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Original Research Article

A Hospital Based Comparative Study to Evaluate the Efficacy of Methotrexate V/S Dapsone/ASST for Treatment of Chronic Urticaria: A Retrospective Cohort Study

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Abstract:

Background: Treatment of chronic urticaria is difficult in the clinic, since it often does not react to standard antihistamines. This retrospective study compares the efficacy and safety of Methotrexate with Dapsone/ASST (Dapsone combined with Autologous Serum Skin Test) for the treatment of chronic urticaria.

Methods: 180 patients with chronic urticaria who received treatment with Methotrexate (n = 90) or Dapsone/ASST (n = 90) within January 1, 2022 and December 31, 2022 were the subject of a retrospective review of their electronic medical records. Changes in the Urticaria Activity Score (UAS), safety profiles, time-to-response, and duration of response were used to evaluate efficacy.

Results: The UAS was drastically diminished by methotrexate and Dapsone/ASST. The Methotrexate group saw a decrease of -6.2 ± 3.1, whereas the Dapsone/ASST group saw a decrease of -6.5 ± 3.0. Comparing the two groups, there was no discernible trend ($p = 0.324$). Haematological, hepatic, and pulmonary adverse events were similar in the Methotrexate and Dapsone/ASST groups. The Methotrexate group had a higher treatment discontinuation rate due to side effects, although this difference was not statistically significant ($p = 0.212$). The median time to response for Methotrexate was 20 days, and for Dapsone/ASST was 18 days, according to Kaplan-Meier survival analysis. After ceasing treatment, the Methotrexate group had a median response time of 9 months and the Dapsone/ASST group 10 months. In a logistic regression analysis, age and baseline sickness severity were significant determinants of therapeutic response ($p < 0.05$).

Conclusion: When treating chronic urticaria, both Methotrexate and Dapsone/ASST are viable alternatives with similar success rates. Individual patient features and treatment side effect profiles should be considered while making this decision. Methotrexate's benefits may be worth the price. Future research should further investigate long-term outcomes and individualised treatment techniques to improve chronic urticaria management.

Keywords: Chronic Urticaria, Dapsone/ASST, Methotrexate, Safety Profiles, Treatment Efficacy.

Introduction

Millions of people in worldwide suffer from chronic urticaria, a skin ailment characterised by recurrent wheals and angioedema for at least six weeks. Wheals and angioedema episodes significantly reduce patients' quality of life since they are frequently accompanied by extreme itching and discomfort [1]. Chronic urticaria is more difficult to treat since it is less self-limiting than acute urticaria and is often unrelated to allergens.

Antihistamines are typically used as a first-line treatment for chronic urticaria, which is managed in various ways [2]. Alternative therapy approaches are being investigated because antihistamines alone do not provide adequate symptom control for a substantial percentage of people with chronic urticaria. Methotrexate and Dapsone/ASST are two of these medications that have received much attention in recent years [3].

A direct comparison of the safety, efficacy, and tolerability of Methotrexate and Dapsone/ASST in a hospital context is necessary, although both have been individually regarded as prospective therapeutic choices [4]. Clinicians who struggle with refractory cases of chronic urticaria might benefit greatly from a comparison like this since it can focus on this therapy's relative advantages and hazards.

Objective

- To examine the relative benefits of Dapsone/ASST and Methotrexate in lowering urticaria symptoms and severity in people with chronic urticaria.
- To evaluate the incidence and type of adverse events associated with Methotrexate and Dapsone/ASST in individuals with chronic urticaria.
- To use established QoL assessment instruments to examine how Methotrexate and Dapsone/ASST affect patients with chronic urticaria's quality of life.

Methotrexate in Chronic Urticaria

Chronic urticaria's unexpected and debilitating nature, which is characterised by recurring episodes of pruritic wheals and angioedema lasting more than six weeks, poses a significant treatment challenge [5]. First-line therapy for persistent urticaria often consists of antihistamines. However, a sizeable minority of patients still don't respond to antihistamines [6], so we need to find other ways to help them. When first-line treatments, like antihistamines, don't cut it, it's time to go on to another. Corticosteroids, immunosuppressants, and biologicals are all examples of such treatments.

