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Original Article

Efficacy of autologous serum therapy in patients with chronic autoimmune urticaria: A prospective, open label study conducted in a tertiary care centre, India

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Abstract

Objective To evaluate the efficacy of repeated autologous serum injections in patients with chronic autoimmune urticaria.

Methods Patients of chronic autoimmune urticaria were prospectively analyzed for the efficacy of eight consecutive weekly autologous serum injections with a post-intervention follow-up of 12 weeks. Total urticaria severity score (TSS) was calculated at the baseline, at the end of treatment and lastly at the end of 12 weeks of follow-up. Response to therapy was judged by the percentage reduction in baseline TSS at the end of treatment and again at the end of 12 weeks of follow-up.

Results Out of the 65 patients enrolled, 4 opted out of study after one or the first few doses. Among the rest of the 61 patients, 16.4% patients showed excellent response and 55.7% showed good to fair response to autologous serum therapy. Poor response was seen in 27.9% of the study population. Among the responders, only 15.9% [out of 72] relapsed at the end of 12 weeks of follow-up and at the end of study protocol we had 60.7% of the study population who could be labeled as completely or partially remitted with the treatment regimen.

Conclusion Autologous serum therapy is an effective therapy in patients with chronic autoimmune urticaria. Better response is seen in female patients with short duration of disease.

Key words
Autologous serum therapy, autologous serum skin test, chronic autoimmune urticaria.

Introduction

Chronic urticaria is characterized by appearance of wheals daily or almost daily for more than 6 weeks. The term chronic idiopathic urticaria (CIU) is used for cases where no cause is found even after thorough history taking and relevant investigations and it is considered as one of the most difficult to treat conditions in dermatology.[1]

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Around 30-40% of patients with CIU have histamine releasing autoantibodies directed against either the high affinity IgE receptor, or less commonly the Fc portion of human IgE and they are labeled as having chronic autoimmune urticaria (CAU). These antibodies are involved in the pathogenesis by activating mast cells or basophils leading to histamine release.[2,3] When autologous serum is injected intradermally in these patients, an immediate wheal and flare reaction is observed and this forms the basis for autologous serum skin test (ASST), a simple screening test to identify these patients.[4] Identification of patients with CAU is important as they suffer from severe urticaria in a

widespread distribution and many require systemic steroids and other immunosuppressives along with antihistamines to alleviate the symptoms.[5] Autologous serum therapy (AST) has been tried by many in patients with CAU with variable results, majority showing beneficial effects. Presence of tolerance generating anti-idiotype antibodies to mast cell degranulating antigens that induce remission of the disease forms the basis of AST and this therapy has been tried in various autoimmune diseases.[6]

We conducted a prospective, open label study to know the efficacy of AST in patients with CAU at the end of treatment protocol, as well as, over next 3 months of follow up.

Methods

Patients of either sex presenting to our out patient department with the diagnosis of chronic urticaria from 1st March 2014 to 30th September 2015 were assessed for any underlying cause by proper history taking, clinical examination and relevant investigations. Patients with no identifiable cause were tested for the presence of autoantibodies by ASST. Patients with positive ASST who were ready to undergo weekly AST and regular follow ups were included in the study after taking written consent. Pregnant and pediatric patients, patients on systemic corticosteroids or other immunosuppressives in the past 6 weeks, those with physical urticaria or any systemic disorder were excluded from the study.

Demographic details of study group were recorded and severity of urticaria was calculated on the basis of total urticaria severity score (TSS). TSS is calculated based on six separate parameters as mentioned in **Table 1**.

Patients were given weekly injections of autologous serum intramuscularly for a total of 8 doses.

Autologous serum was prepared by centrifuging 5ml of venous blood of the patient at 2000rpm for 10 minutes. 2ml of autologous serum thus obtained was injected intramuscularly using a 22 gauge disposable syringe. During the treatment period of 8 weeks, patients were asked to take short-acting antihistamines when ever necessary. Patients were asked to avoid any new systemic drug with out notification. During each follow-up visit, patients were asked about any perceivable reduction in severity of urticaria and need for antihistamines and the information was documented in response chart. At the end of 8 weeks TSS was calculated and patients were instructed to come for follow-up every 2 weeks for a period of 3 months. At every follow-up visit, history of any reappearance of lesions and need for antihistamines were noted carefully and TSS was calculated at the end of follow-up period of 3 months.

Table 1 Calculation of total urticaria severity score

Parameter	*Score 0*	*Score 1*	*Score 2*	*Score 3*
Number of wheals	None	≤10	11-50	>50
Size of wheals	None	<1cm	1-3cm	>3cm
Intensity of pruritus	None	mild	moderate	severe
Duration of wheals	None	<1hr	1-12hrs	>12hrs
Frequency of appearance	None	≤ once a week	2-3 times a week	Daily/almost daily
Frequency of antihistamine use	None	≤ once a week	2-3 times a week	Daily/almost daily

Overall treatment response was assessed by comparing baseline TSS and TSS calculated at the end of treatment and last follow up visit. Response was graded as excellent (76-100% reduction), good (51-75% reduction), fair (25-50% reduction) and poor (<25% reduction). Institutional ethical committee clearance was obtained. Statistical analysis was done using SPPS 20.

Results

Out of 65 patients recruited for the study, 4 patients opted out of the treatment protocol after one or the first few doses, therefore only 61 patients who completed the study were included in the final analysis of the results.

Mean age of the patients was 36.91 years with a range of 20-55 years. Majority of the patients were in the 3rd and 4th decades of their life. The mean duration of urticaria in the study population was 4.9 years with a range from 3 months to 10 years.

