

Efficacy of Autologous Serum Therapy in Chronic Urticaria

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ABSTRACT

Introduction: Chronic urticaria is a common and distressing dermatosis and patients were subjected to high pill burden. Autohemotherapy was regarded as potentially curative therapeutic option in chronic urticaria especially in autoreactive group. Later this procedure was refined by using autologous serum instead of whole blood. The aim of this study was to find out proportion of ASST positive patients among chronic urticaria patients and efficacy of Autologous Serum Therapy (AST) in both ASST positive and negative groups.

Material and Methods: A total of 50 were enrolled into study. Autologous Serum Skin Test (ASST) was done in all patients. In both ASST positive and negative patients, Autologous Serum injections were given weekly for 9 weeks. The effect of AST was recorded by using Urticaria Total Severity Scale at every visit. Patients were followed up for 12 weeks after 9 weekly Autologous serum injections.

Results: A total of 50 patients were enrolled into study. ASST positive group consists of 29 patients and ASST negative group consists of 21 patients. Symptoms of urticaria showed reduction from 4th week of AST in both ASST positive and negative patients. Antihistamine usage declined from 100% baseline in both groups to 37.3% and 57.1% in ASST (+) and ASST (-) groups respectively. At 21 wks, 37.9% of ASST (+) group and 23.8% of ASST (-) group showed complete clearance.

Conclusion: We found that AST prove to be better treatment modality with less side effects to reduce pill burden irrespective of autoimmune nature of urticaria.

Keywords: Autologous Serum Skin Test, Autoimmune, Autologous Serum Therapy, Chronic Urticaria.

INTRODUCTION

Chronic urticaria is a common and distressing dermatosis characterized by the appearance of evanescent wheals almost daily, continuously for six or more weeks.¹ It affects 0.1% of population.²

About 30-50% of patients with chronic urticaria have circulating histamine releasing autoantibodies to the high affinity IgE receptor FcεRIα on basophils or mast cells or, less commonly antibodies to IgE.³ Hide et al⁴ reported that intracutaneous injection of serum known as Autologous Serum Skin Test (ASST) results in immediate hypersensitivity type skin reaction in a subgroup of chronic urticaria patients. This subgroup is known as autoreactive group or autoimmune chronic urticaria. These patients tend to have high itch or wheal score, systemic symptoms and other associated autoimmune diseases.² As circulating histamine releasing factors are responsible for induction of urticarial symptoms in ASST positive CU patients, autohemotherapy is regarded as a promising and potentially curative therapeutic option for this subgroup of CU patients.⁵ Later this procedure was refined by using serum instead of whole blood by Bajaj et al¹ as histamine releasing factors are present in the serum. This made the treatment less painful and

increased compliance.

Patients of chronic urticaria suffer from morbidity that arise from irritable symptoms and are subjected to high antihistamine pill burden. We conducted this prospective open trail to find out efficacy of Autologous Serum Therapy (AST) in chronic urticaria patients and to decrease their pill burden. The aim of this study was to find out proportion of ASST positive patients among chronic urticaria patients and efficacy of AST in both ASST positive and negative groups.

MATERIAL AND METHODS

Patients for this study were enrolled based on inclusion criteria, which were of both sexes of age 16 to 60 years, subjects with a history of daily or almost daily occurrence of urticarial wheals for 6 weeks or more, willingness for the test and weekly injections. Exclusion criteria were patients with history of physical urticaria, systemic steroid or immunosuppressive drug use in past 6 weeks, cholinergic urticaria, known type 1 hypersensitivity reaction, hereditary angioedema or known C1 esterase deficiency, urticaria associated with conditions like neoplasms, connective tissue diseases, any acute or chronic infections, pregnancy and lactation. Dermographic variables were recorded and detailed history regarding atopy was taken. A total of 50 were enrolled into study based on inclusion criteria and exclusion criteria and ASST was done in all after taking informed consent. In both ASST positive and negative patients, 9 weekly injections of Autologous Serum Therapy was given. Weekly followup was advised for 21 weeks from initiation of AST and effect of AST was recorded by using Urticaria Total Severity Score (TSS) which consist of parameters like number and size of wheals, intensity of pruritus, duration of persistence of wheals, frequency of appearance of wheals, and frequency of antihistamine use was recorded in a prescribed proforma (table-1).

