Bronchial Asthma, Chronic Urticaria	Curcuma longa	Positive control = 5 × 6mm, other allergens (-)	Positive control = 11 × 10 mm, dust mite (+ + +) and pollens (+ +)
03	Allergic Rhinitis, Bronchial Asthma	Nigella sativa, Trigonelline	Positive control= < 3 mm	Positive control = 9 × 9mm, dust mite (+ +), pollens (+ + + +) and fungi (+)
04	Allergic Rhinitis, Chronic Urticaria and food allergy	Glycyrhiza glabra, Ocimum tenuflorum, Adhota vasica, Mentha piperita, cyperus rotundus	Positive control = 4 × 4 mm, other allergens (-)	Positive control = 8 × 8mm, dust mite (+ + +) and strongly (+ + + +) for tea, saffron, chicken and potato.
05	Allergic Rhinitis, Chronic Urticaria	Glycyrhriza glabra	Positive control 5 × 5mm and mild dust mite (+)	Positive control = 9 × 9mm, dust mite (+ + +) and some pollens (+ +).
06	Bronchial Asthma	Cyperus rotundus, glycyrhiza glabra	Positive control = 4 × 4mm	Positive control = 10 × 12 mm, dust mite (+ + +) & pollens (+ +)

(+) indicates less than half of histamine but more than 3 mm; (+ +) is equal to half of histamine; (+ + +) more than half of histamine or equal to histamine; (+ + + +) more than Positive Control.

Case 1:

A female patient, with allergic rhinitis and bronchial asthma underwent a skin prick test which was negative for all allergens. The patient was taking a herbal remedy for gyneacological disorders which contained active ingredients *Glycyrhiza glabra* and *Adhota vasica*. Licorice or *Glycyrhizha glabra* is one of the most commonly used traditional medicine in China, Japan and Korea. The components of licorice include glycyrrhizin and flavonoids [21,22]; these components have a number of known pharmacological effects including antiallergic, anti inflammation, anti asthmatic, anti ulcer and anti carcinogenic activities [23,24]. *Adhota vasica* is most well-known for its effectiveness in treating respiratory conditions. The pharmacological uses of *Adhatoda* are a result of its rich concentration of alkaloids [25,26]. The extract containing the alkaloid vascinol and 20% vasicine inhibited ovalbumin-induced allergic reactions [27] while vasicinone has been shown to be a potent anti-allergen in tests on mice, rats and guinea pigs [28]. On repeating the test on the patient after withholding this drug, the SPT result was positive to various aero allergens (Table 1). Hence we presume that the false negative skin prick test result was because of use of these ISM drugs.

Case 2:

Another patient with allergic rhinitis, bronchial asthma and chronic urticaria showed a false negative test which contradicted her allergic history. The patient refused having taken any antihistaminics prior to the testing. However on further investigation, she admitted to the use of a herbal remedy for general weakness. On probing the remedy, it was found to contain curcumin, a compound present in turmeric. Turmeric also called *Curcumae rhizome*, is an everyday herb; not only an essential ingredient of unani and ayurvedic medicines, but it is also an important constituent of traditional Indian cuisine. Curcumin is known to have anti-tumor, anti-inflammatory, anti-oxidative, and anti-allergic effects. Many previous studies demonstrated that curcumin had an inhibitory effect on histamine release from mast cells triggered by IgE, calcium ionophore A23187 or concanavalin A [29,30]. On repeating test after stopping this remedy for 10days, the skin prick test was highly positive to various allergens as was expected by her history.

Case 3:

An atopic patient presenting with classical symptoms of dust allergy showed a negative SPT. The patient had not taken any of the restricted allopathic medicines. However the patient was taking a herbal remedy for controlling diabetes. The Mix consisted of kalungi (Nigella sativa) and methi seeds (*Trigonella foenum-graecum*). The antidiabetic effect of Nigella sativa has been extensively studied [31]. The possible mechanism by which *N. Sativa* exerts its anti inflammatory action has been attributed to its constituent, thymoquinone which is a potent inhibitor of eicosanoid generation [32]. The anti histaminic effect of Trigonelline, an active ingredient of Trigonella foenum-graecum is also known [33]. Repeating the test after stopping the herbal medication for 10 days gave strong positive results.

Other cases:

Similarly the other three patients, showing false negative SPT had been prescribed the use of some tonics by faith healers. The active ingredients of these tonics contained *Ocimum tenuiflorum (tulsi), Mentha piperita (peppermint)* and *Cyperus rotundus. Cyperus rotundus* possesses different biological activities such as antioxidant [34], anti-allergic [35], antipyretic, anti-inflammatory and hypotensive [36]. The broad spectrum of bioactivity of *Mentha piperita* has been ascribed to the flavonoids, which have been proven clinically useful in alleviating the nasal symptoms of allergic rhinitis [37]. *Ocimum tenuiflorum* or tulsi is another herb commonly used in Indian subcontinent. Studies have shown notable properties such as antimicrobial, anti-diabetic, hepato-protective, anti-inflammatory, anti-carcinogenic, radio-protective, neuro-protective, cardio-protective and larvicidal/mosquito repellent of different parts of the Tulsi plant [38].

Therefore, these results indicate the necessity of a thorough history taking prior to the test as well as need to clearly instruct patients to be off any herbal supplementations prior to testing. Interestingly, there are some spices used invariably in our daily diet especially in Indian subcontinent which have been found to have anti histaminic effects. These include turmeric, peppermint, methi seeds and tulsi. Therefore it opens a gateway for allergists to set up a protocol wherein the patients must be mandatorily asked to stop the use of any regional herbs as well as these food ingredients which might interfere with the histamine response during SPT. Correlating the results of SPT with the clinical impression is very instrumental to the approach of assessment of atopic patient. It is therefore extremely important to ask properly the history of intake of alternative system of medicine drugs and other aforementioned dietary ingredients and then insist on its abstinence for 10 days before SPT. Otherwise false negative results can easily mislead the allergists and the whole plan of treatment would be an exercise of futility. It however remains a matter of debate as to precisely how many days of abstinence is required for these herbals. In our study we kept a 10 days of abstinence period roughly corresponding to median time of abstinence for other drugs. A protocol wherein the allergist recommends to stop the use of any regional herbs prior to allergy testing will be the right step in improving the results of allergy testing and preventing false positives.

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Conflicts of interest

The authors report no conflict of interest.

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