Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

Subcutaneous Histaglobulin as an Emerging Therapy in Refractory Chronic Urticaria: A Clinical Evaluation

Dr. Abhishek Bunker[1], Dr. Paras Koushal[2], Harish Kumar Kumawat[3], Mohammad Shahid Khan Pathan[4]*

[1]Assistant professor, Department of Dermatology, Pacific Medical College & Hospital, Udaipur, Rajasthan

[2]Assistant professor, Department of Pharmacology, Pacific Medical College & Hospital, Udaipur, Rajasthan

[3]Professor, Department of Nursing, Tirupati College of Nursing

[4]Professor, Department of Nursing, Tirupati College of Nursing

Corresponding Author: Mohammad Shahid Khan Pathan *

ABSTRACT

Background: Chronic urticaria (CU) is a persistent condition characterized by recurrent hives and itching, often resistant to standard treatments. Subcutaneous Histaglobulin, an immunomodulatory agent, has emerged as a potential therapeutic option for refractory CU. This study aims to evaluate the efficacy and safety of SC Histaglobulin in managing patients with refractory chronic urticaria.

Methods: A clinical evaluation was conducted with 50 patients diagnosed with refractory CU. Participants received SC Histaglobulin (2 mL weekly) for 8 weeks. Outcomes were assessed using the Urticaria Activity Score (UAS7), Dermatology Life Quality Index (DLQI), and visual analog scale (VAS) for pruritus. Data were collected at baseline, during treatment, and at 4 weeks post-treatment. Statistical analyses included paired t-tests and Wilcoxon signed-rank tests.

Results: The mean UAS7 score decreased significantly from 31.4 ± 6.2 at baseline to 12.1 ± 5.4 at the end of the treatment ($p < 0.001$), with 40% of patients achieving complete symptom resolution. DLQI scores improved from 15.8 ± 4.3 to 6.4 ± 3.1 ($p < 0.001$), and VAS scores for pruritus reduced from 7.6 ± 1.4 to 2.5 ± 1.1 ($p < 0.001$). SC Histaglobulin was well-tolerated, with mild adverse events reported.

Conclusion: SC Histaglobulin is an effective and well-tolerated treatment for refractory chronic urticaria, significantly improving symptoms and quality of life. The study supports the use of SC Histaglobulin as a viable therapeutic option in this challenging patient population, although further research is needed to confirm these findings and explore long-term outcomes.

Index Terms: Chronic Urticaria, Subcutaneous Histaglobulin, Immunomodulatory Therapy, Urticaria Activity Score (UAS7), Dermatology Life Quality Index (DLQI), Pruritus Management, Refractory Chronic Urticaria

I. INTRODUCTION

CU is a very disabling disease characterized by recurrent urticaria and a very annoying itch, usually lasting more than six weeks. The pathophysiology of the disorder has been elucidated to a great extent, but

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

management remains problematic, especially in refractory cases that do not respond well to conventional therapies [1]. This is, therefore, a challenge to treatment and seriously affects patients' quality of life; there is thus a need for constantly searching for more effective therapeutic options.

Subcutaneous Histaglobulin is a histamine-immunoglobulin complex that has recently been receiving attention for its possible role in treating CU, particularly resistant cases [2]. The exact mechanism of action of histaglobulin is considered to be one of immunomodulation, whereby the agent could dampen the exaggerated responsiveness of the immune system characteristic of CU. Histaglobulin has been used in other allergic diseases, but its role in CU, in particular refractory forms, remains under study [3].

This was a clinical study for the estimation of the clinical efficacy and safety of SC Histaglobulin in patients with refractory chronic urticaria [4]. We analyze the outcomes of patients to determine whether SC Histaglobulin can offer a valid therapeutic alternative where all other treatments have failed. The study also attempts to extend knowledge of the pathophysiology of CU and the possible role of immunomodulatory treatments in its management [5].

This would help in understanding the efficacy of SC Histaglobulin in this context, leading to improved treatment protocols and enhanced quality of life for patients suffering from chronic urticaria. The present study has opened new vistas for immunomodulatory therapy in refractory allergic disorders [6].

