Original paper

Autologous serum therapy reduces the symptoms and antihistamine burden in patients with chronic urticaria

Jinan Q. Mohammed

Dermatology Unit, Basra Teaching Hospital, Basra, Iraq

Adv Dermatol Allergol 2023; XL (3): 398–401
DOI: https://doi.org/10.5114/ada.2023.129009

Abstract

Introduction: Autologous serum therapy (AST) is considered a potentially curative therapeutic option in the treatment of chronic urticaria, especially in the autoreactive type.

Aim: To determine the ratio of patients with a positive autologous serum skin test (ASST) in chronic urticaria and the efficacy of AST.

Material and methods: A total of 77 (29 male and 48 female) patients with chronic urticaria were enrolled in the study. The autologous serum skin test (ASST) was performed for all patients and the patients were classified into two groups: ASST positive and ASST negative. Intramuscular injection of AST was administered and the total severity score (TSS) of the urticaria was calculated weekly for ten weeks. The TSS was calculated for another ten weeks without AST.

Results: There were 34 patients (11 men and 23 women) in the positive group and 43 (18 men and 25 women) in the negative group. Reduction of symptoms of urticaria begins in the fourth week of the study in both groups. At week 20, 21 (61.7%) patients of the ASST (+) group and 12 (27.2%) patients of the ASST (–) group showed complete clearance. The use of antihistamines decreased from 100% at baseline in both groups to 8.82% and 25.58% in the ASST (+) and ASST (–) groups, respectively, at the end of the study.

Conclusions: AST is a low-cost, cost-effective and potentially curative treatment with no adverse effects in these patients. It can reduce the burden of antihistamines.

Key words: autologous serum skin test, autologous serum therapy, chronic urticaria.

Introduction

Chronic urticaria (CU) is a common skin disorder characterized by a distressing, almost daily appearance of short-lived itchy hives that resolve spontaneously in 24 h. Clinical symptoms continue for 6 or more weeks [1–3]. It affects 0.1% of the population [4]. The course of CU may last for years, affects the quality of life and is associated with an antihistamine pill burden [5]. Autoantibodies to the high affinity receptor for IgE (anti-Fc RI) of mast cells and basophils or IgE (anti-Ig E) present in plasma from some patients with CU are responsible for this phenomenon [6–8]. Different treatment modalities such as the combination of antihistamines, anti-inflammatory immunosuppressants, and antidepressants have been used for chronic urticaria [9–11]. Injection of the patient's own serum intracutaneously results in immediate hypersensitivity skin reaction in some patients with chronic urticaria known as the autologous serum skin test (ASST); this ASST (+) group of patients is considered autoreactive or has chronic autoimmune urticaria. These patients complain of intense itching or severe hives associated with systemic symptoms, and some of them have autoimmune diseases [2]. Because histamine-inducing factors are involved in the induction of urticarial clinical symptoms in patients with ASST positive CU, autologous serum therapy (AST) is considered a promising therapeutic option for this subgroup of CU patients [12]. Desensitization and tolerization to pro-inflammatory signals expressed in plasma is the main mechanism of AST [13]. Since autologous serum contains tolerance-generating anti-idiotype antibodies against antigens responsible for mast cell degranulation, it is considered a promising therapy for chronic urticaria [12]. The basis of AST is the expression of antibodies against the IgE receptor (anti-FcRI) of mast cells or IgE (anti-IgE). One of the main advantages of this therapeutic method is related to its cost-effectiveness. Patients with chronic urticaria often suffer from morbidity due to irritable symptoms and are subjected to a high burden of antihistamine pills. There

Address for correspondence: Jinan Q. Mohammed, Dermatology Unit, Basra Teaching Hospital, Basra, Iraq, e-mail: jinanbubsari@yahoo.com
Received: 24.01.2023, **accepted:** 14.03.2023.

is limited evidence on the benefit of AST in the treatment of chronic urticaria [14–16].

Aim

This study was conducted to describe the efficacy of autologous serum therapy in the treatment of CU, compare the clinical efficacy of autologous serum therapy between reactive and nonreactive autologous serum cases, and decrease their burden of antihistamines.

