Original Research Article

Autologous serum therapy in chronic urticaria

Surendran K A K1,*, Nanjundaswamy B L1, Sathish S1, Bangaru H1, Shruthi Kudari2

1Dept. of Dermatology, Mysore Medical College and Research Institute, Mysore, Karnataka, India
2Dept. of Dermatology, Veerapur Multispeciality Hospital, Haveri, Karnataka, India

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ABSTRACT

Context: Chronic urticaria is one of the most challenging and frustrating therapeutic problem faced by a dermatologist. The simplest screening method to identify chronic autoimmune urticaria was found to be the autologous serum skin test (ASST). Autologous serum therapy (AST) is helpful in chronic urticaria.

Aims: To evaluate the efficacy of autologous serum therapy (AST) in patients with chronic urticaria.

Settings and Design: Prospective study at a tertiary care centre.

Materials and Methods: The study group included 30 adult patients presenting with chronic urticaria. Six separate parameters of disease activity and severity were recorded according to Urticaria Total Severity Score (UTSS) at baseline (0 week) and at the end of treatment (9 weeks). Nine doses of Autologous serum were given intramuscularly at an interval of 1 week. Results were assessed based on the percentage decrease in the UTSS.

Statistical analysis used: Wilcoxon Signed rank test.

Results: Among 30 patients, ASST was positive in 15 patients (50%) and negative in 15 patients (50%). 11 patients (36%) had 31-60% response, 7 patients (23%) had 61-90% response, 4 patients (13%) had 10-30% response and 8 patients (26%) had no response.

Among 15 ASST positive patients, 8 patients (53%) had 31-60% response, 3 (20%) patients had 61-90% whereas among 15 ASST negative patients only 3 (20%) patients had 31-60% response and 4 (26.67%) patients had 61-90%.

Conclusions: AST was found to be effective in the treatment of chronic urticaria. There was statistically significant response both in ASST positive and negative patients.

Key Messages: Autologous serum injection therapy still remains as a cheap, effective and potentially curative therapeutic modality even today in chronic urticaria.

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1. Introduction

Chronic urticaria (CU) is a common and distressing dermatosis characterized by the appearance of evanescent wheals almost daily, continuously for six or more weeks.1 Chronic urticaria may occur at any age but most frequent in the age group of 20-40 years.2 In a number of patients it is associated with various aggravating factors including drugs, food and food additives, infections and infestations, systemic diseases etc. Circulating antibodies against the high affinity IgE receptors and anti FcεRIa antibodies have been detected on mast cells in about 30 to 50% cases of chronic urticaria3 which was termed as chronic autoimmune urticaria.

The simplest screening method to identify chronic autoimmune urticaria (CAU), was found to be the autologous serum skin test (ASST).4 Intradermal injection of autologous serum in these patients elicited an immediate-type wheal and flare response indicating the presence of a circulating histamine-releasing factor. These patients with CAU were reported to have a greater number of wheals with a wider distribution, more severe pruritus and more frequent systemic symptoms.5 In spite of extensive
laboratory investigations, 50% cases of chronic urticaria remain idiopathic. Chronic urticaria (CU) is one of the most challenging and frustrating therapeutic problems faced by a dermatologist. Search for newer effective modalities which can reduce pill burden is a felt need. Recently, few studies reported the efficacy of autologous serum therapy in chronic autoimmune as well as chronic idiopathic urticaria patients.

The present study is undertaken to assess the effectiveness of AST in chronic autoimmune as well as chronic idiopathic urticaria patients.

2. Materials and Methods

The study group included 30 adult patients presenting with chronic urticaria to the Department of Dermatology at Mysore Medical College and Research Institute, Mysore. Informed written consent of the participating patients was taken. Patients above 18 years with itching and wheals occurring daily or near daily (≥3 times/week) for ≥6 weeks were included. Pregnant, lactating women and Patients suffering from immunosuppression due to drug or disease were excluded. Disease assessment was done by using six separate parameters of disease activity and severity were recorded according to Urticaria Total Severity Score (UTSS) at baseline (0 week), end of treatment (9 weeks) and follow up (21-25 weeks). Based on these, a 0-18 total severity score was generated and over-all disease severity classified as clear (TSS=0), mild (TSS 1-6), moderate (TSS 7-12) or severe (TSS 13-18) as shown in the chart below.

