



A STUDY ON EFFICACY OF AUTOLOGOUS SERUM THERAPY (AST) IN PATIENTS WITH CHRONIC URTICARIA

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ABSTRACT

Introduction:

Chronic urticaria (CU) patients suffer from irritable itch and wheals and are also subjected to a huge antihistamine pill burden. A significant number of patients have autoimmune basis where autologous serum therapy (AST) can induce remission from the disease.

Aim and objective:

To study the efficacy of AST in CU patients with positive autologous serum skin test (ASST).

Materials and methods:

30 ASST positive patients were prospectively analyzed for the efficacy of nine consecutive weekly autologous serum injections with a post-intervention follow-up of 12 weeks. Total urticaria severity score (TSS) was monitored at the baseline, at the end of treatment and at the end of 12 weeks of follow up.

Results:

Out of 30 patients 14(46%) patients had excellent response, went into complete remission and remained so over the follow-up period of 12 weeks. 4(13%) had satisfactory response. 12 had no response

Conclusion:

AST is effective in treating autoimmune urticarial. It is economical and cost effective.

KEYWORDS

Chronic urticaria, autologous serum therapy, autologous serum skin test, autoimmune urticaria

INTRODUCTION

Urticaria is defined as a skin lesion consisting of a wheal-and-flare reaction in which localized intracutaneous edema (wheal) is surrounded by an area of redness (erythema) that is typically pruritic. Chronic urticaria (CU) is characterised by episodes of urticaria persisting beyond 6 weeks and is divided into two major subgroups: chronic autoimmune urticaria (CAU) and chronic idiopathic urticaria (CIU).¹ About 30-40% of patients with CIU have histamine-releasing auto-antibodies directed against either the high-affinity IgE receptor, or the Fc portion of human IgE. These patients are labelled as cases of chronic autoimmune urticaria (CAU).^{2,3} Studies have reported that 27-61% of CU patients, had these circulating antibodies in their blood, depending on the method of antibody detection.^{4,5,6,7} These autoantibodies are responsible for causing the activation of basophils or mast cells leading to histamine release, which is the central event in CU. Autologous serum skin test (ASST) is the simplest screening method to identify patients with chronic autoimmune urticaria.⁸ Intra-dermal injection of autologous serum in these patients elicits an immediate-type wheal and flare response indicating the presence of a circulating histamine-releasing factor in the blood. Patients with CAU suffer from a more severe urticaria with a greater number and wider distribution of wheals, more severe pruritus, and more frequent systemic symptoms.⁹ Antihistamines being first line of treatment for CU, effectiveness of antihistamine is limited during the period of its use. Autologous serum containing tolerance-generating anti-idiotypic antibodies to mast cells degranulation antigens has been tried for disease remission in various autoimmune diseases. In recently conducted studies,^{10,11,12} AST have been found to be effective in CAU. Our study was to assess the effectiveness of AST in CAU patients.

MATERIALS AND METHODS

Patients of either sex with chronic urticaria with positive ASST, age >18 years, and willingness for weekly follow-up and injections

were included in the study. Exclusion criteria were pregnant females, patients with negative ASST, patients on systemic corticosteroid or immunosuppressive drug in the past 6 weeks and other systemic illnesses requiring treatment. After getting informed consent, ASST positive patients (30) were prospectively analyzed for the efficacy of nine consecutive weekly autologous serum injections with a post-intervention follow-up of 12 weeks.

AUTOLOGOUS SERUM SKIN TEST

Serum was separated by centrifuging 2ml of patients' blood at 2000 rpm for 10 min. 0.05 ml of autologous serum was injected intra-dermally into the patients left flexor forearm 2 inches below the antecubital crease and 0.05 ml sterile normal saline was injected as control into the right forearm using 31G sterile disposable 1ml insulin syringe, avoiding sites of whealing in the past 24 h and results were read at 30 min. ASST was considered positive when the average of two perpendicular diameters of the autologous serum wheal was 1.5 mm more than the normal saline wheal.¹³ Longacting antihistamines were withdrawn at least 3 weeks before and the short-acting ones 48 h prior to the test.

AUTOLOGOUS SERUM THERAPY

5 ml blood was drawn and serum was separated. 2.5 ml of the serum was given as deep intramuscular injection into the gluteal region with a 22 gauge needle for nine successive weeks. Tablet Desloratidine at the dose of 5mg was given as rescue antihistamine in the run-in period; no other drugs were permitted.

