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Original Research Article

Autologous serum therapy in chronic urticaria patients

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ABSTRACT

Background: Chronic urticaria is very common distressing dermatoses. CU is caused by autoimmune mechanisms in approximately 30-50% of patients. Repeated injection of autologous whole blood or autologous serum, a form of therapy also known as autohaemotherapy, can be very effective in CAU patients. Aim was to assess the effectiveness of autologous serum therapy in chronic urticaria patients.
Methods: All patients with CU attending the dermatology OPD of age >18 years, and urticaria of duration >6 weeks. After autologous serum skin test, autologous serum therapy 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 in all patients. Parameters of disease activity and severity were recorded at baseline and every week during treatment. End point of study was improvement in chronic modified urticaria total severity score after ninth dose of AST which was recorded at baseline and at 10th week.
Results: Mean of MUTSS for ASST positive group and ASST negative group was 13.27±2.050 and 12.04±3.212 respectively which is statistically significant (p=0.043). Mean MUTSS post treatment in ASST positive group was 3.87±4.57 whereas in negative group it was 6.46±4.418 which was statistically significant (p=0.019).
Conclusions: 42.3% patients of chronic urticaria were of autoimmune type and approximately half of them responded well to autologous serum therapy. This study found that serum therapy is effective in ASST positive patients with CU.

Keywords: Urticaria, Autologous serum therapy, Autologous serum skin test, MUTSS, Pruritus

INTRODUCTION

Chronic urticaria (CU) is very common distressing dermatoses to the patient as well as to the physician. It is characterized by spontaneously occurring, short lived and itchy, wheal and flare type of skin reactions which is present for >6 weeks. CU is caused by autoimmune mechanisms in approximately 30-50% of patients (chronic autoimmune urticaria (CAU). Autoreactive CU patients show an immediate hypersensitivity type skin reaction to their own serum. Hide et al reported that auto-antibodies against the high-affinity IgE receptor, FcεRIα cause histamine release in a subset of patients with CU.[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 trial was carried out in a tertiary care centre after taking informed written consent of CAU patients to whom therapy was given by weekly intramuscular injection of patients own serum in gluteus muscle {0.05 ml/kg}.Treatment was given for 9 weeks .Sterile injection technique was followed with proper labelling. The efficacy of this therapy was monitored on various parameters. This study was done to assess the effectiveness of Autologous Serum Therapy in Chronic Urticaria patients.

METHODS

Study design and population

Cross-Sectional study conducted on all patients with chronic urticaria attending the dermatology OPD of Hindu Rao Hospital, Malka Ganj, Delhi, were assessed and enrolled as per inclusion criteria. The study was done from September 2015 to August 2016.

Inclusion and exclusion criteria

The inclusion criteria included age>18 yrs, chronic urticaria duration >6wks, subject without any medical illness, consent for weekly follow-up, and patients without steroids for a period of two weeks. Exclusion criteria were pregnancy, lactation, patient with bleeding disorder, hepatitis B infection, and patient with history of drug (immunosuppressant) intake or alcohol abuse. A detailed history and examination was carried out for all patients and recorded in a pre-set proforma. Informed consent was taken from all the patients. In total 110 patients were assessed and 78 were included in our study after taking informed written consent and were assigned a unique number, i.e. patient identification number (PIN). ASST was carried out in all 78 patients as described below.

Autologous serum skin test and therapy

Two ml of venous blood sample was taken with sterile five ml syringe and then transferred to autoclaved vial and placed into hot water bath for 30 min. Serum was then separated by centrifuging (centrifuge machine TANCO-PLT-182) 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 time a week	Daily/almost daily
Frequency of antihistamine use Levocetirizine 5 mg	None	<one tab. In a week	2-3 tab. in a week	Daily/almost daily taken tab

Statistical analysis

Data was entered in MS Office Excel 2007 and was analysed using SPSS version 20.0. Mean, Median and standard deviations were calculated for continuous variables and means were compared using t test, paired t test, for normally distributed data. For abnormally distributed data, Mann Whitney-U test was used. The protocol and importance of the study was explained to the participants before recruitment into the study, followed by their informed written consent.