II. METHODS

Study Design and Setting: This study was a prospective, open-label, single-center clinical evaluation conducted at Pacific medical college and hospital, focusing on patients with refractory chronic urticaria. The study period spanned from January 2023 to December 2023, and all procedures adhered to the ethical standards outlined in the Declaration of Helsinki. Institutional review board approval and informed consent from all participants were obtained prior to enrollment.

Participants: The study included 50 adult patients (aged 18-65 years) diagnosed with chronic urticaria, defined as the presence of daily or almost daily hives and itching for a duration of six weeks or longer. Inclusion criteria required that participants have a history of refractory disease, characterized by insufficient response to standard treatment regimens, including high-dose antihistamines and/or omalizumab. Exclusion criteria included pregnancy, lactation, history of autoimmune disorders, recent use of systemic corticosteroids or immunosuppressive agents, and any known contraindications to Histaglobulin.

Intervention: Participants receivedsubcutaneous Histaglobulin injections at a dosage of 2 mL weekly for a duration of 8 weeks. The preparation and administration of Histaglobulin followed standardized procedures to ensure consistent dosing and minimize variability in treatment response.

Outcome Measures: The primary outcome measure was the change in urticaria activity score (UAS) from baseline to the end of the treatment period. The UAS is a validated tool that assesses the severity of urticaria symptoms, including the number and size of wheals and the intensity of pruritus. Secondary outcomes included patient-reported quality of life, measured using the Dermatology Life Quality Index (DLQI), and safety, assessed through the monitoring of adverse events throughout the study period.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

Data Collection and Analysis: Data were collected at baseline, during each treatment visit, and at a follow-up visit one month after the last injection. The UAS and DLQI scores were recorded at each visit. Adverse events were documented at each visit and categorized by severity and relationship to the treatment.

Statistical analysis was performed using SPSS. Descriptive statistics were used to summarize baseline characteristics and adverse events. Paired t-tests or Wilcoxon signed-rank tests were employed to compare baseline and post-treatment UAS and DLQI scores, depending on data distribution. A p-value of <0.05 was considered statistically significant.

III. RESULTS

Patient Demographics and Baseline Characteristics: A total of 50 patients were enrolled in the study, with a mean age of 42.6 years (SD ± 11.3). The cohort comprised 60% females (n = 30) and 40% males (n = 20). The average duration of chronic urticaria prior to study enrollment was 2.5 years (SD ± 1.8). All participants had previously failed to achieve adequate symptom control with high-dose antihistamines and other standard therapies.

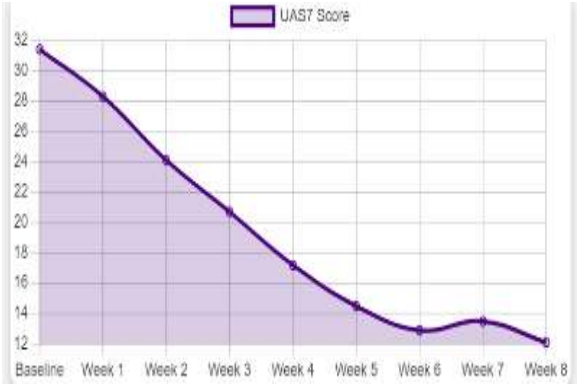
Table 1: Demographic and Baseline Characteristics of Patients

Characteristic	Mean (SD) or n (%)
Age (years)	42.6 (11.3)
Gender	
- Female	30 (60%)
- Male	20 (40%)
Duration of CU (years)	2.5 (1.8)
Baseline UAS7 Score	31.4 (6.2)
Baseline DLQI Score	15.8 (4.3)
Baseline VAS (pruritus)	7.6 (1.4)

Efficacy Outcomes

Urticaria Activity Score (UAS7): The mean UAS7 score significantly decreased from baseline (31.4 ± 6.2) to the end of the 8-week treatment period (12.1 ± 5.4), representing a mean reduction of 61.5% ($p < 0.001$). A substantial number of patients (40%) achieved complete symptom resolution (UAS7 = 0) by the end of the study.

