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Original Research Article

A study of autologous serum therapy in patients of chronic urticaria at a tertiary care center in western India

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ABSTRACT

Background: Chronic urticaria (CU) is a common and troublesome dermatosis for patients. Approximately 30-50% of patients with CU have an autoimmune basis for their condition, as shown by a positive skin test for ASST, this subgroup is known as Autoreactive chronic urticaria. autologous serum therapy (AST) is considered a potential curative for this auto-reactive subgroup. Our study aimed to find out the efficacy of AST in both ASST positive and ASST negative CU patients.
Methods: A cohort of 100 patients of CU were prospectively analyzed for incidence of ASST (+) patients out of total and efficacy of autologous serum injections for sequential 6 weeks in both ASST (+) and ASST (-) CU patients. The response of AST was recorded by the urticaria total severity scale (TSS) every week for 6 weeks and at 18 weeks.
Results: The mean baseline TSS in the ASST (+) group was 12.14±1.66 and in the ASST (-) group was 11.77±1.45 (p-value- 0.5). The mean TSS at 18 weeks in the ASST (+) group was 1.30±1.51 and in the ASST (-) group was 2.17±2.02 (p-value-0.151). At 18 weeks of treatment, complete clearance was present in 44.6% of the ASST (+) group and 31.4% in the ASST (-) group (p value-0.151).
Conclusions: AST can be considered as a first line of treatment, in patients of CU irrespective of the results of ASST, which is cost-effective and has long-lasting effects.

Keywords: Autologous serum skin test, Autologous serum therapy, Autoreactive chronic urticaria, Chronic urticaria, Total severity score

INTRODUCTION

Chronic urticaria (CU) is a common and troublesome dermatosis to patients as well as to the dermatologist characterized by the appearance of evanescent wheals that occur almost daily and continuously for six or more weeks. Incidence of chronic urticaria is 0.1%.[1,2] Approximately 30-50% of patients with chronic urticaria have histamine-releasing autoantibodies to the high-affinity IgE receptors Fc€RIα on basophils or mast cells and 9% have autoantibodies to the IgE. Among patients with chronic urticaria, there is a subgroup known as autoreactive chronic urticaria, in this subgroup, immediate hypersensitivity type skin reaction occurs on intracutaneous injection of autologous serum skin test (ASST).[3,4] This group is known as ASST positive. Urticarial symptoms in ASST positive chronic urticaria patients are caused by serum histamine-releasing factors, autologous serum is thought to be a potentially curative therapy for this auto-reactive subgroup.[5] In autoreactive chronic urticaria patients, autologous serum therapy (AST) results in desensitization or tolerization of the circulatory inflammatory signals.[6] Chronic urticaria patients have a high antihistaminic pill burden due to

irritable symptoms, but the disease course is unpredictable. Second-line therapy for chronic urticaria is immunosuppressants, which require follow-up and laboratory monitoring for the side effects. Biologicals are the specific treatment, but it comes at a high cost. All, the above-mentioned treatment options will finally lead to a financial burden for the patient and health care system. So, in low-middle income countries (LMIC), like India, there is a need for alternative therapy, which has lesser side effects, economical, and leads to longer remission periods. We conducted this trial in chronic urticaria patients to know the proportion of ASST positive patients and to find out the efficacy of autologous serum therapy in both ASST positive and negative patients.

METHODS

Study area

This is a prospective, open-label, interventional study, carried out in the Department of Dermatology, Venereology and Leprosy, Shri M.P. Shah Government Medical College at Jamnagar, Gujarat.

Study period

The study period was from July 2018 to June 2019, total duration of 12 months.

Inclusion criteria

Inclusion criteria were the almost daily appearance of wheals for ≥6 weeks, age between 16 to 60 years, and willingness for weekly follow-up and injections.

Exclusion criteria

Exclusion criteria were patients with a history of physical urticaria, systemic steroids, or immunosuppressive drugs use in the past 6 weeks, cholinergic urticaria, known type 1 hypersensitivity reactions, hereditary angioedema or known C1 esterase deficiency, urticaria associated with conditions like neoplasm, connective tissue diseases or any acute or chronic infection and pregnant females and lactating mothers.

A total of 200 patients with CU were screened. Baseline demographic details were recorded and a detailed history of disease including the history of atopic disorders and thyroid disorders was taken. All patients were subjected to cutaneous examinations. After screening for inclusion and exclusion criteria 100 patients were recruited for the study. Written informed consent was taken in all patients included in the study. Antihistaminic were withdrawn before 48 hours of ASST.

