Original Article

Journal of Dermatology
Volume 6 Number 1, January – June 2021

Autologous Serum Therapy in Chronic Spontaneous Urticaria with Positive ASST as Adjuvant Therapy with Antihistaminics

[1]Sonal G Patel, [2]Rima Joshi, [3]Baldaniya Monika B, [4]Patel Raksha M

How to cite this article:
Sonal G Patel, Rima Joshi, Baldaniya Monika B, Patel Raksha M, Autologous Serum Therapy in Chronic Spontaneous Urticaria with Positive ASST as Adjuvant Therapy with Antihistaminics. RFP Journal ofDermatology 2021; 8(1):9–12.

Author's Affiliations:[1]Assistant professor, Department of Dermatology, Government Medical College, Anandpura, Vadodara, Gujarat 390001, [2]Associate Professor Department of Dermatology, B J Medical College, Ahmedabad, Gujarat 380016, India,[3]3rd year Resident, [4]Professor and Head of the Department, Department of Dermatology, GMERS Medical College and Hospital, Gotri,Vadodara, Gujarat 390021, India.

Corresponding Author: SomanathSahoo, Research scholar, PG Department of Zoology, Berhampur University, Odisha 760007, India.

E-mail: sonalgpatel173@gmail.com

Abstract

Chronic spontaneous urticaria affects 0.5-1% of individuals (lifetime prevalence) and significantly reduces quality of life (QOL) 1. More than half of the patients of chronic urticaria suffer from autoimmune urticaria. Chronic urticaria (CU) is a troublesome problem and patients of CU are affected by the morbidity that arise from irritable itch and wheals and are also subjected to a huge antihistamine pill burden. The symptoms are more profound in autoimmune urticaria (AU) where auto-antibodies in blood flare-up the condition. A vigilant search for a novel modality of treatment which can decrease the pill burden is needed.***Aims:***This study evaluates the effectiveness of autologous serum therapy (AST) in CSU and also determines its usefulness in AU.***Materials and Methods:*** The prospective interventional, randomized single blind studySingle blind, parallel group, randomized, controlled study. Eighteen patients were given AST and seventeen patients were given injection normal saline (placebo), along with Cetrizine given on-demand basis in both groups. AST/Placebo was given weekly for nine weeks and the patient was followed-up for a total period of 24 weeks. Of the 250 patients in whom ASST was performed, 150 were ASST positive of which 115 withdrew (Remote residence from treatment center). 35 ASST positive patients were administered treatment according to below-mentioned groups:*Group A:* 18 ASST positive patients received AST with antihistamines.*Group B:* 17 ASST positive patients received only antihistamines.AU was diagnosed by autologous serum skin test. Urticaria activity score (UAS) was used as primary effectiveness variables. Safety parameters assessed were the spontaneously reported adverse events and laboratory parameters.

Keywords: CSU (Chronic Spontaneous Urticaria); AU(Autoimmune Urticaria); AST (Autologous Serum Therapy)**.**

Introduction

Autologous Serum Therapy (AST)[2,3]

CSU is caused by an auto reactive mechanism in approximately 30-50% of all patients. Patients with auto reactive chronic urticaria (CU) regularly exhibit positive skin test reactions to autologous serum (ASST). In autoimmuneCU patients, expression of autoantibodies directed against the high affinity receptor for IgE (anti-Fcε RI) of mast cells or IgE (anti-IgE) is Responsible for this phenomenon.

Autologous serum therapy is a promising therapy for treatment of resistant urticaria. This is valuable in developing countries as this is an economical option. Therapies aimed at inducing tolerance to circulating histamine-releasing factors in ASST+ CSU patients, e.g. by treatment with autologous serum have been tested.

Our study was done to assess the effectiveness and safety of autologous serum therapy (AST) as an adjunctive therapy to standard antihistamine cetirizine compared to patients receiving cetirizine alone.

Since the effectiveness of antihistamines is limited during the period of its use; a search for a therapeutic modality that can provide extended relief and substantially reduce pill burden is the need of the hour.

Material and Method

The prospective interventional, randomized single blind study was carried out in department of Skin and Venereal Disease in a tertiary care hospital. Approval of the Institutional Human Ethics Committee was taken. Patients having CSU, fulfilling the inclusion criteria attending Dermatology OPD were enrolled. The study period was July 2011 to December 2013.

