ORIGINAL RESEARCH

To evaluate the efficacy of Autologous Serum Therapy in patients with Chronic Urticaria

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ABSTRACT

Aim: To evaluate the efficacy of Autologous Serum Therapy in patients with Chronic Urticaria.**Material and methods:** The inclusion criteria consisted of individuals aged over 18 years, witha duration of chronic urticaria exceeding 6 weeks, absence of any medical conditions, willingness to participate in weekly follow-up, and no use of steroids for a minimum of two weeks. A total of 140 patients underwent assessment, and 100 of them were enrolled in our research after obtaining informed written permission. Each patient was then issued a unique identifier, known as a PIN. ASST was performed on all 100 patients according to the followingdescription. **Results:** ASST was positive in 42 patients (42%). Mean of MUTSS for ASST positive group and ASST negative group was 14.21±3.26 and 13.04±3.65 respectively. This difference is statistically significant (p=0.03). The mean of MUTSS post-treatment in ASST positive group as 4.11±1.34, whereas in negative group it was 6.76±1.31. This difference was statistically significant (p=0.013). Also mean difference in pre and post treatment MUTSS was significantlyhigher in ASST positive group as compared to ASST negative group (p=0.001) indicating higher response of therapy in ASST positive group. **Conclusion:** Out of the whole group of patients with chronic urticaria, 42% were classified ashaving the autoimmune type. Among these individuals, around half saw a positive response toautologous serum treatment. The average value of MUTSS for the ASST positive group was 14.21±3.26, whereas for the ASST negative group it was 13.04±3.65. This difference is statistically significant, with a p-value of 0.03. The mean MUTSS post-treatment in the ASST positive group was 4.11±1.34, whereas in the negative group it was 6.76±1.31. This difference was statistically significant (p=0.013).

Keywords: Autologous Serum Therapy, Chronic Urticaria, MUTSS

INTRODUCTION

Chronic urticaria (CU) is a frequently seen and bothersome skin condition for both patients and physicians. The condition is characterized by the spontaneous occurrence of short-lived and pruritic cutaneous responses in the form of wheals and flares, lasting for more than 6 weeks. Chronic urticaria (CU) is attributed to autoimmune processes in about 30-50% of individuals, known as chronic autoimmune urticaria (CAU). Patients with autoreactive CU have an acute hypersensitive skin response to their own serum. Hide et al. discovered that in a certain groupof individuals with chronic urticaria (CU), auto-antibodies targeting the high-affinity IgE receptor, FcεRIα, are responsible for triggering the release of histamine.[1] The simplest screening method to identify this group of patients having what was termed as chronic autoimmune urticaria (CAU) is autologous serum skin test (ASST).[2] Intradermal injection of autologous serum in these patients elicit an immediate-type wheal and flare response indicating the presence of a circulating histamine-releasing factor (ASST positive). Repeated injection of autologous whole blood or autologous serum, a form of therapy also known as autohaemotherapy, can be very effective in CAU patients. Autohaemotherapy has been used in Indian medicine over the years in a variety of diseases including allergy, chronic inflammation, immunodeficiency vascular diseases, osteoarthritis, atopic dermatitis and various other skin disorders.[3] Multicentric prospective open label trial of autologous serum therapy (AST) has been shown to be useful in

Indian patients.[4] A prospective experiment was conducted at a tertiary care center after obtaining informed written permission from patients with CAU. These patients received treatment with a weekly intramuscular injection of their own serum in the gluteus muscle, with a dosage of 0.05 ml/kg. The duration of the treatment spanned 9 weeks.The sterile injection procedure was adhered to, and appropriate labeling was used. The effectiveness of this treatment was assessed based on many characteristics. The purpose of this research was to evaluate the efficacy of Autologous Serum Therapy in patients with Chronic Urticaria.

MATERIAL AND METHODS

A cross-sectional research was done to analyze and enroll all patients with chronic urticaria who were visiting the dermatology OPD, based on specific inclusion criteria. The inclusion criteria consisted of individuals aged over 18 years, with a duration of chronic urticaria exceeding 6 weeks, absence of any medical conditions, willingness to participate in weekly follow-up, and no use of steroids for a minimum of two weeks. The exclusion criteria included pregnancy, breastfeeding, patients with bleeding disorders, hepatitis B infection, and those with a history of immunosuppressant medication use or alcohol addiction.

A comprehensive history and examination were conducted for all patients and documented in a predetermined proforma. Obtained informed consent from all patients. A total of 140 patients underwent assessment, and 100 of them were enrolled in our research after obtaining informed written permission. Each patient was then issued a unique identifier, known as a patient identification number (PIN). ASST was performed on all 100 patients according to the following description.