Autologous serum skin test

Serum was separated by centrifuging the patient ′ blood at 2000 rpm (centrifuge machine REMI C854/8) for 10 min and 0.1 ml of autologous serum was injected immediately intradermally in the patient's left flexor forearm two inches below the antecubital crease and 0.1 ml of normal saline was injected into the right forearm (control) using 31G sterile disposable insulin syringe. 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.

Autologous serum skin therapy

ASST was performed in all patients and AST (2ml autologous serum deep i.m in gluteal region once weekly for 6 consecutive weeks) was given to them in both ASST positive and ASST negative groups. Patients were advised to follow up every week after 6 weeks of autologous serum therapy for the next 12 weeks and a tablet of levocetirizine (5 mg) was given to patients in both groups on a demand basis (experiencing itching or rash) but not more than a single tablet. Urticaria total severity score (TSS) was used for severity grading. TSS was recorded at baseline and then every week for 6 weeks of autologous serum therapy and at 18th week.

Table 1: Urticaria total sevetity score.

Parameter	Score 0	Score 1	Score 2	Score 3
Number of wheals	None	<or=10	11-50	>50
Sizes of wheals	None	<1 cm	1-3 cm	>3 cm
Intensity of pruritus	None	Mild	Moderate	Severe
Duration of wheals	None	<1 hr	1-12 hr	>12 hr
Frequency of appearance	None	≤once a week	2-3 times a week	Daily or almost daily
Frequency of antihistaminic use	None	≤once a week	2-3 times a week	Daily or almost daily

Disease assessment

Urticaria total severity score used six separate parameters of disease activity. Individual parameters were recorded between 0-3 scores (table 1) at baseline (0 weeks), end of treatment (6 weeks) and follow-up (18 weeks). The response was graded based on urticaria TSS. If TSS >12 it was considered poor response, 9-12 TSS as fair response, 5-8 TSS as good response, 1-4 TSS as excellent response, and 0 TSS as complete clearance. To account

for the powerful placebo effect of weekly injections, we attached less importance to the response immediately after the 6-week treatment period. A period (12 weeks) longer than the treatment duration was allowed to elapse before the follow-up assessment was done to ascertain actual long-lasting improvement/remission. The primary outcome measured was the fall in total severity scores at the 18-week follow-up visit.

Statistical analysis

Data was analyzed using SPSS version 29.0. Mean, Median, and standard deviations were calculated for continuous variables and means were compared using t-test, and paired t-test, for normally distributed data. Nonparametric data was compared by the $\chi 2$ test and parametric comparisons were done by a two-tailed ′ t ′ test. $P<0.05$ was fixed as the limit for the significance of differences.

RESULTS

Based on inclusion and exclusion criteria, 100 patients were enrolled in the study out of which 65 (65%) were ASST (+) and 35 (35%) were ASST (-).

Table 2: Demographic characteristics and analysis of risk factors in CU patients.

S. no.	Risk factor	ASST	
		Positive (%)	Negative (%)
1	Gender		
	Female	43 (66.15)	14 (40)
	Male	22 (33.85)	21 (60)
2	Age (years)		
	16-30	30 (46.15)	15 (42.86)
	31-45	27 (41.54)	12 (34.28)
	46-60	8 (12.31)	8 (22.85)
3	Occupation		
	Student	10 (15.39)	3 (8.6)
	Service	11 (16.92)	5 (14.28)
	Homemaker	29 (44.62)	12 (34.28)
	worker	13 (20.1)	14 (40)
	Miscellaneous	2 (3.1)	1 (2.8)
4	Atopy	26 (40)	11 (32)
5	Angoedema	3 (4.62)	0
6	Family history	2 (3.07)	1 (2.86)
7	Abnormal thyroid function test	3 (4.62)	0

Out of 100 total patients, 43 were males and 57 females with the median age of the ASST (+) group being 31.5 years (25,38.50); in the ASST (−) group, the median age was 35 years (26,50). The median duration of urticaria in the ASST (+) group was 5.5 months (3,12) and in ASST (-) was 6 months (3,12) ($p<0.01$). A positive personal history of atopy in the form of allergic rhinitis, wheezing, or allergic conjunctivitis was present in 26 (40%) ASST (+) and 11 (32%) ASST (-) patients (p value-0.2). In the ASST (+) group, 2 patients had hypothyroidism, 1 had hyperthyroidism, none had hypo or hyperthyroidism in ASST (-) group. The mean baseline TSS in the ASST (+) group was 12.14±1.66 and in the ASST (-) group was 11.77±1.45 (p=0.5). The Mean TSS at 18 weeks in the ASST (+) group was 1.30±1.51 and in the ASST (-) group was 2.17±2.02 (p=0.151).

