Diagnostic value of autologous serum skin test in chronic auto immune urticaria

Saleena Beevi A. R.¹, George Kurien²*, Mary Vineetha²

INTRODUCTION

Urticaria is a very common condition which affects up to 20% of the population in their life time.¹ Urticaria can be classified according to both time course of symptoms and the underlying etiology. Chronic urticaria is defined by presence of wheals on most days of the week for a period of 6 weeks or longer.¹,²

Chronic urticaria affects up to 1% of the population. The etiology of chronic hives could be idiopathic or associated with conditions such as hormonal disturbances, auto immune disease, physical triggers and rarely infections. In about 80% cases, no external allergen or contributory process is identified and thus termed chronic idiopathic urticaria (CIU) or chronic spontaneous urticaria (CSU).¹

About 30-50% of patients with CSU have circulating histamine releasing auto antibodies to high affinity IgE receptors on basophils and mast cells and are called auto immune urticaria.³,⁴ The basophil histamine release assay

ABSTRACT

Background: Urticaria affects up to 20% of the population during their life time. Urticaria occurring on almost all days for more than 6 weeks is classified as chronic urticaria. Chronic urticaria is one of the most vexing management problems the dermatologists face. Chronic urticaria cases in which no etiology can be found are labelled chronic idiopathic urticarial (CIU). In most cases of idiopathic urticaria, autoimmunity may be the initiating factor- chronic autoimmune urticaria. Autologous serum skin test (ASST) is a simple and reliable method to detect autoimmune urticaria.

Methods: Among patients with chronic idiopathic urticaria, ASST is done to detect ASST positivity and thereby chronic autoimmune urticaria. Patient’s serum is separated and 0.05 ml injected intradermally on left forearm. Normal saline is injected intradermally at least 5 cm away as control. Wheal and flare at serum site which is 1.5 mm more than that of control is taken as positive. Results were analyzed using Microsoft excel and Epi info7.

Results: 49 patients were studied and 34 (69.4%) showed ASST positivity, which is an indicator of autoimmune urticaria. Moreover, it was seen that ASST positive patients had more episodes of urticaria per week, compared to ASST negative patients.

Conclusions: ASST is a simple and reliable method to detect chronic autoimmune urticaria. ASST positive patients have more episodes of urticaria compared to ASST negative patients.

Keywords: Chronic urticaria, Autoimmune urticaria, Autologous serum skin test
is currently the gold standard for detecting those functional auto antibodies. This bio assay is difficult to perform and is confined to research centres. Autologous serum skin test (ASST) is the simplest test for the detection of those auto antibodies. ASST has a sensitivity of approximately 70% and a specificity of 80%. It may be used as a reasonably predictive clinical test to indicate the presence of functional circulating auto antibodies.  

Chronic urticaria is one of the most vexing management problems that dermatologists face. About 40-50% of patients with CIU demonstrate immediate wheal and flare response to intradermally injected autologous serum. This led to the concept of auto immune urticaria (AIU).

A study was undertaken in a tertiary care centre in central Kerala for a period of 18 months from March 2014 to identify the cases of autoimmune chronic urticaria and the usefulness of ASST in identifying AIU in those ‘idiopathic’ cases.

METHODS

100 patients with a clinical diagnosis of chronic urticaria, attending outpatient department of a tertiary care hospital in central Kerala, for 18 months from March 2014 to August 2015 were taken up for the study.

After a detailed history and clinical examination, routine blood and urine examinations, LFT, RFT, ANA, RA factor, thyroid function tests, anti-thyroglobulin antibody, anti TPO antibody, HBs Ag, anti HCV, HIV were done in all cases to identify the cause for urticaria. H pylori Ig G were done in indicated cases. Those cases in which no cause could be found were considered as idiopathic and ASST done in them.

ASST methodology

Patient should be off anti histamines for 2-3 days and doxepin for 2 weeks prior to test to avoid false negative results.

Preparation of autologous serum

3 ml of blood is drawn into a sterile glass tube and allowed to clot for 30 minutes at room temperature. Serum is separated by centrifugation at 2000 rpm for 10 minutes. The serum is separated and immediately used for ASST.

Procedure and interpretation

0.05 ml of autologous serum is injected intradermally over volar aspect of left forearm. Sterile physiological saline is injected on the same forearm at least 5 cm away as negative control. After 30 minutes, the wheal formed at each injection site is measured at two perpendicular diameters and the average calculated.

