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Original Research Article

A comparative study of effectiveness of autologus serum therapy with oral antihistamines versus oral methotrexate and oral antihistamines in chronic urticaria patients

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ABSTRACT

Background: Chronic urticaria (CU) is a worrisome problem and patients of CU suffer from the morbidity that arises from irritable itch thus they are subjected to a huge antihistamine pill burden. The symptoms are more prominent in autoreactive urticaria (AU) where auto-antibodies in blood causing recurrent flares. Therefore a need of adjunctive drug to reduce the pill burden is felt need.
Methods: A randomized, controlled study was done. 50 patients were given AST and 50 patients were given oral pulse methotrexate (10-15 mg once weekly) along with levocetrizine in an on-demand basis in both groups. AST was given weekly for nine weeks and followed-up for a total period of 24 weeks. Urticaria total severity score (UTSS) was used to evaluate the effectiveness of treatment. Safety parameters assessed were the spontaneously reported adverse events and laboratory parameters.
Results: UTSS showed significant improvement from baseline, 7th week and 8th week onwards in AST group and methotrexate group respectively. Group comparison showed significant improvement 4th week onwards.
Conclusions: Autologous serum therapy as well as methotrexate both proved effective in chronic urticaria patients. On follow-up improvement is sustained for at least 3-4 months after the last injection in case of AST.

Keywords: Urticaria, Methotrexate, AST

INTRODUCTION

Urticaria is characterized by transient skin or mucosal swellings due to plasma leakage. Superficial dermal swellings are wheals, and deep swellings of the skin or mucosa are termed angioedema. Wheals are characteristically pruritic and pink or pale in the center, whereas angioedema is often painful, less well defined and shows no colour change.[1] It causes a significant decrease in patients quality of life.[2,3] Lifetime prevalence for urticaria is reported as 7.8-22.3%, with point prevalence being around 1%.[4,5] The risk of developing urticaria in a person is throughout his life is around 15-20%.[6] The average duration of the disease is around 1-5 years.[7]

Even after extensive investigation the underlying cause remains unknown and so the term idiopathic is used. In many cases thyroid autoimmunity is positive.[8]

Many times urticaria is associated with aggravating factors like diet, drugs, alcohol, viral infections, local

heat and friction, and mental stress and urticaria can be avoided by sampling avoiding these.

There are various treatment options available including antihistamine which is the first line treatment. The second step of treatment is to increase up to four times the standard dose of a second-generation antihistamine.[9-11]

In refractory cases one can add H_2 antihistamines such as cimetidine, famotidine and ranitidine can be added.[12] In some cases corticosteroids such as prednisone or prednisolone (0.5 to 1 mg per kg per day) may be added initially to control symptoms.[9,13-15]

Other drugs that can be used include leukotriene receptor antagonists, such as montelukast and zafirlukast, can also be added, especially in patients with non-steroidal antiinflammtory drugs intolerance or cold urticaria.[16]

Other treatment modalities for controlling refractory urticaria include high-potency antihistamines like hydroxyzine or the tricyclic antidepressant (doxepin) and other immunomodulatory agents like omalizumab and cyclosporine.[17,18]

Our study compares two such newer modalities autologus serum therapy (AST) and pulse methotrexate dose in controlling urticaria.

METHODS

The present study was carried out in Department of dermatology of tertiary care hospital in Gorakhpur for period of 1 year from January 2017 to January 2018. Ethical committee permission was obtained prior to commencement of study and consent was taken from the patient prior to study. Detailed history and examination was documented in structured proforma.

The study design was prospective interventional study. By systemic random sampling patient were divided into two groups where group 1 received AST and group 2 was given methotrexate 10-15 mg per week. The diagnosis of chronic urticaria (CU) was made clinically.

Baseline investigation performed including complete blood count, liver function test, renal function test, thyroid profile, urine routine and stool routine or microscopy was done.

Autologous serum therapy

Five ml venous blood of the patient was drawn with a sterile, disposable syringe from the antecubital vein in sterile BD vacutainer for serum collection. The blood was subjected to centrifugation using centrifuge machine at the rate of 2000 rpm for 10 min at room temperature. 2-ml deep intramuscular injection was given in alternate buttocks or upper arms. Rescue antihistamine was permitted as in the run-in period; no other drugs were permitted.