Patients in both groups showed a downward trend in TSS from baseline to the end of treatment (6 weeks) and this fall was statistically significant in both ASST (+) group (mean 12.14±1.66 vs 2.18±2.44, p value-0.003) and ASST (-) group (mean 11.77±1.45 vs 4.14±3.55, p value 0.008). This trend continued after the cessation of weekly autologous serum injections with both groups showing statistically significant falls in mean TSS from week 6 until final follow-up at 18 weeks.

As the TSS at baseline was different in both groups, to nullify this, percentage reductions were calculated across groups. Over the next 6 weeks, TSS continued to show further downward trends, and the final reduction in ASST+ and ASST– groups was 17.58% and 35.17% respectively (p=0.005). TSS declined from 100% baseline in both groups to 10.32% and 19.37% in ASST (+) and ASST (-) groups respectively at the end of the study after the 18th week of AST (p value 0.15).

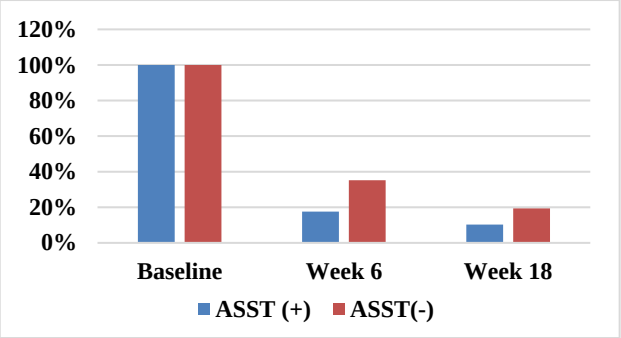

Figure 1: Percentage fall in the TSS in ASST (+) and ASST (-) at 6 and 18 weeks.

At 6 weeks of treatment, complete clearance was present in 35.4% of the ASST (+) group and 22.8% of the ASST (-) group, and the excellent response was present in 48.7% with ASST (+) group, and 31.4% with ASST (-) group, good response was present in 13.8% with ASST (+) group and 28.6% with ASST (-) group, fair response was present in 3.1% with ASST (+) group and 17.2% with ASST (-) group, none had a poor response in both the groups. Response to treatment was statistically significant in both groups (p value- 0.005). At 18 weeks of treatment, complete clearance was present in 44.6% of the ASST (+) group 31.4% of the ASST (-) group, and excellent response was present in 50.8% with the ASST (+) group, and 57.1% with ASST (-) group, good

response was present in 4.6% with ASST (+) group and 11.5% with ASST (-) group, none had fair and poor response in both groups. Though there was a trend towards a more favorable response in the ASST (+) group, it wasn't statistically significant (p value 0.151).

Table 3: Mean TSS and TSS fall from baseline in ASST (+) and ASST (-) groups.

Week	Mean TSS ASST+ (%)	Mean fall from baseline (ASST+) (%)	Mean TSS ASST- (%)	Mean fall from baseline (ASST-) (%)
Baseline	12.4 (100)	-	11.77 (100)	-
1st	10.8 (87)	13	11.34 (96.34)	3.66
2nd	9.10 (73.38)	26.62	9.94 (84.45)	15.55
3rd	7.38 (59.52)	40.48	8.5 (72.22)	27.78
4th	6.5 (52.41)	47.59	5.4 (45.87)	54.13
5th	3.92 (31.4)	68.6	5.4 (45.87)	54.13
6th	2.18 (17.58)	82.42	4.14 (35.17)	64.83
18th	1.28 (10.32)	89.68	2.28 (19.37)	80.63

Table 4: Response to AST at 6 and 18 weeks of treatment.

		ASST		P value
		Positive (%)	**Negative (%)**	
6 weeks	Complete clearance	23 (35.4)	8 (22.8)	0.005
	Excellent	31 (47.7)	11 (31.4)	
	Good	9 (13.8)	10 (28.6)	
	Fair	2 (3.1)	6 (17.2)	
	Poor	0	0	
18 weeks	Complete clearance	29 (44.6)	11 (31.4)	0.151
	Excellent	33 (50.8)	20 (57.1)	
	Good	3 (4.6)	4 (11.5)	
	Fair	0	0	
	Poor	0	0	

DISCUSSION

The goal of AST is to treat the disease until it is gone, so our treatment should follow the basic principles of treating as much as needed and as little as possible. Autologous serum therapy proved blissful for CU patients as AST is a very good adjuvant therapy with antihistaminic to reduce the pill burden and increase the duration of symptom symptom-free period. It improves the quality of life of patients and has no adverse effect. The present study aimed to evaluate the prevalence of autoimmune chronic urticaria among chronic urticaria patients and the efficacy of autologous serum therapy (AST) with shorter duration of treatment for 6 weeks in chronic urticaria and to look for lasting effects till 18 weeks. In our study, AST was effective in both the ASST (+) and ASST (-) groups, similar observations were made in a study done by Bajaj et al. The ASST positive patients (65%) in our study were higher than that observed by Bajaj et al (49.5%) and by Godse et al (26.7%).[5,7]

