

Original Research Article

Autologous plasma skin test in chronic idiopathic Urticaria

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Abstract: Chronic idiopathic urticaria (CIU) is common but one of most frustrating therapeutic problem faced by the dermatologists. About 30% of CIU patients have histamine releasing the auto-antibodies in their blood. The term autoimmune urticaria is increasingly being accepted for this subgroup of patients. The autologous serum skin test (ASST), which indicates the presence of functional circulating auto antibodies to FcεRIα &/ to IgE, is the best invivo test for detection of basophil releasing histamine activity in vitro. Few studies reported that autologous plasma skin test (APST) is positive in more patients of chronic urticaria than ASST. This study aims to find the prevalence of the APST positive cases among Indian patients with CIU. The autologous plasma skin test were done in all patients with chronic urticaria of more than six weeks duration. Physical urticaria, urticarial vasculitis, pregnant & children <12 years patients were not included in the study. Out of the 30 patients examined, 14 patients (46.66%) had positive APST and 16 patients (53.33%) had negative APST with negative controls. Prevalence 46.66% positivity correlates with previous studies. The APST also a simple, less time consuming tool to measure the auto reactivity of the skin like ASST.

Keywords: Chronic idiopathic urticaria, autologous plasma skin test, auto-antibodies

INTRODUCTION:

Chronic urticaria is a frustrating condition for the patients and therapeutic challenge for dermatologists. "Autoimmune urticaria" is a subset of chronic urticaria and has circulating histamine releasing auto-antibodies in the blood. Around 30% of chronic urticaria patients demonstrate these auto antibodies. The basophil histamine release assay is the "gold standard" test to demonstrate these functional auto antibodies in the serum [1], but it is time consuming procedure & difficult to standardize. Other test like western blotting, enzyme linked immune absorbent assay & flow cytometry using chimeric cell lines expressing the human FcεRIα are other options and yet to validate [1]. The autologous serum skin test (ASST), which indicates the presence of functional circulating auto antibodies to FcεRIα &/ to IgE, is the best invivo test for detection of basophil releasing histamine activity in vitro [2]. ASST has a sensitivity of approximately 70% and a specificity of 80% [3]. Thus ASST is the most simple & cost effective screening tool in the diagnosis of autoimmune urticaria. Few studies reported that autologous plasma skin test (APST) is positive in more patients of chronic urticaria than ASST [1, 4]. All the data available is mostly from the western population. This study aims to find the

prevalence of the APST positive cases among Indian patients with chronic idiopathic urticaria (CIU).

MATERIALS AND METHODS:

A clinical prospective study was conducted on patients with chronic urticaria for more than 6 weeks attending the outpatient department of Dermatology, Mandya institute of medical sciences, Mandya. The study was approved by the Institutional Ethics Committee, and informed written consent was obtained from all patients and volunteers before study entry. The study included all chronic urticaria patients, aged at least 12years & willing to perform the APST over a period of 1 year. Patients with urticarial vasculitis, physical urticaria, pregnant and children less than 12 years were excluded. Detailed history including address and occupation with special reference to onset and duration, preceding skin conditions were noted. Also we interrogated about family history of urticaria, personal and family history atopy, and personal and family history of autoimmune diseases (like rheumatoid arthritis, lupus erythematosus, vitiligo, and thyroid diseases).

All patients had stopped systemic treatment at least 3 days before the test and only topical antipruritics like calamine lotion were allowed if the itching was

severe. Prior to the test, adrenaline, injectable methylprednisolone and antihistamines were kept ready for the possibility of an anaphylactic reaction. The autologous plasma skin test (APST) was performed by drawing 5ml of venous blood. Citrated blood was centrifuged 2500 rpm/min for 5 minutes in room temperature to separate the plasma and 0.05 mL of the same is injected intradermally on volar aspect of the patient's forearm at site not affected by a wheal in the last

24 hours; at the same time a control test is done by injecting the same volume of normal saline to other forearm. Both sites were read for wheal at the end of 30 mins. The test is considered positive and the patient is said to have chronic autoimmune urticaria (CAU) if there was a wheal and flare at the tested site (plasma injection site) of a diameter (measured by taking the mean of the largest two diameters) at least 1.5 millimetres more than the wheal and flare induced at the control site (Figure 1).