Thereafter, every week for ten consecutive weeks, 5 ml blood was drawn, serum separated and a 2-ml deep intramuscular injection given in alternate buttocks or upper arms. Rescue antihistamine was permitted as in the run-in period; no other drugs were permitted.

Inclusion criteria

Inclusion criteria were patent having almost daily appearance of wheals for ≥6 weeks; patient willing to take part in study and signed written informed consent; patient willing to come for weekly follow up; age between 18 year to 60 year.

Exclusion criteria

Exclusion criteria were acute urticarial; pregnant and lactating women; patients suffering from immunosuppression due to drug or disease, advanced diseases of vital organs, on steroids; inability to come for weekly follow-ups; addicted to alcohol or other substance abuse, machinery operators, vehicle drivers and in whom sleep/wake cycle alteration could be an issue; drop outs (patient failed to visit at least thrice during study period in 0, 6 and 10 week).

Assessment parameters

Urticaria total severity score

With each parameter having a score of 0-3, maximum score being 18.

Table 1: Urticaria total severity score.

Parameters	Score			
	0	1	2	3
Number of wheals	None	≤10	11-50	>50
Size of wheals	None	<1 cm	1-3 cm	>3 cm
Intensity of pruritus	None	Mild	Moderate	Sever
Duration of persistence	None	< 1 hour	1-12 hour	>12 hour
Frequency of appearance	None	<once or once a week	2-3 times a week	Daily/almost daily
Frequency of antihistamine use	None	<once or once a week	2-3 times a week	Daily/almost daily

Safety parameters

All patients were screened for HIV, HBsAg and VDRL before starting the study.

Proper precaution is taken during handling of blood and serum of the patient.

Clinical adverse events

The adverse events occurring whether or not were considered causally related to study were recorded.

Period of assessment: patients were assessed at 0, 2, 4, 6, 8 and 10 weeks.

Patients were evaluated based upon scores and asked for recurrence and potential side effects. Scores were taken at every visit but for evaluation only scores at start, at end of treatment and at end of 6 months of follow up are taken into consideration.

Statistical method used

Unpaired 't' test was used to compare the data between two groups.

RESULTS

As shown in Figure 1 out of 100 patients, 37 patients were male and rest 63 patients were female. On percentage basis 37% were male and rest 63% were female.

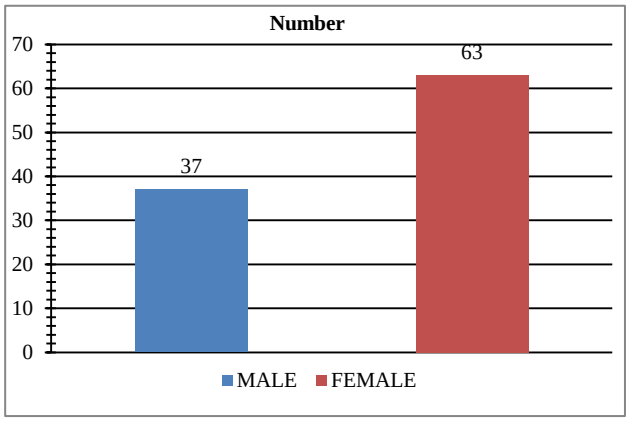

Figure 1: Distribution of patient according to sex.

The age wise distribution is given in Figure 2, out of 100 patients 10 male and 20 female were in age group 15 to 30 years. 20 male and 30 female were in age group 30 to 45 years and 7 male and 13 female were in age group of 45 to 60 years.

Statistical analysis was done by comparing the percentage improvement in two groups and as seen in Figure 3, there was significant improvement in both groups. On comparison of two marks more improvement is seen in group 1 as compared to group 2.

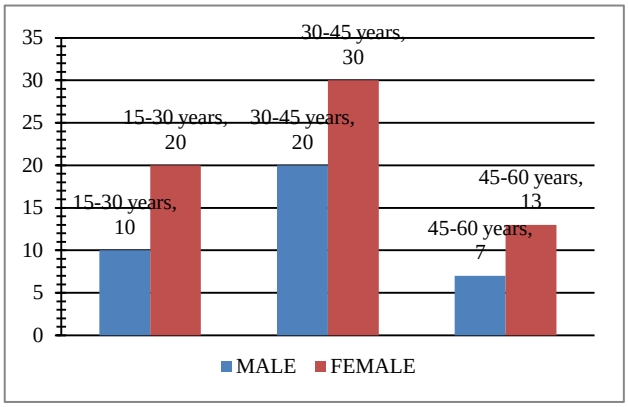

Figure 2: Age wise distribution of patients.