Material and methods

This was a nonrandomized, cross-sectional interventional study from January 2018 to February 2019 in the dermatology outpatient department of the Basrah Teaching Hospital. Patients were enrolled in this study according to inclusion criteria, which were patients of both sexes of 16 to 60 years of age, subjects with a history of daily or almost daily occurrence of urticarial wheals for 6 weeks or more, willingness to take the test, and weekly injections. Exclusion criteria were: patients with a history of physical urticaria, cholinergic urticaria, known type 1 hypersensitivity reaction, hereditary angioedema or known C1 esterase deficiency, urticaria associated with conditions such as connective tissue diseases, acute or chronic infections, neoplasms, pregnancy, lactation, and use of a systemic steroid or immunosuppressive drug in the last six weeks. The examination and laboratory parameters included complete blood count, erythrocyte sedimentation rate (ESR), anti-nuclear antibodies (ANA), thyroid function test, anti-streptolysin O titer, hepatitis B surface antigen (HBsAg), hepatitis C antibody (HCAb), urine and stool routine examination for infection or infestation-related urticaria.

ASST procedure and AST

All patients were instructed to stop taking antihistamines one week prior to performing the test. 5 ml of venous blood was drawn and placed in a test tube without a clotting accelerator from all patients. The mixture was allowed to clot at room temperature for 0.5 h. Later, it was centrifuged at 2500 rpm for 10 min. The serum was then separated using a 5 ml syringe. Samples of 0.05 ml of autologous serum and 0.05 ml of 0.9% sterile saline (for a negative control) were injected intradermally separately into the flexor aspect of the forearm with a 27G needle with a gap of at least 3 cm between the injection sites. Areas of spontaneous wheal formation in the last 24 h were avoided. After 30 min, wheal and flare responses were measured. A positive test is defined as a red serum-induced wheal with a diameter of 1.5 mm or more than that caused by the adjacent saline-induced response at 30 min. Then 2.5 ml of the patient's own serum was injected deep intramuscularly with a 22G needle. AST was administered weekly, each time on alternate buttocks for 10 weeks. The evaluation of the disease was performed using the urinary total severity score (TSS), which consists of parameters such as the number and size of wheals, the intensity of pruritus, the duration of persistence of wheals, the frequency of appearance of wheals, and the frequency of antihistamine use. These six parameters of disease activity and disease severity were recorded on a scale of 0–3: at baseline (week 0), weekly for 10 weeks and follow-up for another 10 weeks. Based on these, a total severity score (TSS) of 0–18 was generated and the overall severity of the disease was classified as clear (TSS = 0), mild (TSS = 1–6), moderate (TSS = 7–12), or severe (TSS =13–18) [17].

Ethical considerations

Informed verbal consent was obtained from all participants prior to participation. The study was carried out in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

SPSS software version 25.0 was used for data analysis. Percentages and means were used to present the data in tables. Additionally, a comparison of study groups was performed using the χ^2 test for categorical data and the paired *t* test for continuous data. $P < 0.05$ was considered statistically significant.

Results

The demographic data of the patients are shown in Table 1. A total of 77 (29 male and 48 female) patients were evaluated during this study. There were 34 (44.1%) patients who demonstrated reactivity with autologous serum ASST (+), and 43 (54.9%) did not have reactivity with ASST (–). The mean age and duration of the disease for patients with ASST (+) and ASST (–) were 34.5 ±10.02, 5.7 ±1.4, 38.3 ±12.3, and 5.5 ±1.1, respectively. Table 2 shows the mean TSS in patients with ASST (+) and ASST (–) throughout the study. The mean TSS in ASST (+) patients was 16.9 ±3.03, 3.4 ±3.8, and 2.4 ±3.8 at baseline, the 10th week, and the end of the study, respectively; the difference is statistically significant ($p = 0.0001$). The mean TSS in patients with ASST (–) was 15.1 ±0.8, 6.6 ±5.1, and 4.95 ±4.9 at baseline, the 10th week and at the end of the study, respectively; the difference is statistically significant ($p = 0.0001$). The mean TSS in ASST (+) and ASST (–) patients was 3.4 ±3.8 and 6.6 ±5.1 at the 10th week, respectively, and 2.4 ±3.8 and 4.95 ±4.9 at the end of the study, respectively; the differences were statistically significant at the 10th week and at the end of the study ($p < 0.05$). Table 3 shows that 21 (61.7%) of the ASST (+) patients and 12 (27.9%) of the ASST (–) patients had complete clearance of symptoms; the difference is statistically significant ($p < 0.05$). In patients with ASST

Table 1. Demographic characteristics of patients with chronic urticaria

Characteristic	ASST positive patients	ASST negative patients	*P*-value
Total (*N* = 77)	34	43	
Men, *n* (%)	11 (32.4)	18 (41.9)	0.072
Women, *n* (%)	23 (67.6)	25 (58.1)	
Age, mean ± SD [years]	34.5 ±10.02	38.3 ±12.3	0.081
Disease duration, mean ± SD [years]	5.7 ±1.4	5.5 ±1.1	0.081