Inclusion Criteria

Participant of all genders, more than 18 years of age, Daily or almost daily appeararadmisednce of wheals for more than 6 weeks and willingness for injections were included.

Exclusion Criteria

- Patients with Physical urticaria, Urticarial vasculitis, children, Pregnancy, willing to be pregnant, lactating women
- Urticaria with known etiology like food, drugs, any infections etc.
- Systemic corticosteroid or immunosuppressive drug use in the past 6 weeks
- Systemic illnesses requiring treatment.

All patients fulfilling the inclusion and inclusion criteria were enrolled.

Informed and written consent were taken from patients in their language prior to enrolment in the study.

Patient's confidentiality was maintained.

Participants were made to understand the process completely and all relevant questions were answered.

Demographic data of all individuals enrolled in the study were recorded.

History regarding onset, frequency of disease, infection, gastrointestinal symptoms, aggravating and associated factors were taken.

Assessment of the severity of the symptoms based on Urticaria Activity Score (UAS) was done(table1). As urticaria symptoms frequently change in intensity, overall disease activity is best measured by advising patients to document 24-h self- evaluation scores for several days. Thus the UAS, is the sum score of 7 consecutive days.[4]

Table 1: Scoring System forUrticaria Patients.[1]

Score	Wheal	Pruritus
0	None	None
1	Mild (<20 wheals/24h)	Mild(present but not annoying or troublesome)
2	Moderate(20-50 wheals/24h)	Moderate(troublesome but does not interfere with normal daily activity orsleep)
3	Intense (>50wheals/24 h or large confluent areas of wheals)	Intense(severe pruritus, which is sufficiently troublesome to interfere withnormaldailyactivityorsleep)

Sum of score: 0-6

of the 250 patients in whom ASST was performed, 150 were ASST positive of which 115 opted out (Remote residence from treatment center).

35 ASST positive patients were administered treatment according to below- mentioned groups:

Group A: 18 ASST positive patients received AST with antihistamine.

Group B: 17 ASST positive patients received only antihistamine.

Method for AST:

- Baseline UAS was recorded.
- Blood for centrifugation to obtain autologous serum was withdrawn immediately before the procedure.
- Weekly intramuscular gluteal injections were administered for 9 weeks (0.05ml/kg/week).
- The improvement of urticaria symptoms and the requirement for antihistaminic rescue medication after therapy was compared.

Pre – requisite for ASST

- Antihistamines were discontinued (at least two days for short acting antihistamines, 6 days for Desloratidine and 2 weeks for Doxepin).
- Systemic steroids were discontinued for at least 2 weeks.
- Forearm has to be free of wheals.

Preparation of serum

Carefully label all tubes and syringes with the patient's name. Collect 5 ml blood into sterile glass tubes without additives. Allow blood to clot at room temperature for 30 minutes. Centrifuge sample, at about 500 RPM for 10 minutes. Suck 0.2ml serum into 1 ml tuberculin syringe in order to inject 0.05 ml intradermally into the volar aspect of forearm.

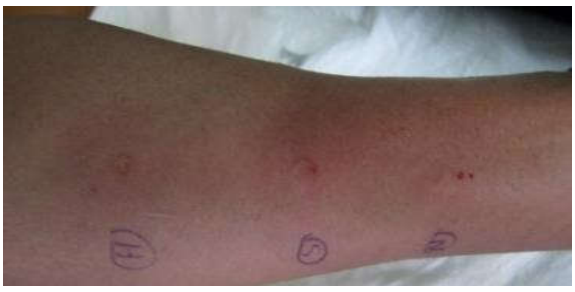
Skin testing technique and interpretation (figure1):

- Forearm is chosen as the test site and cleaned with spirit swab.0.05 ml of fresh undiluted serum is injected intradermally.
- Negative control: intradermal injection of 0.05 ml of sterile saline.
- Positive control: a skin prick test with 10mg/ml histamine solution.
- Skin test reading: at 30 minutes. Wheal and flare response was calculated by measuring two perpendicular diameters (d1 and d2) according to formula $\pi(d1+d2)/4$ (Table2).[5]