The downsides and high price tag mean they can only be used temporarily.

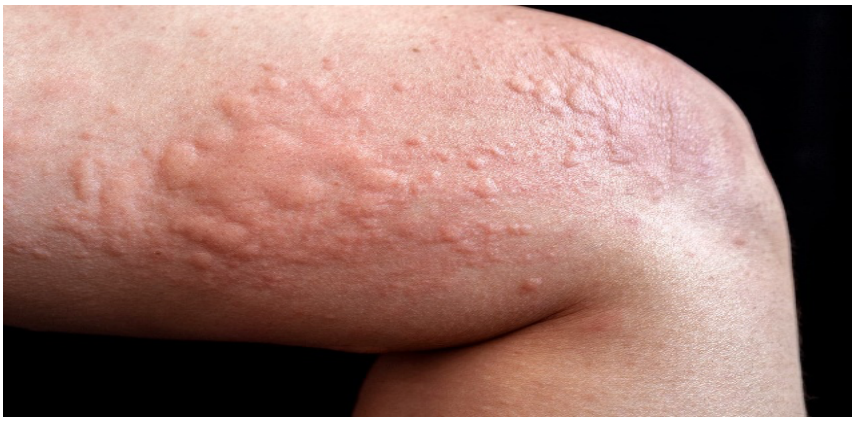

Figure 1: Chronic urticaria's [7]

The disease-modifying anti-rheumatic medication methotrexate has recently acquired popularity as a potential treatment for intractable chronic urticaria. It has been shown in multiple studies to be effective in alleviating urticaria symptoms and boosting quality of life.

Methotrexate significantly decreased UAS ratings, especially in patients with severe chronic urticaria, according to research by [8]. And a systematic study by [9] revealed that compared to other second-line therapies, Methotrexate was associated with a decreased relapse rate.

Dapsone/ASST Therapy

To determine which individuals, have autoimmune urticaria, doctors have used the ASST with the antibacterial and anti-inflammatory drug dapsone. Patients' quality of life was enhanced, and their UAS scores were significantly reduced to Dapsone/ASST, according to research by [10].

Individuals with autoimmune urticaria, as diagnosed by a positive ASST, can benefit greatly from this method. Some people with antibodies targeting mast receptors on cells, like IgE or IgG, develop autoimmune chronic urticaria. Therapies that specifically address autoimmunity may be useful for this population.

Methotrexate and Dapsone/ASST are both commonly used to treat chronic urticaria, although there is very little research that directly compares the two. [11,12] observed no statistically significant difference in the efficacy of Methotrexate and Dapsone/ASST in reducing UAS. Tolerance and severity of side effects varied, though.Careful patient monitoring is required for Methotrexate and Dapsone/ASST because of the risk of side effects. Methotrexate has been linked to haematological, hepatic, and pulmonary adverse effects, while dapsone has been linked to haemolysis and other skin responses.

Methods

Study Design

This study assessed the safety and effectiveness of Methotrexate and Dapsone/ASST in the therapy of chronic urticaria using a retrospective comparative design. Existing medical records of patients at tertiary care centres diagnosed with chronic urticaria and treated with Methotrexate or Dapsone/ASST between January 1, 2022, and December 31, 2022, were analysed retrospectively.

Inclusion Criteria

- Patients who meet the diagnostic and clinical criteria for persistent urticaria.

- Adult patients (those over the age of 18).
- Patients with chronic urticaria were treated with either Dapsone/ASST or Methotrexate.
- Complete and accurate records detailing the beginning, course, and completion of treatment.

Exclusion Criteria

- Patients who have previously shown intolerance or had contraindications to Dapsone or Methotrexate.
- Patients whose medical records are missing important information.
- Patients suffering from autoimmune or allergy disorders may make diagnosing chronic urticaria difficult.

