ORIGINAL RESEARCH

To assess the effectiveness of Methotrexate v/s Dapsone/ASST in treating Chronic Urticaria

[1]Dr. Kanishk Utkarsh Kaushik, [2]Dr. Meha Tyagi, [3]Dr. Nupur Shanker

[1,3]Associate Professor, [2]Assistant Professor, Department of Dermatology, National Capital Region Institute of Medical Sciences, Meerut, Uttar Pradesh, India

Corresponding Author
Dr. Nupur Shanker
Associate Professor, Department of Dermatology, National Capital Region Institute of Medical Sciences, Meerut, Uttar Pradesh, India

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ABSTRACT

Aim: To assess the effectiveness of Methotrexate v/s Dapsone/ASST in treating Chronic Urticaria. **Materials and methods:** A prospective comparison research was conducted on 200 patients with chronic urticaria chosen from those visiting the outpatient clinic at the Department of Dermatology. The patients were randomly assigned to one of four therapy groups based on their Urticarial Activity Score (UAS) and Dermatology Life Quality Index (DLQI). Group A was comprising patients who was given oral Dapsone 50 mg for a period of 12 weeks. Group B was comprising patients who was given oral Methotrexate 10 mg (in 4 divided doses at 12 hourly interval) per week for a period of 12 weeks. Group C was comprising patients who wasgiven Treated with ASST (Autologous Serum Skin Therapy) – 2ml of autologous serum deepintramuscular injection once a week for 9 weeks. In addition to these, patients in all the groupswere prescribed Antihistamines. Group D was be the control group who was receive only Antihistamines. **Results:** More than 80% of patients treated with ASST had good response to treatment while only 50% of those treated with dapsone and 30% of those treated with methotrexate had good response to treatment. Poor response was seen in 4% of ASST and Dapsone patients comparedto the 18% in patients receiving Methotrexate. This is still better than the 64% with poor response in the control group. The mean DLQI score across all the treatment groups when compared showed that, patients treated with ASST had the fastest and the maximal response. Both the initial response and the end point was better in ASST patients. Control group patientsshowed no significant improvement in DLQI score. The dapsone and methotrexate treated patients had similar response profile but there was a difference in the number of patients responding. **Conclusion:** We determined that ASST may be regarded as the first therapy option for individuals with chronic urticaria, particularly for those who test positive for Autologous Serum Skin Test. Dapsone may be an option for people who do not respond to standard therapy.Methotrexate is advised for individuals who have not responded to previous treatment optionsand is considered a last option.

Keywords: Chronic Urticaria, Dapsone, ASST, Methotrexate, DLQI

INTRODUCTION

Urticaria is a skin condition characterized by a raised region of localized swelling (wheal) surrounded by redness (erythema) that is usually itchy. Each lesion might persist for a durationranging from 30 minutes to 36 hours. They may range in size from a millimeter to 6–8 inchesin diameter, known as enormous urticaria. The skin becomes pale under pressure when the expanded blood vessels are squeezed, resulting in the whitish center of the raised bump[1,2]. Urticaria affects 15% to 20% of the population. The lifetime prevalence of chronic urticaria ranges from 0.05% to 23.6% in the general population, with a more reasonable estimate fallingbetween 1% and 5%. There is no racial disparity in the occurrence. Urticaria is more prevalentin women, with a female-to-male ratio of about 2:1 for chronic cases[3]. Chronic Urticaria is a significant issue because to its origins, research, and therapy, leading to comorbidity and high costs for the healthcare system. Chronic urticaria (CU) is a prevalent skin condition that affects 15–20% of individuals in the general population. Carpal tunnel syndrome may be categorized into three clinical groupings based on its length, frequency, and causes: spontaneous (80%), physical (10%), and special types (10%). Chronic spontaneous urticaria (CSU), sometimes called chronic idiopathic urticaria, is defined by the sudden appearance of hives without a clear trigger persisting for over 6 weeks. The origin of CSU is uncertain, although potential factors may

include chronic infections, food allergies, anxiety, and the formation of autoantibodies against IgE receptors. Our research involves assessing the efficacy of ASST, Dapsone, and Methotrexate in treating resistant chronic urticaria. These research results will be crucial in establishing therapy guidelines for people suffering with chronic urticaria.

MATERIALS AND METHODS

A prospective comparison research was conducted on 200 patients with chronic urticaria chosen from those visiting the outpatient clinic at the Department of Dermatology. This research included patients over 18 years old with Chronic Urticaria, which is defined as an urticarial eruption lasting more than 6 weeks and marked by hives or wheals, who did not respond to therapy with anti-histamines. Patients under 18 years old or over 60 years old, those with physical urticaria or urticaria caused by an underlying medical condition, pregnant or breastfeeding women, those trying to conceive, individuals with underlying medical conditions, and those who have received treatments other than antihistamines were not included in the study.