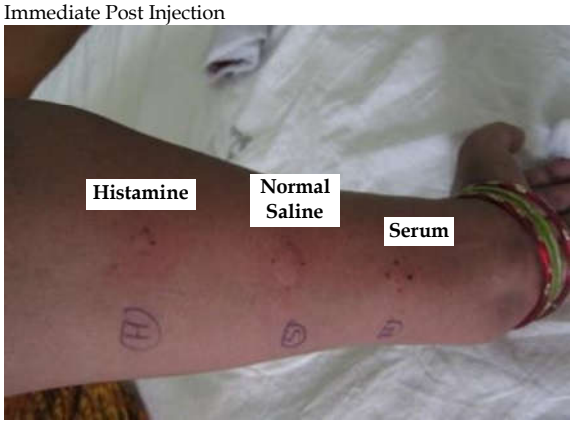
Table 2: Interpretation of Asst.[5]

Positive test	Negative test	Uninterpretable
A serum induced red wheal with diameter 1.5mm or more than the saline induced response at 30 minutes with a positive histamine test.	Serum wheal response palerather than uniformly red with a positive histaminetest.	Red wheal develops at the saline injections sites or histamine skin prick testis negative.

Statistical Methods:Chi-squared test



Immediate Post Injection



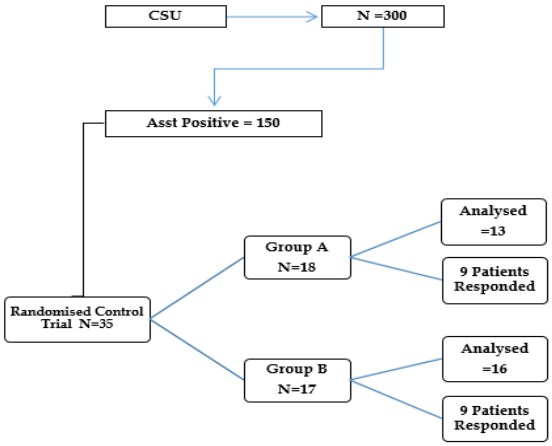
30 Min Post Injection.

Fig. 1: Skin testing technique and Interpretation.

Results

Autologous Serum Therapy

Out of 35 randomized patients (intention-to-treat population) 29 patients completed the study (per protocol population).Reasons for drop out included requirement for systemic treatment with glucocorticoid and failure to document symptoms.



of 13 ASST positive CSU patients, 9 showed significant improvement of UAS after repeated injections of AST. Improvement on treatment group was statistically significant ($p<0.05$) compared to ASST positive group receiving antihistamine only.

Disease Activity

ASST positive patients showed 50% improved UAS after AST therapy ($p < 0.05$) as compared to UAS levels before therapy.Whereas UAS did not improve significantly in ASST positive CSU patients that had received antihistamine only.(table3)

Table 3: Improvement in UAS after AST Therapy.

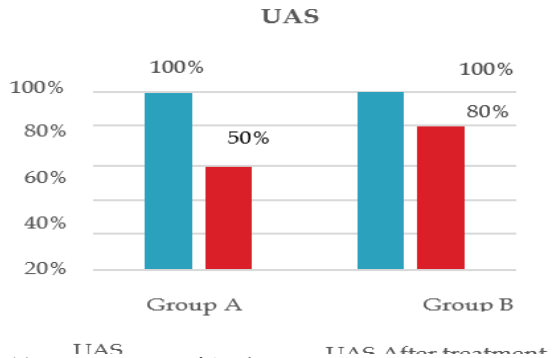
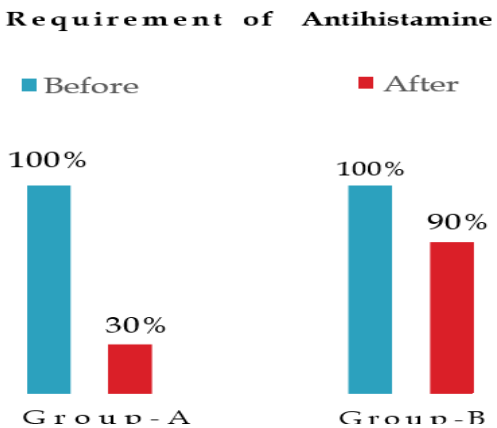


Table 4: Requirement of Antihistamine.