Fig 1: APST positive showing test and control site. Test site (left forearm) showing wheal of >1.5mm than control (right forearm) at the end of 30mins

RESULTS:

Thirty consecutive adult patients with CIU, attending the outpatient department of Dermatology, Mandya institute of medical sciences, Mandya were included in the study. CIU was diagnosed on the basis of the appearance of continuous or recurrent hives with or without angio edema for more than 6 weeks. Of the 30 patients examined, 13(43.33%) were male & 17(56.66%) were females (Table-1). They were in age range of 15-60 years with a mean age of 35.6 yrs. Duration of urticaria

was between 6 weeks to 1 year with average duration being 6.4 months.

A total of 14 patients (46.66%) had positive APST and 16 patients (53.33%) had negative APST (Table 1). If the wheal of 1 mm is considered, then the positivity increases to 56.7%. In contrast sensitivity decreases if the reading time is prolonged (Table 2). Maximum positivity is noted when plasma induced wheal of 1.5 mm is taken as positive response at the end of 30 mins (Table 3).

Table-1: Prevalence of APST positive among CIU Patients*

APST	MALE	FEMALE	TOTAL
POSITIVE	6	8	14(46.66%)
NEGATIVE	7	9	16(53.33%)
TOTAL	13	17	30

* Wheal size of 1.5mm at the end of 30 mins is considered as positive response

Table-2: Clinical assessment of size of the wheal at the end of 30 mins

Parameters	No. Of patients
Plasma induced wheal diameter of 1.0 mm	17
Plasma induced wheal diameter of 1.5mm	14
Plasma induced wheal diameter of 2mm	7
Plasma induced wheal of diameter of 3mm	4

Table 3: APST positivity with fixed wheal diameter (1.5mm) at variable reading time

Size of the wheal	1.5mm
At the end of 20 min	11
At the end of 30 min	14
At the end of 60 min	11
At the end of 90 min	4

DISCUSSION:

Chronic urticaria (CIU) is a common skin disorder but cause cannot be ascertained in majority of patients. Such idiopathic cases are termed chronic idiopathic urticaria. A portion of CIU patients demonstrate functional auto antibodies (anti-FcεRI and /or anti-IgE) or histamine releasing factors in the serum [5]. The term chronic autoimmune urticaria (CAU) is applied for this subgroup of patients. ASST is a simple investigation for the demonstration of circulating auto antibodies. Intradermal injection of patient's own serum will produce erythema and wheal in the subjects with auto antibodies. Thus ASST is a surrogate marker for the detection of CAU. Asero *et al.*; demonstrated generation of thrombin, a serine protease able to activate mast cells and to cause relevant increase in permeability of endothelium leading to increased positivity in APST group than ASST group [4].

There are many studies demonstrating various prevalence rate of ASST in CAU and frequency varies from 4.1 – 76.5 [6-9]. Similar studies with APST are lacking. Highest frequency of 86% APST was demonstrated by Asero *et al.*; [4] and least by Metz *et al.*; [9] (43%). Present study demonstrated a frequency of 46.7% which is similar to many other studies [4, 9, 10, 11]. Asero *et al.*; observed that APST was positive in 97

and 86% of urticaria patients in two different studies and recommended using APST instead of ASST [4, 12]. But Kocaturk *et al.*; reported that ASST was superior to APST and had the ability to detect more patients with auto reactive urticaria than APST [13].

ASST positivity varies when diameter of wheal considered varies. Similar observation was noted with APST. Present study was compared with Sabroe RA *et al.*; [3] study where ASST positivity at different wheal size was considered at fixed time of reading (At 30 mins) (Table 4). It was noted that APST is marginally superior to ASST when wheal diameter of 1.5 -2.0mm was considered as positive at the end of 30 mins.

Initial appearance of a positive ASST response varies with time if reading. Many studies have considered 30 mins as standard for ASST test in CIU. Similar studies with APST are lacking. Present study demonstrated highest positivity when reading was taken at the end of 30 mins.

ASST is the surrogate marker of CAU. It is simplest and inexpensive test to demonstrate auto reactivity. Similarly APST was simple office based test which is slightly superior to ASST. Thus both ASST and APST can be considered while evaluating chronic urticaria.

Table 4: Comparison of ASST (Sabroe RA *et al.*; [3]) with APST (Present study) positivity considering various diameters as positivity criteria with fixed reading time of 30 mins

ASST positivity criterion (mm)	Positive ASST (Sabroe RA [3])	Positive APST (Present study)
≥0.5	66.5%	----
≥1	54.2%	56.7%
≥1.5	44.5%	46.7%
≥2	34.8%	23.3%
≥2.5	24.5%	13.3%

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