METHODOLOGY

Two ml of venous blood sample was taken with sterile five ml syringe and then transferred toautoclaved vial and placed into hot water bath for 30 min. Serum was then separated by centrifuging for three minutes. 0.05 ml of serum was injected immediately intradermally in patient's left flexor forearm two inches below anticubital crease and 0.05 ml of normal saline was injected into the right forearm (control) using 31G sterile disposable BD insulin syringe. Reading of wheal was taken at 30 min. After ASST, autologous serum therapy (AST) was administered using autologous serum in a dose of 0.05 ml per kg body weight, injected IM in gluteus muscle weekly for nine weeks to all patients irrespective of test result positive or negative.

Table 1: Criteria for ASST

Diameter of wheal	Interpretation
>1.5 mm of control perpendicular diameter	Positive ASST
≤ 1.5 mm of control perpendicular diameter	Negative ASST

DISEASE ASSESSMENT

Parameters of disease activity and severity were recorded at baseline and every week during treatment. Parameters assessed were number of wheal per day/week, intensity of pruritus, frequency of appearance and frequency of antihistamine use. End point of study was improvement in chronic modified urticaria total severity score (MUTSS) after ninth dose of AST. Modified urticaria total severity score (MUTSS) was recorded at baseline and at 10th week. Also, degree of improvement was graded as poor, moderate, good and complete depending upon MUTSS.

Table 2: Modified urticaria total severity score.

Parameter	Score			
	0	**1**	**2**	**3**
Number of wheals	None	≤10	11-50	≥50
Intensity of pruritus	None	Mild	Moderate	Severe
Duration of persistence	None	<1 hr	1-12 hr	>12 hr
Frequency of appearance	None	<once a week	2-3 week a time	Daily/almost daily
Frequency of antihistamine use Levocetirizine 5 mg	None	<one tab. In a week	2-3 tab. In a week	Daily/almost taken daily tab

STATISTICAL ANALYSIS

The data was inputted into MS Office Excel 2007 and analyzed using SPSS version 22.0. Mean, median, and standard deviations were computed for continuous variables. Means were compared using t-tests and paired t-tests for normally distributed data. The Mann Whitney-U test was used for data that had anomalous distribution. Prior to enrolling participants in the study, the procedure and significance of the research were clearly communicated, and individuals were required to provide informed written permission.

Table 3: Scoring system

Mild	**0-5**
Moderate	5-10
Severe	10-15
Very severe	≥15

Table 4: MUTSS analysis system.

Poor	**<25%**
Moderate	25-50 %
Good	>50%
Complete	Complete cessation

RESULTS

Based on inclusion and exclusion criteria, 100 patients were enrolled in the study out of which40 were males and 60 female (Table 5), aged between 18 yrs to 67 yrs, with mean age of 36.36±2.65 years.

Table 5: Gender of patients

Gender	Number	Percentage
Males	40	40
Females	60	60
Mean age	36.36±2.65	

The overall duration of disease was from three months to 18 years, with mean duration being 40.57±6.58 months. As shown in (Table 6), ASST was positive in 42 patients (42%).

Table 6: ASST in OPD patients and Median duration of urticaria in these patients.

ASST status	ASST positive		ASST negative		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
	42	42	58	58	100	100
Median duration of urticaria (months)	37		19		-	

Table 7: Mean of MUTSS for ASST groups.

Mean of MUTSS	ASST positive	ASST negative	P value
	14.21±3.26	13.04±3.65	0.03

Both ASST positive and negative groups were statistically comparable by age, sex and age of onset of signs and symptoms. Median duration of urticaria was 37 months in ASST positive while it was 19 months in ASST negative patients. Baseline disease attributes in two groups were noted and MUTSS for urticaria was calculated and patients were stratified into four groupsdepending upon the score (ie 0-5/ 6-10/11-15/>15). Mean of MUTSS for ASST positive group and ASST negative group was 14.21±3.26 and 13.04±3.65 respectively. This difference is statistically significant (p=0.03) as shown in (Table 7).

The (Table 8) shows mean of MUTSS post-treatment in ASST positive group as 4.11±1.34, whereas in negative group it was 6.76±1.31. This difference was statistically significant (p=0.013). Also mean difference in pre and post treatment MUTSS was significantly higher in ASST positive group as compared to ASST negative group (p=0.001) indicating higher response of therapy in ASST positive group. Also, the difference of pre and post treatment score in ASST positive was 10.10 while it was 6.28 in ASST negative, which was highly significant (p=0.001).

Table 8: Mean of MUTSS post-treatment in ASST groups.