We found that autologous serum therapy significantly reduced CSU activity by 50% and antihistamine requirement by 70% in ASST positive CSU patients after nine weekly AST were given.(Table 4)

Discussion

Chronic urticaria is a disease with an unpredictable course and the treatment is continued till the disease goes into remission. Chronic urticaria patients with a positive ASST (autoimmune subgroup) are more likely to be associated with HLA DR4, to have autoimmune thyroid disease, a more prolonged disease course and may be recalcitrant to H1-antihistamine treatment than those with a negative ASST.[5]

A new modality that can supplement antihistamines and leukotriene inhibitors in combating CU, while also decreasing the pill burden is long felt, and will be appreciated by patients and physicians alike.

Potential of whole blood in the treatment of urticaria was documented by Fleck M 6 and Stuabach et al.,[7] in separate studies and later use of serum in the treatment of urticaria was highlighted by Bajaj et al.[9]

The possible mechanism of action of AST was thought be induction of anti- idiotypes, which have recently been shown to inhibit the function of disease-inducing antibodies in pemphigus and also to shift the Th2 cytokine profile to Th1 in ASST+ patients.[8, 7]

The reduction in pill-burden gives a sense of well-being that is reflected in the improvement of quality of life which was found to be significant in those receiving AST in ASST positive CSU present study.

Our results are slightly lower than the figure of 60% reported by Bajaj AK et al, who also concluded that autologous serum therapy is effective in a significant proportion of ASST positive patients with CSU.[3]

Present study revealed that AST has a vast potential in the treatment of urticaria. The reduction in the symptom is accompanied by reduction in pill-burden and decrease in UAS score. It should be focused that in autoimmune urticaria, a subgroup of urticaria otherwise refractory to conventional therapy, AST has proved itself as an excellent adjuvant therapy. The goal of therapy in chronic urticaria is to maintain a symptom free period and to ensure that the treatment is associated with minimum
side effects and less monitory burden.

Conclusion

In patients with chronic urticaria, AST is a useful adjunct which reduces the pill burden and improves the quality of life. Autoimmune urticaria patients also benefited from this method and thus AST finds its place in the therapeutic armamentarium of clinicians treating chronic spontaneous urticaria.

References

1. Zuberbier T.A Summary of The New International Eaaci/Ga2len/Edf/Wao Guidelines In Urticaria. Wao Journal 2012; 5:S1-S5.
2. Staubach P. Onnen K. Vonend A, Metz M. Siebenhaar F, Tschentscher I, Et Al.Autologous Whole Blood Injections To Patients With Chronic Urticaria And A Positiveautologous Serum Skin Test. A Placebo Controlled Trial. Dermatology 2006; 212:150-9.87.
3. Bajaj Ak. Saraswat A. Upadhyay A. Damisetty R. Dhar S. Autologous Serum Therapy In Chronic Urticaria: Old Wine In A New Bottle. Indian J. Dermatologyvenereolleprol 2008: 74: 109-13.
4. ZuberbierT.Eaaci/Ga2len/Edf/Wao Guideline: Definition, Classification And Diagnosis Of Urticaria. Allergy 2009; 64:1417-1426.
5. Kaplan Ap. Chronic UrticariaAnd Angioedema. N Engl J Med 2002;246:175- Back To Cited Text No.34.
6. Fleck M. Urticaria. In :Gottron H, Schönfeld W, Editors. Dermatologie Und Venerologie. Vol. 3. Stuttgart: Thieme; 1959. P. 265-98.
7. Staubach P, Onnen K, Vonend A, Metz M, Siebenhaar F, Tschentscher I, 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.
8. Alvarado-Flores E, Avalos-Diaz E, Diaz L, Herrera-Esparza R. Anti-Idiotype Antibodies Neutralize In Vivo The Blistering Effect Of Pemphigus Foliaceus Igg. Scand J Immunol 2001;53:254-8.
9. Bajaj Ak, Saraswat A, Upadhyay A, Damisetty R, Dhar S. Autologous Serum Therapy In Chronic Urticaria: Old Wine In A New Bottle. Indian J DermatolVenereolLeprol 2008;74:109-13.