Autologous serum skin test performed in all study subjects and Autologous serum therapy was given to study subjects irrespective of ASST positivity, intramuscularly for 9 doses at an interval of 1 week.

After Autologous serum injections the response to treatment was graded as very good, good and nil response respectively as shown below.

2.1. Autologous serum skin test

Serum was separated by centrifuging patient’s blood at 3000 rpm for 10 min and 0.1 ml of autologous serum and normal saline were injected intradermally 5 cm away from each other on the volar aspect of the forearm and results were read after 30 minutes. ASST was considered positive when the wheal size at the test site was 1.5 mm more than the normal saline wheal (control site). Anti-histamines were withdrawn at least 48 hrs. before testing.

2.2. Autologous serum therapy

5 ml of blood was collected in a plain (red top) vacutainer, centrifuged at 3000 rpm for 10 mins, serum was separated and 2 ml of serum was injected deep intramuscularly in the gluteal region. Procedure was repeated once weekly for nine weeks.

Results were assessed based on the percentage decrease in the UTSS.

3. Results

Among 30 patients, females outnumbered males i.e. 18 patients (60%) were females and 12 (40%) were male. Minimum age was 20 years and maximum age was 53 years, mean age was 37 years. Majority of the patients belonged to the age group 20-30 years i.e. 17 patients (56%) belonged to age group 20-30 years.

Minimum duration of urticaria was 1 year and maximum was 7 years. Majority of the patients had duration between 2 to 5 years (19 patients). Mean duration of urticaria was 3.6 years.

Among 30 patients, 21 patients had severe urticaria (UTSS 13-18) and 9 patients had moderate urticaria (UTSS 7-12).

At the end of 9 weekly doses of AST in 30 study patients, 15 patients (50%) showed improvement with UTSS 1-6, 8 patients (27%) with UTSS 7-12; 7 patients (23%) still remained with UTSS score of 13-18.

Five patients had association with thyroid disease and all these 5 were positive for ASST.

Among 30 patients, ASST was positive in 15 patients (50%) and negative in 15 patients (50%).

Among 15 ASST positive patients, 8 patients (53.3%) showed good improvement with reduction in UTS score, 4 patients (26.6%) showing very good response with UTS score reduction from severe to mild grade and 3 patients (20%) showed nil response to AST with persisting UTS score.

Among 15 ASST negative patients, 5 patients (33.3%) showed good improvement with reduction in UTS score, 4 patients (26.6%) showed very good response with UTS score reduction to mild grade from severe and 6 patients (40%) showed nil response to AST with UTS score remaining without any change in them.

Statistical analysis was done by using Wilcoxon Signed rank test which showed significant change in UTSS score before and after AST (p=0.000). There was significant improvement in the UTSS score after AST in both ASST positive (p=0.001) and ASST negative patients (p=0.003).

 Patients who had thyroid association showed varied response. 4 patients (80%) showed good response with reduction in UTSS and 1(20%) remained with nil response.

Among 11 patients who had Urticaria of less than 2 years duration, 8 patients showed response to treatment with reduction in UTSS and 3 patients remained same without any change in UTS score.

In study patients, 17 patients were in the age group of 20-30 years among which 14 patients (82%) showed good response to AST.
Table 1:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Number of wheals</td>
<td>None</td>
</tr>
<tr>
<td>Size of wheals</td>
<td>None</td>
</tr>
<tr>
<td>Intensity of pruritus</td>
<td>None</td>
</tr>
<tr>
<td>Duration of persistence</td>
<td>None</td>
</tr>
<tr>
<td>Frequency of appearance</td>
<td>None</td>
</tr>
<tr>
<td>Frequency of antihistamine use</td>
<td>None</td>
</tr>
</tbody>
</table>

Table 2:

<table>
<thead>
<tr>
<th>Response to AST</th>
<th>UTS score reduction before &amp; after AST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very good</td>
<td>UTSS reduction from severe to mild grade</td>
</tr>
<tr>
<td>Good</td>
<td>UTSS reduction from severe to moderate/mild grade</td>
</tr>
<tr>
<td>Nil</td>
<td>No change in UTS score</td>
</tr>
</tbody>
</table>

4. Discussion

Chronic urticaria is a nuisance disorder of skin with varied etiology. About 30%-50% of patients with chronic idiopathic urticaria have circulating histamine releasing autoantibodies to the high-affinity IgE receptor FcεRI α on basophils and mast cells or, less commonly, antibodies to IgE. The term autoimmune urticaria is increasingly being accepted for this subgroup of patients.