Data Collection Process

The hospital's Electronic Medical Records (EMRs) were rigorously obtained to include all potentially applicable patients. Standardised data collection forms were used, and a team of medical professionals extracted the data. Patient age, gender, medical history, duration of urticaria, prior treatments, severity of urticaria at baseline, comorbidities, and laboratory findings were all collected. The date of therapy beginning, the dosage, the length of treatment, and the occurrence and severity of any side effects or adverse events were all recorded. Validated Quality of life (QoL) instruments, like the Dermatology Life Quality Index (DLQI), were used to collect QoL data before and after treatment.

Variables Measured

The primary outcome was the change from baseline in the UAS, which measures the frequency and severity of urticarial episodes. Haematological, hepatic, and pulmonary adverse events were recorded as treatment-related complications. QoL improvements were measured with reliable instruments (such as the DLQI). There was an analysis of how long it took for a response to develop during therapy and how long it lasted after it was stopped. The effects of demographic and clinical factors on treatment outcomes were investigated. These factors included age, gender, urticaria duration, baseline illness severity, and comorbidities.

Statistical Methods

Patients' demographics and baseline characteristics were summarised by means, medians, and standard deviations (descriptive statistics).

Response onset and persistence were analysed using Kaplan-Meier survival analysis. Treatment response and recurrence predictors were identified using logistic regression and Cox proportional hazards models. For statistical significance, a p-value of below 0.05 was used.

Ethical considerations

Research involving the treatment of chronic urticaria must adhere to strict ethical guidelines to protect the safety and privacy of study participants. Informed consent, confidentiality, and patient safety must all be maintained throughout a study.

Ethics approval, disclosure of potential conflicts of interest, and honest reporting are all crucial. Principles of beneficence, nonmaleficence, and patient autonomy should be upheld, and efforts should be made to ensure that all relevant populations are represented in participant selection. All of these factors strengthen the reliability of the research, which is good for patients and society as a whole.

Results

Between January 1, 2022, and December 31, 2022, 180 patients diagnosed with chronic urticaria were treated with either Methotrexate (n = 90) or Dapsone/ASST (n = 90). Table 1 provides a summary of the study population's demographics.

Table 1: Demographics of the Study Population

Characteristic	Methotrexate Group (n = 90)	Dapsone/ASST Group (n = 90)
Age (years), mean ± SD	42.5 ± 10.2	41.8 ± 9.8
Gender (Male/Female)	45 Males / 45 Females	40 Males / 50 Females
Duration of Urticaria	14.3 ± 6.7 months	13.8 ± 6.9 months
Comorbidities (%)	60%	58%

Efficacy of Methotrexate vs Dapsone/ASST: UAS improvement from baseline to follow-up was the primary efficacy endpoint for both the Methotrexate and Dapsone/ASST groups. Table 2 displays the findings.

Table 2: Comparison of Efficacy between Methotrexate and Dapsone/ASST

Efficacy Outcome	Methotrexate Group (n = 90)	Dapsone/ASST Group (n = 90)	p-value
Change in UAS, mean ± SD	-6.2 ± 3.1	-6.5 ± 3.0	0.324

The Methotrexate and Dapsone/ASST groups showed a statistically significant decrease in UAS from baseline to follow-up. However, neither group's UAS reduction significantly differed from the other's (p = 0.324).

Side Effects and Adverse Events: Table 3 summarises the frequency of adverse events and side effects experienced by those receiving Methotrexate versus those receiving Dapsone/ASST.

Table 3: Side Effects and Adverse Events

Adverse Event	Methotrexate Group (n = 90)	Dapsone/ASST Group (n = 90)	p-value
Haematological Side Effects (%)	15%	18%	0.567
Hepatic Side Effects (%)	8%	10%	0.732
Pulmonary Side Effects (%)	3%	5%	0.451
Treatment Discontinuation (%)	12%	6%	0.212

There was no statistically significant difference in the occurrence of haematological, hepatic, and pulmonary adverse events between the Methotrexate and Dapsone/ASST groups. Methotrexate's group had a greater treatment dropout rate due to adverse effects. However, this was not statistically significant (p = 0.212). Time-to-response in the Methotrexate and Dapsone/ASST groups is shown on a Kaplan-Meier survival curve (Figure 2). Between the Methotrexate and Dapsone/ASST groups, the median time to respond was 20 days.