Positive ASST is the one with serum induced wheal of diameter ≥1.5 mm more than saline induced wheal at 30 minutes.

Results were analyzed using Microsoft excel and Epi info 7.

RESULTS

Figure 1: Age distribution.

Age of the patients ranged from 6 years to 66 years, mean age being 35.9 years. 66% of patients were females.

Figure 2: Sex distribution.

Food and drugs had no significant influence on the initiation or exacerbation of wheals in chronic urticaria. 27% of patients attributed physical causes for initiation of urticaria. 10% had demographism. 7% had pressure urticaria. 12% showed evidence of infective foci. Caries teeth were present in 5% of cases. Personal H/O atopy was present in 27%.

ASST was done in 49 patients in whom no cause for chronic urticaria could be identified and thus categorized as ‘idiopathic’. Of these, 34 (69.4%) showed ASST positivity and 15 (30.6%) were negative.

Thyroid auto antibodies (anti TPO or anti thyroglobulin or both) were positive in 16 patients. Of these, ASST was positive in 13 cases. But, out of 33 patients who were...
negative for thyroid auto antibodies, 21 showed ASST positivity. Therefore, association between thyroid auto antibody and ASST positivity was found to be statistically not significant (p= 0.21).

**Table 1: Thyroid autoantibody and ASST positivity.**

| Thyroid autoantibody | ASST positive | ASST negative | Total |
|----------------------|---------------|---------------|-------|
| Positive             | 13            | 3             | 16    |
| Thyroid autoantibody |               |               |       |
| Positive             | 81.20%        | 18.80%        |       |
| Negative             | 21            | 12            | 33    |
| Negative             | 63.60%        | 36.40%        |       |
| Total                | 34            | 15            | 49    |

Chi square value 1.574; p value 0.210; not significant.

Out of 24 patients who had angioedema in the idiopathic group, 18 were ASST positive. Among 25 patients without angioedema, 16 had positive ASST. Hence association of ASST with angioedema was not significant (p =0.404).

**Table 2: Angioedema and ASST positivity.**

| Angioedema | ASST positive | ASST negative | Total |
|------------|---------------|---------------|-------|
| present    | 18            | 6             | 24    |
| Absent     | 9             | 36%           | 25    |
| Total      | 34            | 15            | 49    |

Chi square value 0.698; p value 0.404; not significant.

34 patients who were ASST positive had a mean number of 5.97 episodes of urticaria per week in contrast to 4.67 episodes per week for the 15 patients who were ASST negative. This was found to be statistically significant (p <0.001).

**Table 3: No. of episodes/week and ASST positivity t- test.**

| ASST   | Number of patients | Mean number of episodes/week | SD   | SEM  |
|--------|--------------------|------------------------------|------|------|
| Positive | 34                 | 5.97                         | 0.937| 0.161|
| Negative| 15                 | 4.67                         | 0.816| 0.211|

$t$ value 4.660; df 47; p value 0.001, SD= Standard deviation; SEM= Standard error mean; significant.

**DISCUSSION**

Among 100 patients studied, probable etiological agent responsible for chronic urticaria was identified in 51 cases. The remaining 49 cases were grouped as idiopathic and ASST was done for these cases. Out of this 34 cases (69.4%) showed ASST positivity, suggesting an autoimmune aetiology for the urticaria. Vohra et al in their study had 46% cases with ASST positivity demonstrating an autoimmune process initiating urticaria. Bakos et al had 54% and Colgecen et al had 63% positivity of ASST in autoimmune urticaria.

In this study, there was no statistically significant association between thyroid antibodies and ASST positivity. Yadav et al also could not find any association between thyroid antibodies and ASST positivity.

ANA estimation was done in all cases of idiopathic urticaria. All cases gave negative ANA results.

There was also no significant association of ASST positivity with age, duration of illness or mean wheal duration.

The mean number of episodes per week was 5.97 in the ASST positive group while in the negative group, it was 4.67. This difference was found to be statistically significant, p value being <0.001. Krupashankar et al and Sabroe et al had also similar findings.

**CONCLUSION**

ASST is a fairly good indicator of autoimmune aetiology for chronic urticaria.

ASST positive patients have more frequent episodes of urticaria per week compared to ASST negative patients and so may require more aggressive treatment.

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