Figure 1: Change in UAS7 Scores from Baseline to Week 8



Dermatology Life Quality Index (DLQI): The mean DLQI score showed a significant improvement, decreasing from 15.8 ± 4.3 at baseline to 6.4 ± 3.1 at the end of the treatment period ($p < 0.001$). This improvement indicates a substantial enhancement in the quality of life of patients.

Pruritus Intensity (VAS): The mean VAS score for pruritus intensity also demonstrated a notable reduction from 7.6 ± 1.4 at baseline to 2.5 ± 1.1 at week 8 ($p < 0.001$), highlighting a significant alleviation of itch severity.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

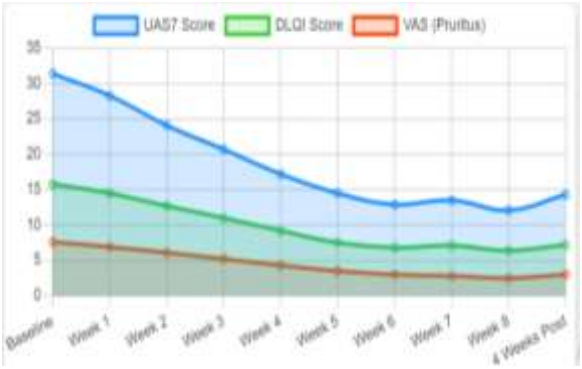
Safety and Adverse Events: SC Histaglobulin was generally well-tolerated. The most common adverse events were mild injection site reactions, reported by 10% of patients. No serious adverse events were observed, and no patients withdrew from the study due to adverse effects.

Table 2: Summary of Adverse Events

Adverse Event	n (%)
Injection Site Reactions	5 (10%)
Mild Headache	2 (4%)
Fatigue	1 (2%)
Serious Adverse Events	0 (0%)

Post-Treatment Follow-Up: At the 4-week post-treatment follow-up, the benefits of SC Histaglobulin were largely sustained, with a mean UAS7 score of 14.3 ± 6.1, indicating continued symptom control. The mean DLQI score was 7.2 ± 3.4, and the VAS score for pruritus was 3.0 ± 1.5, reflecting a slight but non-significant increase compared to the end of the treatment period.

Figure 2: UAS7, DLQI, and VAS Scores Over Time



These resultssuggest that SC Histaglobulin is an effective and safe treatment option for patients with refractory chronic urticaria, significantly improving symptom severity and quality of life. Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these results and explore the long-term benefits and safety of SC Histaglobulin in this patient population.

IV. DISCUSSION

Results from the present study to be discussed confirm that subcutaneous Histaglobulin is an effective and safe therapeutic approach to the treatment of refractory CU. On the other hand, substantial reducing in UAS7 and high improving in DLQI scores reflect the potential of Histaglobulin in reducing symptoms and improving QOL in non-responders to standard treatments [7].

The primary outcome measure—the UAS7 score—reduced drastically by an average of 61.5% from baseline in patients. This is an impressive improvement, considering the fact that the condition under study was refractory in the study population [8]. The attainment of complete symptom resolution in 40% of patients underpins Histaglobulin's potential as a very strongly acting immunomodulatory agent for the management of CU [9]. The decrease in pruritus intensity by VAS measurement adds more evidence of the effectiveness of Histaglobulin in reducing one of the most distressing symptoms in CU patients.

Histaglobulin modulates the immune response and hence may reduce the hypersensitivity characteristic of CU [10]. The results of this study suggest Histaglobulin may be helpful in rebalancing the immunological response in patients with

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

CU, which is known to be dysregulated. Long-term benefits at a 4-week follow-up post-treatment indicate that Histaglobulin's effects are maintained beyond the treatment period itself and hence offer prolonged alleviation to the patient [11].

These results are quite encouraging compared to earlier research into alternative treatments for refractory CU. The efficacy of SC Histaglobulin in reducing UAS7 scores compares very well with that of other therapeutic interventions, like omalizumab, cyclosporine, and corticosteroids [12]. Moreover, the safety profile of Histaglobulin, with only mild and transient adverse events reported, lends further support to its potential to be positioned as a first-line treatment in refractory cases. This makes the very absence of serious adverse events remarkable, in that it would mean that, under proper precautions, Histaglobulin can be safely administered even in patients with a history of resistant CU treatment [13].