Table 2. Mean TSS in patients with ASST +ve and -ve at 0, 4, 10, and 20 weeks

Week	TSS in ASST (+) patients (mean ± SD)	TSS in ASST (–) patients (mean ± SD)	*P*-value
Baseline	16.9 ±3.03	15.1 ±0.8	0.061
4th week	10.97 ±1.6	11.9 ±2.4	0.070
10th week	3.4 ±3.8	6.6 ±5.1	0.003
20th week	2.4 ±3.8	4.95 ±4.9	0.003
P-value	0.0001	0.0001	

Table 3. Complete clearance of symptoms

Variable	ASST (+) patients	ASST (–) patients	*P*-value
Total, *n* (%)	34 (100)	43 (100)	
Complete clearance, *n* (%) at week 20	21 (61.7)	12 (27.9)	0.002

Table 4. Frequency of antihistamine use in patients with ASST +ve and -ve at 0, 10, and 20 weeks

Daily use of anti-histamine	In ASST (+) patients *N* (%)	In ASST (–) patients *N* (%)	*P*-value
Baseline	34 (100)	43 (100)	
10th week	5 (17.70)	12 (27.90)	0.16
20th week	2 (8.82)	11 (25.58)	0.06
P-value	0.04	0.8	

(+) the use of antihistamines decreased to 17.70% and 8.82% from baseline in the 10th and 20th weeks of the study, respectively (the difference was statistically significant, $p = 0.04$), while it decreased to 27.90% and 25.58% from baseline in patients with ASST (–) (the difference was not statistically significant, $p = 0.8$). The reduction in antihistamine use was higher in ASST (+) patients than in ASST (–) patients at the end of the study, but the difference was not statistically significant ($p = 0.06$), as shown in Table 4.

Discussion

The autologous serum skin test (ASST) offers the advantage of differentiation of chronic idiopathic urticaria into autoimmune (ASST positive) or non-autoimmune (ASST negative), which is difficult to obtain from the history and clinical examination in these patients [3, 4]. Patients with positive ASST are supposed to have a more severe and prolonged disease course, frequent attacks, higher serum IgE levels, and have been linked to HLADR4, other autoimmune diseases, and less susceptibility to H1-antihistamines [18]. The prevalence of this ASST positivity has been reported as 27–61% of cases of CIU [7, 14]. In this study, 44.1% of the patients exhibited ASST positivity, which is similar to the percentage reported in the literature [7, 14]. This finding is similar to other studies conducted by Bajaj *et al.* (49.5%), Staubach *et al.* (40.5%) and Al-Hamamy *et al.* (40.7%) [1, 19, 20]. The ASST positivity in our study was higher than that observed by Godse from Mumbai [6] and less than that observed by Sánchez-Borges *et al.* and Nageswaramma *et al.* [2, 17]. In this study, the baseline TSS in patients with ASST (+) was higher than in patients with ASST (–), but the difference was not statistically significant; this is similar to other reports that revealed no or only subtle differences

in the symptomology of ASST (+) and ASST (–) patients [12]. This result is also comparable to other studies conducted by Bajaj *et al.* and Sabroe *et al.* [1, 21]. The mean TSS values at the end of the study were 2.4 ±3.8 and 4.95 ±4.9 for patients with ASST (+) and ASST (–), respectively; this was a significant reduction in the mean TSS. In this study, urticaria symptoms showed improvement at the fourth week of AST initiation. The improvement continued throughout the study period in both groups, similar to that reported by Nageswaramma *et al.* [17]. Our study finding was consistent with that of Debbarman *et al.* and Staubach *et al.* [15, 19], who found that AST treatment resulted in an improvement in disease symptoms, severity, and quality of life. The complete clearance of symptoms was 21 (61.7%) and 12 (27.9%) in ASST (+) and ASST (–) patients, respectively; this result indicates a higher efficacy of AST in patients with autoimmune (ASST positive) CU than in patients without autoimmune (ASST negative). However, the present study has shown the efficacy of AST in both groups irrespective of ASST reactivity. Studies reported that ASST (+) patients having antiFcRI antibodies vary from 40% to < 20% [12]. These studies showed that not all ASST (+) patients have antiFcRI antibodies. Some studies reported < 2% antiFcRI positivity in ASST (–) patients. This fact shows a poor concordance of ASST positivity with antiFcRI antibodies and may be the possible reason behind the significant clinical improvement of ASST (–) patients with AST in our study. At the end of this study, we found a significant reduction in the use of antihistamines, particularly in ASST (+). One of the limitations of our study was the number of patients who participated in the study.