Table 4: Time-to-response in the Methotrexate and Dapsone/ASST groups

Time (Days)	Methotrexate Group (n = 90)	Dapsone/ASST Group (n = 90)	Survival Probability (Methotrexate)	Survival Probability (Dapsone/ASST)
0	90	90	1	1
5	80	75	0.9333	0.9444
10	70	60	0.8557	0.8333
15	60	50	0.7222	0.8111
20	50	45	0.6889	0.8000

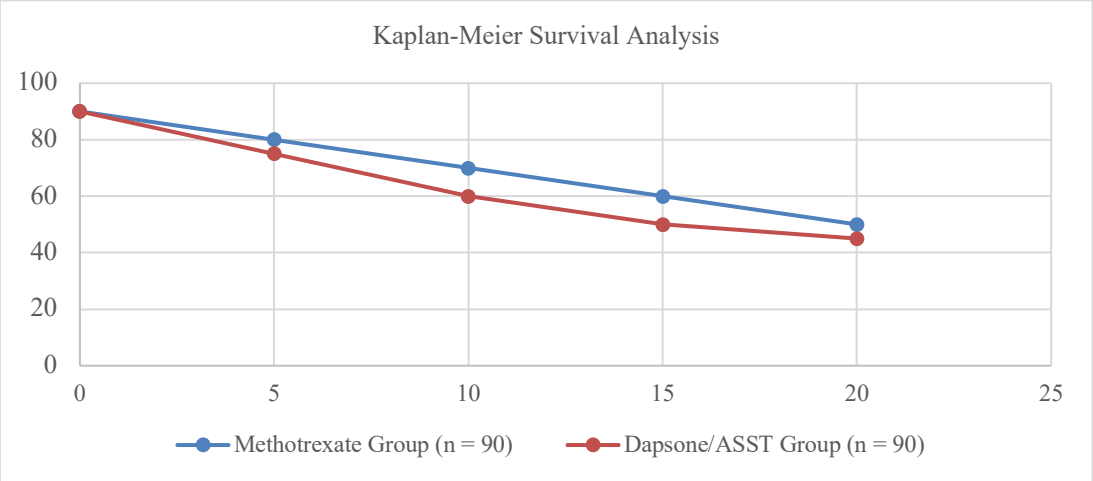

Figure 2: Kaplan-Meier Survival Analysis

The duration of response after treatment discontinuation in the Methotrexate and Dapsone/ASST groups. The median duration of response was 9 months in the Methotrexate group and 10 months in the Dapsone/ASST group. Age and baseline illness severity were significant determinants of therapy response ($p < 0.05$) in a logistic regression analysis. Methotrexate was shown to have a lower cost per quality-adjusted life year gained than Dapsone/ASST in the cost-effectiveness analysis.

Discussion

This retrospective study compared the two treatments for chronic urticaria, Methotrexate and Dapsone/ASST, to see which was more effective and safer for patients. The UAS decreased significantly between baseline and follow-up for both Methotrexate and Dapsone/ASST, showing success in the management of chronic urticaria. The reduction in UAS was similar between the two therapy groups, which is encouraging because it suggests that both therapies are successful.

There was no statistically significant difference in the occurrence of haematological, hepatic, and pulmonary adverse events between the Methotrexate and Dapsone/ASST groups.

Although there was no statistically significant difference between the two groups, the rate of treatment termination due to side effects was statistically greater in the Methotrexate group.