ASST Procedure

5 ml of subject's venous blood is drawn and placed in a test tube without clotting accelerator. It is allowed to clot at room temperature for half an hour. Later it is centrifuged at 2500 rpm for 10mins. Then serum is separated by using 5cc syringe. Samples of 0.05 ml patient's autologous serum and 0.05 ml of 0.9% sterile saline (for negative control) are separately injected intradermally into the flexor aspect of forearm with 27G needle

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Parameter	Scores			
	0	1	2	3
Number of wheals	None	≤10	11-50	>50
Size of wheals	None	<1 cm	1-3 cm	>3 cm
Intensity of pruritus	None	Mild	Moderate	Severe
Duration of persistence	None	<1 h	1-12 h	>12 h
Frequency of appearance	None	<once or once a week	2-3 times a week	Daily/almost daily
Frequency of antihistamine use	None	<once or once a week	2-3 times a week	Daily/almost daily

Age	Males	Females
16-30 yr	8	21
31-45 yr	6	9
46-60 yr	2	4

Table-2: Age-sex distribution

Sex	ASST (+) group	ASST(-) group	Total
Males	11	5	16
Females	18	16	34
Total	29	21	50

Table-3: Based on sex distribution

Week	(Mean) TSS ASST (+)	(Mean) TSS ASST (-)
Baseline	12.2 (100%)	11.3 (100%)
4 th week	11 (90.1%)	10.7 (94.6%)
6 th week	8.8 (72.1%)	9.6 (84.9%)
9 th week	6 (49.1%)	8.5 (75.3%)
21 st week	3.8 (31.2%)	6.3 (55.7%)

Table-4: Mean TSS in ASST +ve and -ve patients at 0, 4, 6, 9, 21 weeks

with a gap of at least 3cm between the injection sites. Areas known to have been involved in spontaneous wheals in the last 24hrs will be avoided. Wheal and flare response measured after 30 mins. A positive test is defined as a red serum induced wheal with a diameter of 1.5 mm or more than that caused by adjacent saline induced response at 30 mins.

Autologous serum therapy

After the ASST is done, all the patients irrespective of the results Autologous serum therapy will be given. 2.5 ml of patient’s own serum will be injected deep intramuscularly with a 22G needle. AST is given weekly, each time on alternate buttocks for 9 weeks

Disease assessment

Disease assessment was done by Urticaria Total Severity Score (TSS) which consist of parameters like number and size of wheals, intensity of pruritus, duration of persistence of wheals, frequency of appearance of wheals, and frequency of antihistamine use. Six separate parameters of disease activity and severity were recorded on a 0-3 scale [Table 1] at baseline (0 week), end of treatment (9 weeks) and follow-up (21weeks). Based on these, a 0-18 total severity score (TSS) was generated and overall disease severity classified as clear (TSS = 0), mild (TSS - 1-6), moderate (TSS -7-12) or severe (TSS -13-18).

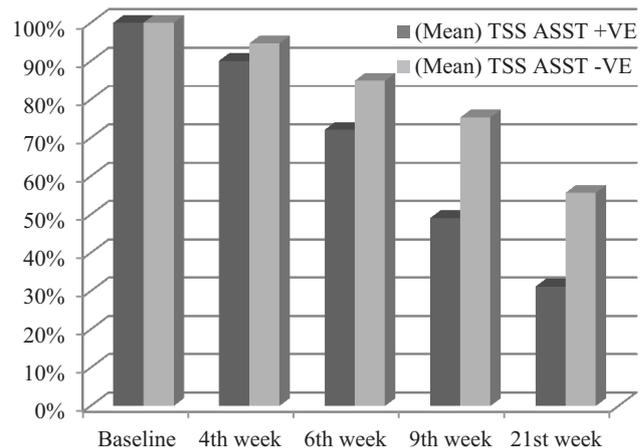


Figure-1: Trend of fall of Mean TSS in ASST (+) and ASST (-) group

STATISTICAL ANALYSIS

Microsoft excel 2007 was used for statistical analysis and making graphs. Descriptive statistics like mean and percentages were used for interpretation of data. P < 0.05 was fixed as the limit for significance of differences. P value was calculated using paired 't' test

