

Chronic Autoimmune Urticaria and Efficacy of Autologous Serum Therapy

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Abstract

Introduction: Chronic idiopathic urticaria (CIU) is defined as widespread, short-lived wheals occurring daily or almost daily for more than 6 weeks, with no obvious cause. Approximately, 30-40% of patients with CIU have chronic autoimmune urticaria. Autologous serum skin test (ASST) is a simple *in vivo* screening test for detecting patients with autoimmune urticaria. Autologous serum therapy (AST) has been found fairly effective in chronic urticaria.

Aim: To study the prevalence of chronic autoimmune urticaria using ASST and epidemiological pattern of the disease and to evaluate the efficacy of AST in the disease.

Materials and Methods: A prospective, interventional study was conducted between October 2009 and September 2011. 200 consecutive patients who attended our outpatient department were selected for the study. ASST was done with patient's serum and AST was given intramuscularly every week for 9 consecutive weeks, and the results were studied.

Results: Among 200 patients, 85 were males and 115 were females. 47 were positive and 153 were negative for ASST. No statistically significant difference was seen with age and sex distribution, atopy, number of wheals, and wheal size, and statistically significant difference was seen with angioedema, pruritus score, average hold time use, duration of wheals, and total severity score (TSS) among ASST positive and ASST negative patients. AST was given to 46 ASST positive patients. At the end of treatment, none had severe TSS, 9 patients were free from symptoms, and the majority had only mild TSS.

Conclusion: In patients with chronic autoimmune urticaria, AST is a cheap, cost-effective, and potentially curative modality of treatment.

Key words: Autologous serum skin test, Autologous serum therapy, Histamine-releasing autoantibodies, Total severity score

INTRODUCTION

Urticaria commonly called as “hives” has a long and rich history dating back to the 10th century BC.¹ Urticaria is a distressing dermatosis of skin characterized by transient erythematous edematous wheals which are very itchy. Activation of cutaneous mast cells liberates various mediators predominantly histamine which increases the

permeability of capillaries and venules which in turn produces urticaria. Chronic idiopathic urticaria (CIU) is defined as widespread, short-lived wheals occurring daily or almost daily for at least 6 weeks, with no obvious cause. Approximately, 30-40% of patients with CIU have histamine-releasing autoantibodies directed against either high-affinity immunoglobulin E (IgE) receptor or less frequently IgE itself and are categorized as having chronic autoimmune urticaria. The presence of autoantibodies may be important clinically in severely affected, treatment-resistant patients where immunomodulatory drugs may be helpful.² The autologous serum skin test (ASST) is a simple *in vivo* screening test for detecting patients with autoimmunity, which has a sensitivity of 70% and specificity of 80%.³ A positive test is suggestive but not diagnostic of an autoimmune basis. Confirmation is needed by

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testing the patient's serum for anti-FcεRIα or the anti-IgE autoantibodies. Basophil histamine release assay is the gold standard for detecting functional autoantibodies.⁴ However, it is available only in a few research centers and cannot be used routinely. CIU can be extremely disabling in its severe form and can be difficult to treat with conventional antihistaminic and need immunomodulators. Autologous serum therapy (AST), a modified form of autologous whole blood therapy, has been found to be fairly effective in chronic urticaria.⁵ We had the opportunity to study the various clinical parameters in patients with chronic autoimmune urticaria, the role of ASST in these patients, and the efficacy of AST in the management of these patients.

Aims

To study the clinico-epidemiologic features in a patient with positive or negative ASST and to evaluate the efficacy of AST in patients with chronic autoimmune urticaria.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of Dermatology, Madras Medical College. Informed consent and Institutional Ethics Committee approval were obtained. 200 consecutive patients of CIU (defined by having at least 2 episodes per week for more than 6 weeks) who attended our dermatology outpatient department were selected for the study. Other causes of urticaria were excluded by history and clinical examination. Pregnant and lactating mothers, children less than 12 years, patients who had taken antihistaminic within the past 3 days to 1 week, and who have taken steroids within 30 days to 3 months were excluded from the study. Severity of the disease based on history was graded with various scores such as a number of wheal, pruritus, frequency of wheal, duration of wheal, size of wheal, and score for antihistamine use. Total severity score (TSS) was calculated by adding the various scores, and patients' disease severity was graded according to TSS (Table 1).

AST was given to ASST positive patients who were willing for weekly injections and regular follow-up. AST was given for 9 consecutive weeks and was asked to follow up after 3 months. Repeat scoring and TSS were calculated at the follow-up.

Table 1: TSS

TSS score	Grade
0	Clear
1-6	Mild
7-12	Moderate
13-18	Severe

TSS: Total severity score

RESULTS

Of the total 200 patients, 85 (42.5%) were males and 115 (57.5%) were females. 153 (76.5%) patients were ASST negative and 47 (23.5%) patients were ASST positive. There was no statistically significant difference seen in sex distribution ($P = 0.504$), age distribution ($P = 0.535$), duration of disease ($P = 0.142$), association with atopy ($P = 0.852$), number of wheals score ($P = 0.926$), and wheal size score ($P = 0.057$) among ASST positive and ASST negative patients. Statistically significant difference was seen in angioedema ($P = 0.002$), frequency score ($P < 0.001$), pruritus score ($P = 0.022$), average hold time (AHT) use ($P < 0.001$), duration of wheals ($P = 0.0015$), and mean TSS ($P < 0.001$) among the two groups. Out of the 47 ASST positive patients, only 44 patients completed 9 weeks of AST. 1 patient denied treatment and 2 patients dropped out. Out of 44 patients who completed AST, 9 had complete clearance, 31 had mild symptoms, and 4 had moderate symptoms based on TSS at the end of treatment. 7 out of 9 patients who had complete clearance, remained clear during follow-up, 1 patient lost to follow-up, and 1 patient relapsed back to have severe symptoms. None of the patients reached their baseline TSS value in the follow-up period (Table 2).