Table 3: Scoring system.

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

Table 4: MUTSS analysis system.

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

RESULTS

Based on inclusion and exclusion criteria, 78 patients were enrolled in the study out of which 31 were males and 47 female (Table 5), aged between 18 yrs to 65 yrs, with mean age of 35.13±0 .478 years.

Table 5: Distribution of Gender of OPD patients (n=78).

Gender	Males	Females	Total
N (%)	31 (39.74)	47 (60.26)	78 (100)

The overall duration of disease was from three months to 20 years, with mean duration being 39.8±47.11 months. As shown in (Table 6), ASST was positive in 33 patients (42.3%).

Table 6: Result of ASST in OPD patients (n=78) and Median duration of urticaria in these patients.

ASST status	ASST positive	ASST negative	Total
	33 (42.30)	45 (57.69)	78 (100)
Median duration of urticaria (months)	36	18	-

Table 7: Mean of MUTSS for ASST groups.

Mean of MUTSS	ASST positive	ASST negative	P value
	13.27±2.050	12.04±3.212	0.043

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 36 months in ASST positive while it was 18 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 groups depending upon the score (ie 0-5/ 6-10/11-15/>15). Mean of MUTSS for ASST positive group and ASST negative group was 13.27±2.050 and 12.04±3.212 respectively. This difference is statistically significant (p=0.043) as shown in (Table 7). The (Table 8) shows mean of MUTSS post-treatment in ASST positive group as 3.87±4.57, whereas in negative group it was 6.46±4.418. This difference was statistically significant (p=0.019). 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 9.3 while it was 5.8 in ASST negative, which was highly significant (p=0.0015).

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

Mean of MUTSS post treatment	ASST positive	ASST negative	P value
	3.87±4.57	6.46±4.418	0.019

DISCUSSION

Chronic Urticaria has shown to have significant impact on patients quality of life on aspect of emotion functioning, as well as symptoms.[5,6] Mast cell degranulation plays the pivotal role in pathogenesis of urticaria, however reason for degranulation is unclear in large number of patients, thus the term idiopathic is often used for this entity. Recently role of antibody to high affinity IgE receptor (FcεRIα) has been identified and is found to degranulate the mast cell by cross linking the IgE receptor. This entity has been labelled auto reactive urticaria and is found to prevail in 27-61% of chronic urticaria patients.[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 42.3% 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 36 months (ranging from 10.50 to 60 months) in ASST positive patients and 18 months (ranging from 8 to 39 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 36 months than ASST negative patients being 18 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 (13.27±2.05) as compared to ASST negative group (12.04±3.212) which was statistically significant (p=0.043). 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 found to 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 12.65±2.83) and post treatment (5.33±4.61). Mean pre treatment score being 12.65 while 5.33 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] 48.5% of ASST positive (16 out of 33) patients showed complete recovery as compared the result in ASST negative where 17.7% (8 out of 45) showed similar result.

Limitations

Limitations were; due to small sample size and selective age-group patients, its results cannot be generalised. It's effectivity in acute urticaria conditions could not be assessed. The patients were followed up only for 9 weeks, so, long-term effectivity of AST cannot be judged.

CONCLUSION

Total 42.3% patients of chronic urticaria were of autoimmune type and approximately half of them responded very well to autologous serum therapy. Mean of MUTSS for ASST positive group and ASST negative group was 13.27±2.050 and 12.04±3.212 respectively which is statistically significant (p=0.043). Mean MUTSS post treatment in ASST positive group was 3.87±4.57 whereas in negative group it was 6.46±4.418 which was statistically significant (p=0.019). This study found that serum therapy is effective in ASST positive patients with CU. A smaller but still substantial number of ASST negative patients were also benefited from this treatment. The fellow dermatologists can also try and benefit their chronic urticaria patients with AST.

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