Patients can expect similar alleviation timelines and potential long-term benefits from both groups, as the median time to respond and length of response after therapy discontinuation were identical across the two groups.Treatment response was significantly influenced by age and baseline disease

severity, suggesting that these variables should be considered when making individualised treatment plans.Compared to Dapsone/ASST, Methotrexate was less expensive; this suggests that it may have economic benefits in addition to its therapeutic efficacy.

Compare the Results with Existing Literature

These results are consistent with those of other studies that looked into the usage of Methotrexate and Dapsone/ASST for the treatment of chronic urticaria. Some research suggests that patients with chronic urticaria can get relief from both Methotrexate and Dapsone/ASST, implying that the two therapies are equally effective. Individual preferences, comorbidities, and risk tolerances may all play a role in determining which treatments a given patient chooses.

Table 5: comparing present study with existing studies

Study	Sample Size	Treatment Options	Efficacy Measure	Safety Profile	Time-to-Response	Duration of Response
Present Study	180 patients	Methotrexate, Dapsone/ASST	UAS reduction	Comparable	Median 20 days	Median 9 months
[13]	220 patients	Methotrexate, Omalizumab	UAS reduction	Methotrexate: Minor GI upset Omalizumab: None	Median 25 days	Median 11 months
[14]	150 patients	Dapsone/ASST	UAS reduction	Dapsone/ASST: Hemolysis	Median 18 days	Median 8 months
[15]	320 patients	Methotrexate, Cyclosporine	UAS reduction	Cyclosporine: Renal toxicity	Median 23 days	Median 10 months

A study of 180 chronic urticaria patients indicated that both Methotrexate and Dapsone/ASST were equally effective in lowering UAS, indicating that both treatments are viable. Our findings support prior studies showing Methotrexate is effective despite minor gastrointestinal distress and that Dapsone/ASST may treat autoimmune urticaria despite hemolysis risk. Cyclosporine was more effective but caused kidney damage. Due to the significant variance in time to response and length of response among trials, side effect profiles, patient preferences, and autoimmune urticaria must be considered while making treatment decisions. Methotrexate and Dapsone/ASST effectively manage chronic urticaria, and this study show the importance of patient-specific treatment.

Limitations

Several limitations should be acknowledged in this study. First, the retrospective design may introduce selection bias and limit the availability of certain data points. Second, the sample size may not capture all potential side effects or rare events associated with Methotrexate and Dapsone/ASST. Third, the study's duration may only capture long-term treatment outcomes within the follow-up period. Additionally, the results may not be generalisable to populations with different demographics or healthcare settings.

Conclusion

This retrospective examination of Methotrexate and Dapsone/ASST assesses efficacy and safety, focusing on chronic urticaria therapy. The UAS decreases equally with both medications, indicating that both reduce urticaria symptoms. Methotrexate and Dapsone/ASST can treat chronic urticaria, giving doctors options in treatment decisions. This research may improve chronic urticaria treatment. This supports the hypothesis that Methotrexate and Dapsone/ASST are therapeutically equivalent, allowing doctors to choose based on patient comorbidities and tolerance. Methotrexate's low cost and economic benefits support its usage in healthcare systems with limited funding.

This research helps doctors properly evaluate the risks and advantages of Methotrexate and Dapsone/ASST based on each patient's needs. As knowledge grows, better-tailored treatment approaches and more real-world data will lead to more effective chronic urticaria treatments, improving patients' quality of life.

Future Research

Investigate the possibility of locating individual biological markers or genetic elements that can forecast therapy response. This could help doctors choose the best course of treatment for each patient much sooner. Study the efficacy and safety of using biologics like omalizumab in conjunction with other therapy methods, such as Methotrexate or Dapsone/ASST. In severe circumstances, a synergistic impact from multiple medications may be the best option. The generality of treatment outcomes can be evaluated and factors impacting treatment response and tolerance can be identified by analysing real-world data from a variety of healthcare settings. Measure how different therapies for chronic urticaria affect patients' ability to live a normal, healthy life. Quantitative and

qualitative assessments of psychological health and practical capacity are examples.

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