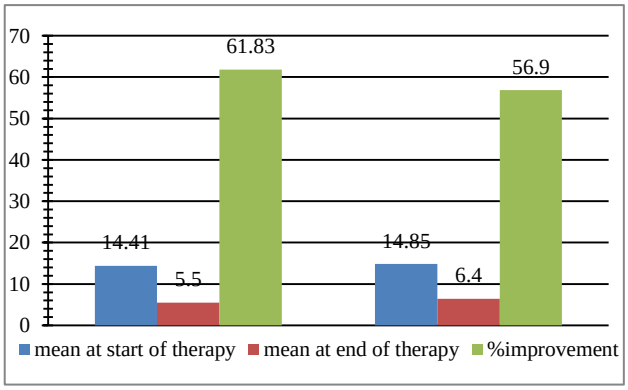

Figure 3: Improvement of UTSS in two groups after start and end of therapy.

DISCUSSION

The time consuming and frustrating management of CU and associated direct and indirect health costs with socio-economic implications, about 20-30% reduction in performance was assessed.[19,20] It is well versed in literature that resistant urticaria- a steroid dependent rash is poorly responsive to multiple antihistaminic and immunosuppressive agents.[21] Okubo et al defined resistant urticaria in patients not responding to 10 mg cetirizine per day for 1 week.[22] The guidelines by European Union consensus defines- resistant urticaria as the rash which is not controlled after increasing the four times dose of usual dosing of non-sedative H1 antihistamines, but they indicate that this recommendation is based on low quality evidence.[23]

A study conducted by Sagi et al, with methotrexate it was seen that out of 8 patients with CU who had responded poorly to antihistamines, oral steroids and other immunosuppressants and subsequently treated with weekly 15-25 mg methotrexate, 7 showed complete remission with onset of effect seen at 3-5 weeks, maintained for 2-15 months.[24] Similarly a study by Perez et al showed 16 patients of steroid dependant chronic

urticaria- 10 chronic urticaria, 4 urticarial vasculitis and 2 angioedema treated with methotrexate in doses ranging from 5-15 mg/week showed marked improvement.[21] Twelve out of 16 patients responded to therapy, 2 were able to discontinue steroids completely and seven being able to taper their oral steroids.. In our study there is marked improvement in UTSS after taking methotrexate which is consistent with these studies. Onset of therapeutic effect of methotrexate was noted at periods varying from 3 weeks to more than 6 months. Hair thinning and fatigue were common side effects noted while rarely hepatitis and bone marrow suppression was noted.

Autohemotherapy (repeated intramuscular injection) is one of the oldest modalities used in treating urticaria and other viral or allergen.[25,26] The mechanism of action is by inducing tolerance against offending antigen like that in immunotherapy.[27,28]

In a study conducted by Bajaj et al it was seen that there is significant percentage of improvement in CSU patients and responding really well to autologous serum injection treatment.[29] While in other study AST and autologous whole blood injections in 88 CU patients did not found significant difference in terms of improvement between two groups.[30]

In our study we found that patient showed significant improvement after AST and this improvement was sustained in follow up period.

CONCLUSION

The aim of the study was to see effectiveness of autologous serum therapy and oral methotrexate. The comparative analysis was carried out in 100 patients of CU which were divided into two groups as group 1 (methotrexate group) in which autologous serum therapy was given along with oral antihistamines on SOS basis and in group 2 (AST group) only oral antihistamines given on SOS basis. At the end of the study, following conclusions were drawn: Autologous serum therapy is proved effective in CU patients statistically in group 2, effect of autologous serum therapy as well as methotrexate started appearing 4th week onwards, AST was well-tolerated and none of the patients reported any side effects except local soreness lasting from 12 to 24 hrs. On follow up improvement is sustained for at least 3-4 months after the last injection.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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