Mean of MUTSS post treatment	ASST positive	ASST negative	P value
	4.11±1.34	6.76±1.31	0.013

DISCUSSION

Chronic Urticaria has been shown to have a substantial influence on the emotional well-being and symptom experience of patients, affecting their overall quality of life.[5,6] The process of mast cell degranulation is crucial in the development of urticaria. However, the specific causeof degranulation remains unknown in many individuals, leading to the adoption of the term "idiopathic" to describe this condition. A recent study has discovered the involvement of antibodies to the high affinity IgE receptor (FcεRIα), which has been reported to trigger

degranulation of mast cells by binding to and activating the IgE receptor. This condition is referred to as auto reactive urticaria and is seen in 27-61% of individuals with chronic urticaria.[7-10] Thus, the aim of the present study was to evaluate the prevalence of autoimmune chronic urticaria among chronic urticaria patient and efficacy of autologous serum therapy (AST) in chronic urticaria of more than 6 weeks duration. Similar to most previous reports ASST positivity was seen in 42% patients with chronic urticaria which was comparable to that seen in other studies which varied from 25% to 60%.[11-19] Females outnumbered the males in both ASST positive and negative groups 1.5:1 and 1.4:1 respectively. Overall age and sex profile of our patients in both groups was statistically similar and comparable to that reported by most workers.[14-20] The median duration of urticaria in our ASST positive patients was 37 months (ranging from 11 to 61 months) in ASST positive patients and 19 months (ranging from 9 to 40 months) in ASST negative patients. Sabroe et al noted that median duration of urticaria was 10 months and 22 months among ASST positive and negative patients respectively.[11,21] Mamatha et al also noted a median duration of 12 months in ASST positive patients as compared with 15 months in ASST negative patients.[12] Taubi et al demonstrated a positive correlation between the chronicity of urticaria and positive ASST in 5 year follow up study.[15] Although not statistically significant median duration of urticaria was longer in ASST positive patients being 37 months than ASST negative patients being 19 months. Similar observations were made by Vohra et al and Stanbach et al MUTS scoring was done.[22,23]

Patients in ASST positive group had higher mean severity score (14.21±3.26) as compared to ASST negative group (13.04±3.65) which was statistically significant (p=0.03). Our results were in concordance with study by Bajaj et al[4] Sabroe et al.[2] They reported that ASST positive patients had more widespread lesions and significantly more severe disease with systemic symptoms. Similarly higher TUSS was seen in ASST positive patients as compared to ASST negative patients in study by Vohra et al.[22] Toubi et al also demonstrated a trend towards a significant association between the severity of chronic urticaria and ASST positivity.[12] However there are reports that revealed no or only subtle differences in symptomatology of ASST positive and ASST negative patients; slightly longer duration and higher antihistaminc use.[12,16] Differences could be due to variations in clinical parameters assessed and different severity scores used for assessment of disease. We assessed the patients at week 0 which was taken as baseline, then weekly assessment was done till ten weeks. Severity of disease was foundto be more severe in ASST positive patients. Total severity score at week zero was taken as baseline, while at week ten was taken as post treatment score. AST was well tolerated by our patients and none of the patients reported any side effects. Our follow up evaluation was done at 10th week to study the effects of autologous serum therapy.

Overall we noted significant difference between mean severity score pre (14.21±3.26) and post treatment (4.11±1.34). Mean pre treatment score being 14.21 while 4.11 being post treatment score (p=0.001). These were similar to observations made by Bajaj et al and Stanbach et al.[4,23] Thus AST was an effective treatment even in some ASST negative patients. These findings were similar to Bajaj et al (who resume for ASST positive 13.27±2.050 and for ASST negative it was 12.04±3.212 and post treatment score for ASST positive is 3.87±4.57 and for ASST negative 6.46±4.418).[4]

CONCLUSION

Out of the whole group of patients with chronic urticaria, 42% were classified as having the autoimmune type. Among these individuals, around half saw a positive response to autologous serum treatment. The average value of MUTSS for the ASST positive group was 14.21±3.26, whereas for the ASST negative group it was 13.04±3.65. This difference is statistically significant, with a p-value of 0.03. The mean MUTSS post-treatment in the ASST positive group was 4.11±1.34, whereas in the negative group it was 6.76±1.31. This difference was statistically significant (p=0.013). This research revealed that serum treatment is efficacious in individuals with chronic urticaria who test positive for ASST. A lower but significant proportion of patients who tested negative for ASST also saw benefits from this medication.