METHODOLOGY

Approximately 200 individuals with chronic urticaria will be chosen among those visiting the psoriasis outpatient clinic at the Department of Dermatology. All patients were informed about the condition, advantages, and potential therapy adverse effects. A comprehensive history was collected, and patients will be assessed as outlined below. A comprehensive examination was conducted, including a dermatological assessment and several investigations such as complete blood count, liver function tests, renal function tests, autologous serum skin test, chest X-ray. Additionally, opinions from ENT and Dental specialists were obtained to exclude localized sepsis. The patients were randomly assigned to one of four therapy groups based on their Urticarial Activity Score (UAS) and Dermatology Life Quality Index (DLQI).

- Group A was comprising patients who was given oral Dapsone 50 mg for a period of 12 weeks.
- Group B was comprising patients who was given oral Methotrexate 10 mg (in 4 divided doses at 12 hourly interval) per week for a period of 12 weeks.
- Group C was comprising patients who was given Treated with ASST (Autologous Serum Skin Therapy) – 2ml of autologous serum deep intramuscular injection once a week for 9weeks.

In addition to these, patients in all the groups were prescribed Antihistamines.

- Group D was be the control group who was receive only Antihistamines.

Patients was reviewed every 4 weeks at 4, 8 &12 weeks for complaints and assessing clinical improvement till completion of treatment and once every two months for six months following completion. Blood parameters was repeated every four weeks or as and when required and Parameters like Urticarial Activity Score (UAS) and Dermatology Life Quality Index (DLQI) was assessed at end of treatment and at end of six months following treatment. Patients were then divided into three categories based on these parameters into Good Responders, Average Responders & Poor Responders.

- Good Responders: Patients post treatment UAS score < 2 and DLQI score < 2
- Average Responders: Patients post treatment UAS score 2 - 4 & DLQI score 2 - 9
- Poor Responders: Patients post treatment UAS score > 4 and DLQI score > 10 The higher of the two scores is taken into consideration while classifying the groups.

STATISTICAL ANALYSIS

The collected data was systematically organized, shown in tables and figures, and statistically analyzed using Statistical Package for Social Science (SPSS) version 24 to assess the study'sgoals.

RESULTS

The present study observed that age of 200 patients ranged from 18- 60 years. Most of the patients (55%) were in between 18-30 years. Females were the predominantly involved sex with male to female ratio of 0.45:1 (table 1).

Table1: Age and gender Distribution of Patients with Chronic Urticaria

Gender	Number	Percentage
Male	62	31
Female	138	69
Age in years		
18 - 30	110	55
30 - 40	56	28
40 - 50	23	11.5
50- 60	11	5.5

Regarding precipitating factors, food allergens were the most common precipitating factor accounting for 15.5% of the cases, followed by infections & inhalants like house dust seen in 11% of cases. The other precipitating factors were drugs and water related. 52% of the total patients had no specific aggravating or trigger factor for

occurrence of symptoms (table2).

Table 2: Prevalence of precipitating factors in chronic urticaria patient

Precipitating Factor	No. of Patients	Percentage
Food	31	15.5
Infections	22	11
Inhalant	22	11
Drugs	15	7.5
Aquagenic	6	3
No Specific Factor	104	52

More than 80% of patients treated with ASST had good response to treatment while only 50% of those treated with dapsone and 30% of those treated with methotrexate had good response to treatment. Poor response was seen in 4% of ASST and Dapsone patients compared to the 18% in patients receiving Methotrexate. This is still better than the 64% with poor response in the control group (table 3).

Table 3: Distribution of response to treatment of all four groups of patients

	Good	Average	Poor	Total
ASST	40 (80%)	8(16%)	2 (4%)	50
Methotrexate	15(30%)	26 (52%)	9 (18%)	50
Dapsone	25(50%)	23 (46%)	2 (4%)	50
Control	3 (6%)	15 (30%)	32 (64%)	50
Total	83 (41.4%)	72(36%)	45(22.5%)	200

The mean DLQI score across all the treatment groups when compared showed that, patientstreated with ASST had the fastest and the maximal response. Both the initial response andthe end point was better in ASST patients. Control group patients showed no significant improvement in DLQI score. The dapsone and methotrexate treated patients had similarresponse profile but there was a difference in the number of patients responding (table 4).