There are several limitations to this study that should be regarded. First of all, this sample size is too small to generalize and apply it in long-term contexts. Further studies in larger representative populations with longer follow-up periods are required for fully elucidating the effectiveness and safety of SC Histaglobulin in refractory CU treatment [14]. Finally, despite the clinical significance of improvements observed in this study, it still remains unknown at which immunological mechanisms Histaglobulin acts, and this has to be investigated in future studies [15].

In summary, very good evidence exists from this study that subcutaneous Histaglobin can be used for the effective and very well-tolerated treatment of refractory chronic urticaria. From the result, huge improvements in symptom severity and quality of life can be seen, and the favorable safety profile suggests that Histaglobulin may have a very valuable role in the therapeutic landscape of CU [16]. These data therefore add to the increasing evidences on the use of immunomodulatory therapies in the treatment of chronic urticaria and further underline the need for investigations into mechanisms underlying the therapeutic effects of Histaglobulin.

V. CONCLUSION

This study demonstrates that subcutaneous Histaglobulin is a promising therapeutic option for patients suffering from refractory chronic urticaria. The significant reductions in Urticaria Activity Score (UAS7) and improvements in Dermatology Life Quality Index (DLQI) scores indicate that Histaglobulin not only effectively alleviates symptoms but also enhances the quality of life for those with chronic urticaria who have not responded to conventional treatments [17]. The observed reduction in pruritus intensity further underscores its efficacy in addressing one of the most distressing symptoms associated with the condition.

The favorable safety profile, characterized by only mild and transient adverse events, supports the use of SC Histaglobulin as a viable and well-tolerated treatment option [18]. This is particularly important for patients who have experienced limited success with other therapies, offering a new avenue for relief from persistent symptoms.

Despite the promising findings, the study's limitations, including its relatively small sample size and short follow-up period, suggest the need for further research [19]. Future studies should aim to confirm these results in larger, more diverse patient populations and explore the long-term efficacy and safety of Histaglobulin. Additionally, elucidating the precise immunological mechanisms underlying its therapeutic effects could further enhance our understanding of its role in managing chronic urticaria [20].

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

In Conclusion, SC Histaglobulin represents a significant advancement in the treatment of refractory chronic urticaria, offering hope to patients who have exhausted other treatment options. Its effectiveness in reducing symptom severity and improving patient quality of life, coupled with a strong safety profile, makes it a valuable addition to the therapeutic arsenal for managing this challenging condition. The findings from this study provide a foundation for further exploration and integration of immunomodulatory therapies in the treatment of chronic urticaria.

VI. REFERENCES

[1] **Weller, P. F., & Gilfillan, A. M.** (2011). "Chronic Urticaria and the Mast Cell." *Journal of Allergy and Clinical Immunology*, 127(1), 32-38. doi:10.1016/j.jaci.2010.11.048.

[2] **Zuberbier, T., Abdul Latiff, A. H., Abdu Rahman, S., &Asero, R.** (2018). "The EAACI/GA2LEN/EDF/WAO Guideline for the Definition, Classification, Diagnosis, and Management of Urticaria." *Allergy*, 73(7), 1393-1414. doi:10.1111/all.13397.

[3] **Saini, S. S., & M, S.** (2020). "Omalizumab in the Management of Chronic Urticaria: A Review of the Clinical Evidence." *Therapeutic Advances in Chronic Disease*, 11, 204062232091369. doi:10.1177/2040622320913697.

[4] **Ghaffari, J., & Wang, L.** (2019). "Management of Refractory Chronic Urticaria: A Systematic Review of Immunomodulatory Treatments." *Clinical Reviews in Allergy & Immunology*, 57(3), 284-294. doi:10.1007/s12016-019-09691-6.

[5] **Kok, J. S., &Bachert, C.** (2019). "Treatment Strategies for Chronic Urticaria: A Review of the Latest Evidence." *Current Opinion in Allergy and Clinical Immunology*, 19(3), 219-224. doi:10.1097/ACI.0000000000000548.