In our study, improvement started within 1 week of AST in the ASST (+) group in comparison to the ASST (-) group, which was statistically significant (p value 0.005). While in a previous study by Debbarman et al and Nageswaramma et al reported that symptoms of urticaria showed improvement by 4th week of initiation of AST in both groups.[8,9] Within the ASST (+) and ASST (-) groups, there was a downward trend in TSS from baseline to the end of treatment (6 weeks) and this fall was statistically significant in both the ASST (+) group and ASST (-) group. In our study at 6 weeks of treatment, response to treatment was more favorable in ASST (+) group as compared to ASST (-) group, which was statistically significant. But at 18 weeks of treatment, though there was a trend towards a more favorable response in ASST (+) group, it was not statistically significant. It suggests that ASST (-) patients also had a late favorable response to AST.

Mean percentage reductions in TSS clearly show that there was a faster and more dramatic decline in severity in the ASST (+) group during the treatment phase. This trend continued for the next 12 weeks and ASST (+) scores were still lower than the ASST (−) scores at the final 18-week follow-up. In comparison, Staubach et al, reported a significant reduction only in ASST (+) patients (41%) while ASST (−) patients showed only a 21% fall in severity scores, which was not different from the placebo group. Complete clearance has been seen in 44.6% of

ASST (+) and surprisingly, 31.4% of ASST (-) patients also had complete clearance at 18 weeks.

A study conducted by Nageswaramma et al reported 37.9% of ASST (+) and 23.8% of ASST (-) patients showed complete clearance by the 21st week.[9] Staubach et al performed a follow-up evaluation 4 weeks after the last (8th) injection using autologous whole blood in their study. We specifically chose three times longer follow-up duration than Staubach and co-workers did to accurately assess the longevity of the suppressive effect of this form of treatment. AST was well-tolerated and none of the patients reported any side effects, also there was no bruising at injection sites though it was reported in previous studies.[5]

The limitation of this study was its uncontrolled and unblinded nature. We could have chosen a placebo arm in this study. A larger placebo-controlled study with unselected CU patients is warranted to assess the utility of this therapy in our patients.

CONCLUSION

In conclusion, our experience has shown that AST can be considered as a first line of treatment, in patients with chronic urticaria irrespective of the results of the Autologous serum skin test, which is cost-effective and has long-lasting effects.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bajaj AK, Saraswat A, Upadhyay A, Damisetty R, Dhar S. Autologous serum therapy in chronic urticaria: Old wine in a new bottle. Indian J Dermatol Venereol Leprol. 2008;74:109-13.
2. Krupashankar DS, Shashikala K, Rama Madala. Clinical and investigative assessment of patients with positive versus negative autologous serum skin test: A study of 80 south Indian patients. Indian J Dermatol. 2012;57(6):434-8.
3. Godse KV. Autologous serum skin test in chronic idiopathic urticaria. Indian J Dermatol Venereol Leprol. 2004;70:283-4.
4. Hide M, Francis DM, Grattan CE, Hakimi J, Kochan JP,Greaves MW. Autoantibodies against the high affinity IgE receptor as a cause of histamine release in chronic urticaria. N Engl J Med. 1993;328:1599-604.
5. Staubach P, Onnen K, Vonend A, Metz M, Siebenhaar F, Tschentscher I, et al. Autologous whole blood injections to patients with chronic urticaria and a positive autologous serum skin test: A placebo-controlled trial. Dermatology. 2006;212:150-9.
6. Asero R, Ferrer M, Kocaturk E, Maurer M. Chronic spontaneous urticaria: The role and relevance of autoreactivity, autoimmunity, and autoallergy. J Allergy Clin Immunol Pract. 2023;11(8):2302-8.
7. Godse KV. Autologous serum skin test in chronic idiopathic urticaria. Indian J Dermatol Venereol Leprol. 2004;70:283-4.
8. Debbarman P, Sil A, Datta PK, Bandhyopadhyay D, Das NK, Autologus serum therapy in chronic urticaria: A promising complements to antihistaminics. Indian J Dermatol. 2014;59:375-82.
9. Nageswaramma S, Sarojini VL, Pujitha BB, Shirisha G, Bindu GS. Efficacy of Autologus serum therapy in chronic urticaria. ICV. 2015;77:83.

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