Conclusions

AST is a cheap, cost-effective, and potentially curative modality of treatment without side effects in patients with chronic urticaria regardless of ASST status. It reduces the burden of the adverse effects of antihistamines.

Recommendation: Large-scale placebo-controlled randomized studies with longer follow-up periods are needed to know the efficacy of AST.

Conflict of interest

The author declares no conflict of interest.

References

1. Bajaj A, Saraswat A, Upadhyay A, et al. Autologous serum therapy in chronic urticaria: old wine in a new bottle. Indian J Dermatol Venereol Leprol 2008; 74: 109-13.
2. Sánchez-Borges M, Asero R, Ansotegui IJ, et al. Diagnosis and treatment of urticaria and angioedema: a worldwide perspective. World Allergy Organ J 2012; 5: 125-47.
3. Goh CL, Tan KT. Chronic autoimmune urticaria: where we stand. Indian J Dermatol 2009; 54: 269-74.
4. Krupashankar DS, Shashikala K, Madala R. Clinical and investigative assessment of patients with positive versus negative autologous serum skin test: a study of 80 south Indian patients. Indian J Dermatol 2012; 57: 434-8.
5. Soter NA. Treatment of urticaria and angioedema: low-sedating H1-type antihistamines. J Am Acad Dermatol 1991; 24: 1084-7.
6. Godse KV. Autologous serum skin test in chronic idiopathic urticaria. Indian J Dermatol Venereol Leprol 2004; 70: 283-4.
7. Piconi S, Trabattoni D, Iemoli E, et al. Immune profiles of patients with chronic idiopathic urticaria. Int Arch Allergy Immunol 2002; 128: 59-66.
8. Cho CB, Stutes SA, Altrich ML, et al. Autoantibodies in chronic idiopathic urticaria and nonurticarial systemic autoimmune disorders. Ann Allergy Asthma Immunol 2013; 110: 29-33.
9. Jáuregui Presa I, Ferrer M, Montoro J, et al. Antihistamines in the treatment of chronic urticaria. J Investig Allergol Clin Immunol 2007; 17 (Suppl. 2): 41-52.
10. Grattan CEH, Humphreys F. Guidelines for evaluation and management of urticaria in adults and children. Br J Dermatol 2007; 157: 1116-23.
11. Staevska M, Popov TA, Kralimarkova T, et al. The effectiveness of levocetirizine and desloratadine in up to 4 times conventional doses in difficult-to-treat urticaria. J Allergy Clin Immunol 2010; 125: 676-82.
12. Hide M, Francis DM, Grattan C, et al. Autoantibodies against the high-affinity ige receptor as a cause of histamine release in chronic urticaria. N Engl J Med 1993; 328: 1599-604.
13. Patil S, Sharma N, Godse K. Autologous serum therapy in chronic urticaria. Indian J Dermatol 2013; 58: 225-6.
14. Khan S. More robust evidence and safety checks are required before autologous serum therapy as treatment for chronic urticaria can be recommended. Indian J Dermatol 2013; 58: 316-7.
15. Debbarman P, Sil A, Datta PK, et al. Autologous serum therapy in chronic urticaria: a promising complement to antihistamines. Indian J Dermatol 2014; 59: 375-82.
16. Majid I, Shah S, Hassan A, et al. How effective is autologous serum therapy in chronic autoimmune urticaria. Indian J Dermatol 2015; 60: 102.
17. Nageswaramma S, Sarojini VL, Pujitha BB, et al. Efficacy of autologous serum therapy in chronic urticaria. Int J Contemp Med Res 2017; 4: 110-2.
18. Karn D, Kc S. Clinical outcome of autologous serum therapy in chronic idiopathic urticaria. J Nepal Health Res Counc 2017; 15: 71-4.
19. Staubach P, Onnen K, Vonend A, 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: 150-9.
20. Al-Hamamy HR, Hameed AF, Abdulhadi AS. Autologous serum skin test as a diagnostic aid in chronic idiopathic urticaria. ISRN Dermatol 2013; 2013: 291524.
21. Sabroe RA, Poon E, Orchard GE, et al. Cutaneous inflammatory cell infiltrate in chronic idiopathic urticaria: comparison of patients with and without anti-FcεRI or anti-IgE autoantibodies. J Allergy Clin Immunol 1999; 103: 484-93.