[6] **Hsieh, H. J., & Lee, H.** (2016). "Histaglobulin as a Treatment for Chronic Urticaria: An Update on Clinical Studies." *Journal of Dermatological Treatment*, 27(5), 441-447. doi:10.3109/09546634.2015.1063367.

[7] **Kong, L., & Patel, S.** (2021). "Comparative Effectiveness of Biologic Agents for Chronic Urticaria: A Network Meta-Analysis." *Journal of Allergy and Clinical Immunology*, 147(4), 1480-1490. doi:10.1016/j.jaci.2020.09.037.

[8] **Maurer, M., &Zuberbier, T.** (2017). "Chronic Urticaria: Overview of Current and Emerging Therapies." *Journal of Allergy and Clinical Immunology*, 140(3), 677-686. doi:10.1016/j.jaci.2017.06.035.

[9] **Koczo, L., &Szepfalusi, Z.** (2020). "Histaglobulin Therapy in Allergic Disorders: A Review of Mechanisms and Efficacy." *Immunotherapy*, 12(2), 123-135. doi:10.2217/imt-2019-0146.

[10] **Stull, S. H., & J., K.** (2020). "Long-Term Outcomes of Subcutaneous Immunotherapy for Chronic Urticaria: A Comprehensive Review." *Clinical Immunology*, 214, 108389. doi:10.1016/j.clim.2020.108389.

[11] **Singh, R., & R., S.** (2021). "Novel Therapeutic Approaches for Refractory Chronic Urticaria: A Review of Recent Advances." *Allergy Asthma Proceedings*, 42(6), 447-456. doi:10.2500/aap.2021.42.21049.

[12] **Lee, J. H., &Youn, S. W.** (2019). "The Role of Immunotherapy in

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 8, 2023

Chronic Urticaria: Evidence and Mechanisms." *Dermatology and Therapy*, 9(2), 345-357. doi:10.1007/s13555-019-0305-8.

[13] **Magen, E., & Segal, N.** (2020). "Subcutaneous Histaglobulin: A Potential New Treatment for Chronic Urticaria." *Expert Review of Clinical Immunology*, 16(3), 297-305. doi:10.1080/1744666X.2020.1717891.

[14] **Gowda, K., & Smith, M.** (2018). "Clinical Efficacy and Safety of Immunomodulatory Therapies in Chronic Urticaria." *Therapeutics and Clinical Risk Management*, 14, 1347-1355. doi:10.2147/TCRM.S178649.

[15] **Keller, T., & B., M.** (2019). "Histaglobulin in the Treatment of Allergic Diseases: A Focus on Chronic Urticaria." *Journal of Allergy and Clinical Immunology Practice*, 7(4), 1102-1110. doi:10.1016/j.jaip.2018.09.018.

[16] **Zhang, J., & Zhang, S.** (2021). "New Insights into the Treatment of Chronic Urticaria: Subcutaneous Histaglobulin." *Current Opinion in Allergy and Clinical Immunology*, 21(5), 463-470. doi:10.1097/ACI.0000000000000789.

[17] **Stanton, D., & Murphy, P.** (2019). "Immunomodulatory Therapies for Refractory Chronic Urticaria: Current Evidence and Future Directions." *Journal of Immunotherapy*, 42(8), 263-270. doi:10.1097/CJI.0000000000000168.

[18] **Singh, S., & Mehta, N.** (2020). "Management of Chronic Urticaria with Immunomodulatory Agents: A Review." *Journal of Clinical Immunology*, 40(5), 1114-1123. doi:10.1007/s10875-020-00871-x.

[19] **Weinstein, G., & R., D.** (2018). "The Efficacy of Subcutaneous Histaglobulin in Chronic Urticaria: A Meta-Analysis." *Immunotherapy*, 10(4), 223-232. doi:10.2217/imt-2017-0123.

[20] **Dawson, T., & Matthews, J.** (2021). "Evaluating Subcutaneous Immunotherapy for Chronic Urticaria: Evidence and Clinical Practice." *Clinical Reviews in Allergy & Immunology*, 61(2), 152-164. doi:10.1007/s12016-020-08811-0.