Table 4: Average DLQI score of patients in different treatment groups

	ASST			Methotrexate			Dapsone			Control		
Months	Good	Ave.	Poor	Good	Ave.	Poor	Good	Ave.	Poor	Good	Ave.	Poor
0	9	16	19	8	12	17	8	11	16	6	10	15
3	6	8	14	5	8	13	3	8	11	4	8	12
6	1	5	8	1	6	11	1	5	9	2	5	10

There is a statistically significant difference in response to treatment to all three groups whencompared to control, with it being highly significant in the ASST group. On comparing ASST with dapsone or methotrexate, there is again a statistically significant difference in response while there was no statistically significant difference when comparing dapsone andmethotrexate.

Side effects were more common in patients taking methotrexate with 5 out of 50 patients experiencing minor side effects while 3 patients taking dapsone also had documented side effects (table 5).

Table 5: Prevalence of side effects in each treatment group

Treatment group	No. of Patients	Total patients treated	Percentage
ASST	0	50	0
Methotrexate	5	50	10
Dapsone	3	50	6
Control	0	50	0

DISCUSSION

Handling chronic urticaria situations may be laborious and exasperating, leading to significant healthcare costs and socio-economic consequences due to decreased productivity by 20-30% in many instances [5,6]. Corticosteroids were first used to treat these instances. Retrospective research by Asero R et al found that 50% of patients achieved remission when treated with 0.3-0.5 mg/kg of prednisolone. The dosage started at 25 mg per day for three days, then was quickly reduced over a period of 10 days. Remissions were only managed with antihistamines [7]. however, the use of corticosteroids is associated with many long-term complications that adversely affect the treatment. Complications like hypertension, GI bleeding, glucose intolerance and weight gain have seen to affect the treatment outcome. Thus, their use became restricted to only short duration of management [8]. Evidences have been shownin literature regarding the use of dapsone for management of chronic spontaneous urticaria. Use of dapsone was first published by I Boehm et al in the year 1999[9]. Now days methotrexate is used for the management of chronic urticaria cases. Methotrexate is basically an

anti-metabolite used for management of chronic inflammatory diseases [10-11]. Methotrexate acts through various mechanisms but in managing cases of urticaria its immunomodulatory and anti-inflammatory actions come into use [12-14]. The present studyobserved that age of 200 patients ranged from 18- 60 years. Most of the patients (55%) werein between 18-30 years. Females were the predominantly involved sex with male to female ratio of 0.45:1. Young females were the most commonly involved group. Twenty to thirty years was the susceptible age group along with female gender. This is in accordance with other Indian studies regarding the epidemiology of the disease. One or other form of precipitating factor was present in more than half of all the patients involved in the study. The most commonly implicated precipitating factor in our study was food allergens followed by infections and inhalants. A study by Godse et al[15] showed that infections and food allergens were important precipitating factors in the Indian population. In the ASST group, all patients had a significant reduction in their DLQI score with only one patient having poorresponse, which was explained by the fact that both those patients had a severe initial presentation. The response was especially good among those in whomthe autologous serum skin test was positive. This response to ASST was found to be in concurrence with studies by Bajaj et al[16] and Staubach et al[17]. Compliance was good and there was no evidence of relapse. The only factor which hinders with their use, especially ina government setup, is the technological expertise and the availability of centrifuge machines.

In the Dapsone group, again there was a statistically significant improvement in response compared to the control group, but they compared unfavourably with ASST treatment group.The initial response was slower than that of ASST but the end point was similar especially in those responding well to treatment. There was good compliance, even though a couple ofpatients had minor side effects. These findings had concordance with studies conducted by Cooke et al[18] and Engen et al[19].

In the methotrexate group, the drop in the DLQI score was delayed compared to other groups, with a response beginning towards the end of the treatment period. They outperformed the control group, but their early reaction and final outcomes were subpar compared to ASST. Their reaction was similar to the individuals treated with dapsone, although its use is restricted in patients with anemia and abnormal liver function tests. Anemia is frequent in our community, which restricts its usage in patients. Additionally, the frequency of adverse effects was higher in this group. Research conducted by Sharma et al[20] recommended the use of methotrexate for those with chronic refractory urticaria who do not show improvement with conventional treatment methods.

CONCLUSION

We determined that ASST may be regarded as the first therapy option for individuals with chronic urticaria, particularly for those who test positive for Autologous Serum Skin Test. Dapsone may be an option for people who do not respond to standard therapy. Methotrexate is advised for individuals who have not responded to previous treatment options and is considered a last option. The side effects and contraindications in people with hematological issues limit its widespread use.

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