Forty-four (72.1%) of 61 patients showed some response as evidenced by the reduction in their TSS while on treatment with the weekly injections and these were considered as responders. Out of these 44 responders, 10 patients (16.4% of the study population) were categorized as showing an excellent response, 20 patients (32.8% of the study population) as showing good response and 14 patients (22.9% of the study population) showing a fair response at the end of the treatment regimen. 17 (27.9%) out of 61 patients showed poor response to the treatment with no significant change in their TSS while on treatment and were considered as nonresponders.

Both the responders as well as nonresponders were followed up for the next 3 months for any relapse and any further changes in TSS. While all the nonresponders continued to remain unresponsive during this follow-up period with the regular need for H1 antihistamines, relapse was seen in 7 (15.9%) patients among the responder group within this period. Thus, at the end of 3 month follow-up we had 37 (60.6% of the study population) who could be labeled as completely or partially remitted with the therapeutic regimen.

The mean duration of urticaria in responders and nonresponders was 25.0227 months (2 years) and 59.7500 months (5 years), respectively. This difference in the duration of urticaria was found to be statistically significant (P = 0.0000, paired T test). The mean baseline TSS score among responders and nonresponders was 14.6818 and 15.1875, respectively and difference was insignificant (P=0.40184), **(Table 2)**.

Table 2 Comparison of disease parameters between responders and nonresponders.

Parameter	*Responders*	*Nonresponders*	*P value*
No. of patients	44	17	
Age (mean)	36.18±9.8	38.8±7.4	0.3, NS
Sex (female/male)	29/15	9/8	
Mean duration of urticaria in (months)	25.0227	59.7500	0.0000,S
Mean TSS baseline	14.6818	15.1875	0.40184,NS
Mean TSS 8 weeks	3.8	12.9	<0.001,S

NS: not significant, S: significant, TSS: total urticaria severity score.

Table 3 Comparison of parameters of total severity score in responders.

Parameters	*At baseline (mean)*	*At the end of therapy (mean)*	*P value*
Number of wheals	2.32	0.409	0.0000, S
Size of wheals	2.500	0.250	
Intensity of pruritus	2.59	0.727	
Duration of wheals	2.25	0.318	
Frequency of appearance	2.66	0.636	
Frequency of antihistamine use	2.50	0.455	

S: significant

The mean age recorded in the responder group was 36.18±9.8 years in comparison with 38.8±7.4 years for the nonresponders group (*P* = 0.3) and the difference was not significant. The female to male ratio was 29:15 among responders against 9:8 among nonresponders.

Among the responders there was significant reduction of all parameters of TSS at the end of therapy when compared to baseline TSS **(Table 3)**.

Discussion

The aim of our study was to evaluate the efficacy of AST in CAU of more than 3 months duration. We used autologous serum therapy in place of autohemotherapy as the circulating autoreactive factor is present in the serum, not in the cellular components of blood.

We had 61 patients of CU with positive ASST who completed the study protocol. The treatment protocol was tolerated well without any significant side effects except for mild discomfort at injection site lasting for 24 hours in four patients. The percentage of responders appears to be quite high in our study, when compared to studies done by Majid *et al*.[7] (32% vs. 72.13%) and Bajaj *et al*.[8] (60% vs. 72.13%). The number of patients showing excellent response (75-100% decrease in the baseline TSS) were also high in our study as compared to Majid *et al*.[7] (16.4% vs. 9% of the study population) and it was higher than ours in Bajaj *et al*.[8] (35.5%).

In contrary to study by Majid *et al*.[7], the therapeutic efficacy in responders of our study was maintained in majority, with only 15.9% of the responders showed relapse during follow-up, whereas in the former study, 36.8% of the responders experienced relapse of symptoms.

The duration of urticaria in responders was low when compared to nonresponders (25.0227 months vs. 59.7500 months, *P*=0.0000], whereas in Majid *et al*.[7] study the difference was found to be insignificant. This could be the reason behind the higher percentage of responders in our study, as longer duration of disease in nonresponders could be an indicator of resistant form of disease.

In Debbarman *et al*.[9] study conducted on CAU, patients receiving AST showed significant reduction of TSS from 5th week on wards, while in ours it was little earlier (4th week).

In Majid *et al*.[7] study responders were significantly younger than the nonresponders (28.3±8.9 years vs. 37.5 ±10.7 years, *P*=0.002), but in our study the difference was insignificant (36.18±9.8 vs. 38.8±7.4 years, *P*=0.3) and responders were predominantly females in both the studies (65.0% and 89.47%). The mean baseline TSS and TSS at the end of the study protocol among responders showed significant reduction in all the parameters with marked improvement in size and duration of wheal.

Chronic urticaria has an unpredictable course and patient needs treatment till he goes into

remission. Antihistamines and leukotriene inhibitors targeting two of the many mediators in the pathogenesis of urticaria form the mainstay of therapy. Sometimes immunosuppressive agents, which act through inhibition of degranulation by preventing antibody formation like corticosteroids, methotrexate, cyclosporine, adalimumab etc. are needed for control urticaria symptoms. Though these agents are effective in chronic urticaria, their use is limited by side effects and high cost.[10]

Our study found AST as an effective therapy in patients with chronic autoimmune urticaria. Better response is seen in female patients with short duration of disease. Lack of a parallel arm of controls is the limitation of our study.

Conclusion

Though the concept of AST in chronic urticaria was introduced long ago, there are only a few documented studies in the literature. We consider autologous serum therapy as an effective, economical and safe treatment modality in patients with chronic autoimmune urticaria.

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