REFERENCES

1. Godse KV, Nadkarni N, Patil S, Mehta A. Subcutaneous Autologous Serum Therapy in Chronic Spontaneous Urticaria. Indian J Dermatol. 2017;62(5):505-7.
2. Sabroe RA, Grattan CE, Francis DM, Barr RM, Kobza Black A, Greaves MW. The autologousserum skin test: A screening test for autoantibodies in chronic idiopathic urticaria. Br J Dermatol. 1999;140(3):446-52.
3. Datta A, Chandra S, Saha A, Sil A, Das NK. Exploring the safety and effectiveness of subcutaneous autologous serum therapy versus conventional intramuscular autologous serum therapy in chronic urticaria: An observer-blind, randomized, controlled study. Indian J Dermatol Venereol Leprol 2020;86:632-642.
4. 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(2):109-13.
5. Maurer M, Ortonne JP, Zuberbier T. Chronic urticaria: A patient survey on quality of life, treatment usage and doctor-patient relation. Allergy. 2009;64(4):581-8.
6. Yuan Y, Xiao Y, Chen X, Li J, Shen M. A systematic review and meta-analysis of health utility estimates in chronic spontaneous urticaria. Front Med 2020; 7: 543290.

7. Surendran K A K , Nanjundaswamy B L , Sathish S , Bangaru H , Kudari S. Autologous serum therapy in chronic urticaria. Indian J Clin Exp Dermatol 2019;5(4):275-279.
8. Fiebiger E, Maurer D, Holus H, Reininger B, Hartmann G, Woisetschläger M, et al. Serum IgG autoantibodies directed against the alpha chain of Fc epsilon RI: A selective marker and pathogenetic factor for a distinct subset of chronic urticaria patients? J Clin Invest. 1995;96(6):2606-12.
9. Ferrer M, Kinet JP, Kaplan AP. Comparative studies of functional and binding assays for IgG anti Fc epsilon Riα (αsubunit) in chronic urticaria. J Allergy Clin Immunol. 1998;101(5):672-8.
10. Piconi S, Trabattoni D, Iemoli E, Fusi ML, Villa ML, Milazzo F, et al. Immune profile of patients with chronic idiopathic urticaria. Int Arch Allergy Immunol. 2002;128(1):59-66.
11. Sabroe RA, Fiebiger E, Francis DM, Maurer D, Seed PT, Grattan CE, et al. Classification of anti-Fc-RI and anti-IgE autoantibodies in chronic idiopathic urticaria and correlation with disease severity. J Allergy Clin Immunol. 2002;110(3):492-9.
12. Toubi E, Kessel A, Avshovich N, Bamberger E, Sabo E, Nusem D, et al. Clinical and laboratory parameters in predicting chronic urticaria duration: A prospective study of 139 patients. Allergy. 2004;59(8):869-73.
13. O'Donnell BF, Francis DM, Swana GT, Seed PT, Black AK, Greaves MW. Thyroid autoimmunity in chronic urticaria. Br J Dermatol. 2005;153(2):331-5.
14. Bakos N, Hillander M. Comparison of chronic autoimmune urticaria with chronic idiopathic urticaria. Int J Dermatol. 2003;42(8):613-5.
15. Mamatha G, Balachandran C, Smitha P. Chronic idiopathic urticaria: Comparison of clinical features with positive autologous serum skin test. Indian J Dermatol Venereol Leprol. 2008;74(2):105-8.
16. Nettis E, Dambra P, D'Oronzio L, Cavallo E, Loria MP, Fanelli M, et al. Reactivity to autologous serum skin test and clinical features in chronic idiopathic urticaria. Clin Exp Dermatol. 2002;27(1):29-31.
17. Fusari A, Colangelo C, Bonifazi F, Antonicelli L. The autologous serum skin test in the follow-up of patients with chronic urticaria. Allergy. 2005;60(2):256-8.
18. Godse K. Methotrexate in autoimmune urticaria. Indian J Dermatol Venereol Leprol. 2004;70(6):377.
19. Baskan EB, Turker T, Gulten M, Sukran T. Lack of correlation between Helicobacter pylori infection and autologous serum skin test in chronic idiopathic urticaria. Int J Dermatol. 2005;44(12):993-5.
20. Swerdt AD, Keybus CV, Kasran A, Cadot P, Neyens K, Coorevits L, et al. Detection of basophil-activating IgG autoantibodies in chronic idiopathic urticaria by induction of CD63. J Allergy Clin Immunol. 2005; 116(3):662-7.
21. Sabroe RA, Seed PT, Francis DM, Barr RM, Black AK, Greaves MW. Chronic idiopathic urticaria: Comparison of the clinical features of patients with and without anti-Fc-RI or anti-IgE autoantibodies. J Am Acad Dermatol. 1999;40(3):443-50.
22. Vohra S, Sharma NL, Mahajan VK, Shanker V. Clinicoepidemiologic features of chronic urticaria in patients having positive versus negative autologous serum skin test: A study of 100Indian patients. Indian J Dermatol Venereol Leprol. 2011;77(2):156-9.
23. Stanbach 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(2):150-9.