The basophil histamine release assay is currently the “gold standard” for detecting functional autoantibodies in patients with chronic idiopathic urticaria. However, this bioassay is difficult to standardize because it requires fresh basophils from healthy donors and is time consuming. The
autologous serum skin test (ASST) is currently the best in vivo clinical test for detection of in vitro basophil histamine-releasing activity. AST was well-tolerated and none of the patients reported any side effects except local soreness lasting from 12 to 24 h. We did not notice any bruising at injection sites.

Similar to most previous reports in CU patients, almost half of the patients (50%) had a positive ASST which was higher than that observed by Godse from Mumbai (26.67%) and Bajaj from Allahabad (49.5%). In our study there was no significant difference in the severity of urticaria in ASST (+) patients and ASST (-) patients. Bajaj et al reported that significantly higher proportion of ASST (+) patients were classified as severe compared to the ASST (-) group. In 1999, Sabroe et al. reported that ASST (+) patients had more widespread lesions and significantly more severe pruritus and systemic symptoms. However, other reports have revealed no or only subtle differences in the symptomatology of ASST (+) and ASST (-) patients with slightly longer disease duration and higher antihistamine use. However, while UTSS at the 9th week was significantly lower in the ASST (+) group. Our results indicate that almost 53% of ASST (+) patients showed a significant improvement in their signs and symptoms after nine weekly ASTs were given. This is slightly lower than the figure of 70% reported by Staubach et al. and 60% reported by Bajaj et al. However, the two studies are not easily comparable since they used somewhat different methods for analysis. Subgroup analysis of those who received AST revealed significant decline irrespective of their ASST positivity.

ASST positive patients took more time for significant decline from baseline UTSS than ASST negative patients, although the intergroup comparison showed no significant difference at every follow up.

We found significant reductions in UTSS and dramatic decline in severity in the ASST (+) and ASST (-) group during the treatment phase which is comparable with the study conducted by Bajaj et al. However in a study done by Staubach et al. reported 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.

Our study showed that AST was an effective treatment even in ASST (-) patients, although number of patients was lower than that reported by Godse from Mumbai. This is especially important from a management viewpoint since immunosuppressive therapies can also be tried if conventional approaches of management are unsuccessful. As the mechanism of action of AST is an enigma, we can only surmise as to the mechanisms behind the significant improvement in almost half of all ASST (-) patients in our study.

Bradykinin is released when serum is separated and the complement factor C5 gets activated to C5a. Both can cause false positive immediate type reactions. Moreover, there is a poor concordance of ASST positivity with circulating antibodies to IgE or FcεRIα. Reported rates of ASST (+) patients actually having antiFceRIα antibodies vary from 40 to <20%. This means that most of the patients who react to ASST do not have circulating antiFceRIα/IgE antibodies. On the other hand, while initial studies reported <2% antiFceRIα positivity in ASST (-) patients, recent studies have detected these antibodies in as many ASST (-) patients as ASST (+) ones and even in healthy controls. Matters are further complicated by the different methods employed to detect antiFceRIα antibodies with immunoblotting being less sensitive than histamine release assays.

5. Conclusion

To conclude, we have observed that the Autologous serum injection therapy still remains as one of the cheap, effective and potentially curative therapeutic modality even today in chronic urticaria. Although there was a statistically significant improvement in the UTSS score after AST among both ASST positive and negative patients, there was slightly better response in ASST positive group compared to ASST negative group.

6. Source of Funding
None.

7. Conflict of Interest
None.

References

Author biography

Surendran K A K Associate Professor

Nanjundaswamy B L Professor and Head
Sathish S Senior Resident
Bangaru H Associate Professor
Shruthi Kudari Consultant Dermatologist