DISEASE ASSESSMENT

Total severity score (TSS)¹⁰ [Table 1] was recorded on a 0-3 scale and disease severity was classified as, clear (TSS = 0), mild (TSS 1-6), moderate (TSS 7-12) or severe (TSS 13-18), at baseline (0 week), end of treatment (9th week) and follow-up (12th week). TSS is a more holistic parameter than Urticaria Activity Score (UAS) as it reflects the pill burden along with disease activity. Response to the

treatment protocol was assessed based on reduction in the TSS from the baseline value. Excellent response (TSS-0), good response (TSS- 1-6), fair response (TSS- 7-12), and poor response (TSS- 13-18).

Clinical parameters	0	1	2	3
No. of wheals	None	<10	11-50	>50
Size of wheals	None	<1cm	1-3cm	<3cm
Intensity of itch	None	Mild	Moderate	Severe
Duration of persistence of wheals	None	<1hr	1-12hrs	>12hrs
Frequency of appearance of wheals	None	Once a week	2-3 times/week	Daily
Frequency of antihistamine use	None	Once a week	2-3 times/week	Daily

TABLE-1: Urticaria Total Severity Score (TSS)

RESULTS

AST was given to 30 ASST(+) patients (M: F = 4:1; age range = 18-55 years; duration of disease = 6 months to 5 years). 14(46%) patients had excellent response, went into complete remission and remained so over the follow-up period of 12 weeks. 4(13%) had satisfactory response. 40% had no response.

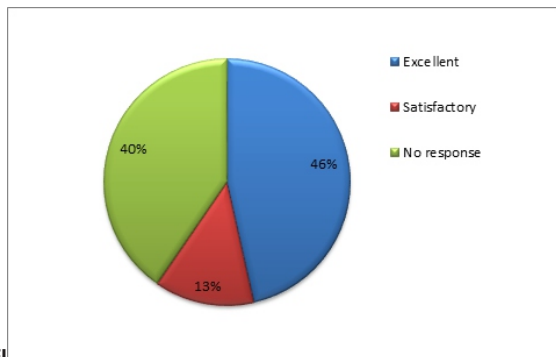


FIGURE-1: Response to autologous serum therapy

DISCUSSION

CU remains a major problem in terms of etiology, investigations and management. Mast cell degranulation plays the pivotal role in the pathogenesis of urticaria. Antibody to high-affinity IgE receptor (FcεRI) is identified and is found to degranulate the mast cell by crosslinking the IgE receptors. This entity is regarded as autoimmune urticaria and is found to prevail in 27-61% of chronic urticaria.⁴ Treatment of CU is most of the times quite challenging for the treating physician. This is because of the fact that the moment antihistamines are withdrawn in these patients, they tend to develop a relapse. Since patients are not able to control their symptoms by antihistamines alone, they need systemic steroids or other immunosuppressive drugs on a regular or recurrent basis.

In a placebo controlled study,¹⁴ auto-hemotherapy (injection therapy with the patients' own blood) was shown to have a beneficial role in CAU patients.¹⁰ Since this mode of treatment had largely been abandoned in recent times as being unscientific, a multicentre, prospective, open-label trial of autologous serum therapy (AST) in patients with CU done by Bajaj et al,¹¹ refined Autologous Whole Blood by removing the cellular components of blood for intramuscular injections as histamine-releasing factors are present in the serum. This made the treatment less painful for the patients and easier to administer for the clinician without reducing its efficacy. Patients with CU were given weekly intramuscular injections of autologous serum and were monitored for any improvement in urticaria total severity score (TSS). The study showed AST to be effective in a significant proportion of ASST (+) patients with CU. A smaller but still substantial number of ASST (-) patients also benefited from this treatment. A study done by Majid et al¹³ on AST in ASST positive patients, 12% of patients went into complete remission and they were disease free during their 12 weeks of follow-up. Patil et al¹⁴ conducted a study on AST

in CU, AST was given to ASST positive patients and 45% of patients had excellent response.

Aim of our study was to evaluate the efficacy of AST in CAU. We have found encouraging results in a small study. Almost half of the patients (46%) had excellent response and went into complete remission during the 12 weeks follow-up period. Our findings were comparable with previous studies. Patients did not complain of any side effects during treatment except for the mild pain during injection.

Autoimmune urticaria, which is refractory to conventional therapy, AST has proved itself as an excellent adjuvant therapy. The goal of therapy in chronic urticaria is to maintain a symptom free period and to ensure that the treatment is not associated with significant side effects and monetary burden.

CONCLUSION:

Heberden who described urticaria and said "...the greatest number (of patients) experience no other evil from it besides the intolerable anguish arising from the itching.",¹⁵ till this 21st century, urticaria has shown to have significant impact of patient quality-of-life on the aspect of emotion, functioning as well as symptoms. Treatment of CU is most of the times quite challenging for the dermatologist. Autologous serum therapy can be useful in India as it is economical, cost-effective and does not involve use of various expensive drugs like cyclosporine and omalizumab. Large trials are needed to confirm the above findings.

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