DISCUSSION

In our study with 200 CIU patients, the prevalence of patients with autoimmune urticaria was 23.5%. The prevalence of ASST in patients of chronic urticaria ranges from 25% to 60%. Historically, Grattan *et al.* were the first to use ASST to differentiate chronic autoimmune urticaria from CIU.⁶ Study done by Bajaj *et al.* among 394 patients, ASST positivity was 49.5%.⁵ Godse conducted study on 45 patients and found 26.67% were ASST positive.⁷ Out of 96 patients, 53% were positive in a study by Asero *et al.*⁸ The prevalence of ASST positivity in our study was little lower compared to other studies.

In our study, male to female ratio among ASST positive and negative groups was 0.8:1 and 1:1.42, respectively, which was comparable with the study conducted by Vohra *et al.* where it was 1:1.25 and 1:2.07, respectively.⁹ Mean age in ASST positive and negative groups was 36.77 ± 15 and 35.42 ± 13 years, respectively, which was comparable with the study conducted by Azim *et al.* where it was 34 ± 10 and 30 ± 11 years.¹⁰ Mean duration of disease in our study among ASST positive and negative patients was 4.36 ± 3 and 3.8 ± 3 years, which was comparable with studies conducted by Staubach *et al.*¹¹ Association with atopy was seen in 30-28% patients of ASST positive and negative patients, respectively, which was in concordance with study

Table 2: TSS after 9 weeks of ASST

Time	Number of patients	TSS (Mean)	TSS grade in number of patients			
			Clear	Mild	Moderate	Severe
Baseline	44	13.68	0	1	18	25
End of treatment	44	3.68	9	31	4	0
Follow-up	41	3.98	7	25	8	1

TSS: Total severity score, ASST: Autologous serum skin test

conducted by Bajaj *et al.*,⁵ where it was 46.7% and 38.5%, respectively, and with study conducted by De Swerd *et al.* where it was 32-31%, respectively.¹² No statistical difference was seen in the above parameters in our study and also in other studies.

In our study, 59.57-33.98% of ASST positive and negative patients had angioedema, where the difference was statistically significant. In studies conducted by Vohra *et al.* and Azim *et al.*, it was 59% and 52% and 46.7% and 40%, respectively, where the difference was not significant.^{9,10} In our study, the frequency score of 3 among ASST positive and negative patients was 68% and 21.56%, respectively, which was statistically significant ($P < 0.001$) and was comparable to another study conducted by George *et al.* ($P = 0.038$).¹³ There was no statistically significant difference seen in number of wheals score among ASST positive and negative patients, which was comparable to studies conducted by Bajaj *et al.* and Sabroe *et al.*^{5,14} Significant difference was seen in the mean values for pruritus score, 2.3 ± 0.6 and 1.98 ± 0.7 and AHT use score, 2.59 ± 0.6 and 1.42 ± 0.8 among ASST positive and negative patients, which was in concordance with the study conducted by Staubach *et al.* and Sabroe *et al.*^{11,14} Statistically insignificant results between ASST positive and negative groups was seen for wheal size score ($P = 0.0623$), which was similar to studies conducted by Bajaj *et al.* and Staubach *et al.*^{5,11}

The majority of ASST positive patients had severe TSS score, while the majority of ASST negative patients had moderate TSS score in our study, which was significant. Study by Bajaj *et al.* with similar scoring system showed no significant difference in mean TSS between two groups.⁵

Mean baseline TSS value of 44 ASST completed patients was 13.68, and at the end of treatment, it was 3.68 in our study. This was a significant reduction in mean TSS. Although there was an increase in actual TSS during follow-up in some patients, it did not reach baseline values. Only a few studies with AST on chronic urticaria patients are available. Staubach *et al.* used autologous whole blood for therapy.¹¹ Bajaj *et al.* used AST and found that ASST positive patients had a dramatic decline in severity score and lower TSS score compared to ASST negative patients.⁵ Since only limited studies are conducted on chronic urticaria patients

using AST, large-scale placebo-controlled randomized studies with longer follow-up period are needed to know the efficacy.

CONCLUSION

Prevalence of autoimmune urticaria among patients with chronic urticaria was 23.5%. ASST is a simple, cost-effective, easy to perform screening test which can be done as an outpatient procedure to identify autoimmune etiology, in patients previously categorized as having CIU. AST is a cheap, cost-effective, and potentially curative modality of treatment with no side effects in patients with chronic autoimmune urticaria. Especially, in those patients with severe intensity who often require steroids and immunomodulators which are well known for their adverse effects on long-term use, AST emerges to be a better therapeutic option.

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