RESULTS

A total of 50 patients were enrolled into study. 34 were females and 16 were males (tables-2,3). These 50 patients were divided into ASST positive and negative groups based on Autologous serum skin test. ASST positive group consists of 29 (58%) patients of which, 18 were females and 11 were males. ASST negative group consists of 21 (42%) patients of which, 16 were females and 5 were males. The median age of ASST (+) group and (-) group was 26 years (range 17 – 60years) and 27 years (range 18- 50 years) respectively. The duration of urticaria ranged from 2 mon to 10 years in ASST (+) and 8 mon – 7 years in ASST (-) group. A positive history of atopy was present in 21 patients in ASST (+) group and 15 in ASST (-) group. Antihistamine usage declined from 100% baseline in both groups to 37.3% and 57.1% in ASST (+) and ASST (-) groups respectively at the end of the study. Symptoms of urticaria showed reduction from 4th week of AST in both ASST (+) and (-) group. At 4th week TSS in ASST (+) and ASST (-) group was 90.1% and 94.6% respectively. At 6th week TSS was 72.1% and 84.9% in ASST (+) and ASST (-) groups respectively. The fall in TSS at 9th week in ASST (+) and ASST (-) groups was 50.9% and 24.7% respectively. Over next 12 weeks TSS continued to

show further downward trend and final reduction in ASST (+) group and ASST (-) group was 68.8% and 44.3% respectively. TSS at the 21st week was lower in the ASST (+) group than ASST (-) group, but it was not statistically significant (P value > 0.05). In ASST (+) group, at the final follow up visit i.e at 21 weeks 37.9% showed complete clearance and 27.5% showed mild disease. In ASST (-) group 23.8% showed complete clearance and 19% showed mild disease (table-4, figure-1).

DISCUSSION

Chronic urticaria is a disease of unpredictable course and the treatment is continued till the disease goes into remission. The need for newer therapeutic modality to supplement the antihistamines and leukotriene inhibitors is long felt and any adjuvant therapy that can reduce the pill-burden while achieving symptom free period is welcome by the patients and physicians alike.³

The aim of our present study was to evaluate the efficacy of autologous serum therapy in chronic urticaria. We chose to use autologous serum in place of whole blood for the following reasons:

- The circulating autoreactive factor is present in the serum, not in cellular components of blood.
- Finer needles can be used for injecting serum compared to those with whole blood, reducing patient discomfort and increasing compliance.
- Whole blood must be injected as quickly as possible after being drawn to avoid the possibility of clotting, requiring increased patient cooperation.

In our study 58% were found to exhibit ASST positivity which is similar to that reported by Krupashankar et al.² However ASST positivity was higher than that observed by Godse from Mumbai.³

ASST (+) patients did not show significant differences ($p > 0.05$) in total severity scores (lesion size, frequency, number, pruritus, antihistamine use, persistence) as compared to ASST (-) patients. This is similar to other reports that revealed no⁶ or only subtle differences in symptomology of ASST (+) and ASST (-) patients.⁵

Staubach et al⁵ performed follow up evaluation 4 weeks after the last injection using autologous whole blood. In our study we performed follow up evaluation 12 weeks after last injection to assess the longevity of the suppressive effect of this therapy. In our study, symptoms of urticaria showed improvement by 4th week of initiation of AST in both groups which is similar to that reported by Debbarman et al.⁷

37.9% of ASST (+) and 23.8% of ASST (-) patients showed complete clearance by 21 weeks. The reduction in the symptom is accompanied by reduction in pill burden and decrease in TSS. Mean percentage reduction in TSS show that there was a dramatic decline in severity in the ASST (+) group. There was remarkable decrease in TSS in ASST (-) group but the scores were still higher than ASST (+) group at the end of study. However the difference was statistically not significant ($P > 0.05$). This reduction in TSS was similar to that observed by Bajaj et al.¹ 11 patients who had complete clearance after 9 injections of AST remained symptom free for 3 months to 1 year in ASST (+) group.

Mast cell degranulation plays a pivotal role in pathogenesis

of urticaria, however the reason for degranulation is still a mystery. In recent times antibody to high affinity IgE receptor (FcεRI) is identified and is found to degranulate mast cell by cross linking the IgE receptors.⁷ But reported rates of ASST (+) patients having antiFcεRI antibodies vary from 40%⁸ to $< 20\%$.⁵ This shows that all ASST (+) patients do not have antiFcεRI antibodies. Some studies reported $< 2\%$ antiFcεRI positivity in ASST (-) patients.⁸ Recent studies have detected these antibodies in as many ASST (-) as ASST (+) patients and even in healthy subjects.¹ This shows poor concordance of ASST positivity with antiFcεRI antibodies. This may be the possible reason behind significant clinical improvement of ASST (-) patients with AST in our study.

We did not notice any adverse effects like bruising or soreness at injection sites although it was reported in some patients treated with autologous whole blood for chronic urticaria in previous study.⁵

CONCLUSION

The exact mechanism how AST works is not known but it may prove to be cost effective and better curative modality to reduce pill burden and shows a promising role in treatment of the chronic urticaria regardless of the autoimmune nature.

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