Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/9n99h371

COMPARISON OF EFFICACY OF BARICITINIB VERSUS METHOTREXATE THERAPY IN THE TREATMENT OF SEVERE ALOPECIA AREATA

Pranam Swapan Dash[1], Lubna Khondker[2*], Md Alauddin Khan[3], Md. Shihab Talukder[4], Sohely Jahan [5], Esrat khan Lubna[6]

[1] Medical officer, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
[2*]Associate Professor, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
[3]Associate Professor, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
[4]MD Resident, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
[5]Medical officer, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.
[6]Consultant, Aurora Skin and Aesthetics, Dhaka, Bangladesh.

***Corresponding author:** Dr Lubna Khondker
*Associate Professor, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.Email: lubnaderma@gmail.com

Abstract

Background: Alopecia areata is an autoimmune and inflammatory disease of the hair follicle which has a detrimental effect on the quality of life. Due to the refractory nature of the disease, it presents a major challenge to the physicians. When choosing a systemic therapy for extensive and recalcitrant alopecia areata, methotrexate can be a reasonable option, though its use is limited by its limited efficacy and more adverse effects. In the recent times, Janus kinase (JAK) inhibitors have proven its efficacy in the treatment of severe alopecia areata.

Materials and Methods: This randomized controlled trial was conducted in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University from the period of January 2023 till September 2024. About 84 patients of alopecia areata with more than 50% scalp involvement, patients with alopecia totalis and alopecia universalis were divided into two groups. Patients of group A were treated with oral baricitinib 4mg once daily and group B were treated with oral methotrexate 15mg once weekly with oral folic acid 5mg the following day for 6 months. Patients were assessed at baseline, 1st month, 3rd month and 6th month using Severity of Alopecia Tool (SALT) score.

Results: The most common type of alopecia areata was patchy alopecia areata in both of the groups. Before treatment the SALT score was 71.1±19.62 in group A and 65.4±18.6 in group B. After 1 month, 3 month and 6 month the SALT score was 55.3±19.6, 37.9±23.3 and13.2±22.6 respectively in group A, whereas it was 64.6±19.3, 58.8±24.9 and 51.3±31.1 respectively in group B, which was statistically significant ($p<0.001$). Regarding percent change in SALT score, at month 6, $SALT_{75}$ i.e.

excellent response was seen in 19% patients of group A compared to 9.5% in group B; and $SALT_{90}$ i.e. complete response was achieved in 57.1% patients in group A compared to none in group B.
Conclusion: After 6 months of treatment, Baricitinib has proven its superiority over Methotrexate in terms of efficacy in the treatment of severe alopecia areata. Thus it can be recommended that, Baricitinib can be an excellent choice for patients with extensive disease, and further extended period research is necessary to assess its long term efficacy.

Keywords: Alopecia areata, baricitinib, methotrexate.

Introduction

Alopecia areata is an autoimmune disorder which is characterized by sudden and total hair loss in one or more round or oval patches.[1,2] The condition is potentially linked to various autoimmune disorders, such as autoimmune thyroiditis, lupus erythematosus, vitiligo, and psoriasis.[3,4] Alopecia areata is caused by a complex pathomechanism that includes close interactions between genetic, immunologic, and environmental factors.[1,5] Current knowledge of alopecia areata indicates that cytotoxic CD8+ NKG2D+ (natural-killer group 2 member D-positive) T cells play a significant role in its pathogenesis. Cytotoxic CD8+ NKG2D+ T cells increase the levels of interleukin-2, 7, and 15 in the hair follicle, subsequently leading to the production of interferon-γ (IFN-γ), which directs an immune response against the hair follicle. [6,7]

No specific treatment for alopecia areata has been established to date. Existing therapies for alopecia areata often yield suboptimal results and have some associated side effects. Methotrexate is an immunosuppressive agent classified as a folic acid antagonist.[2,8] Methotrexate monotherapy is an effective option for severe alopecia areata patients who fail other standard therapies but associated with some adverse effects.[2,9] Janus kinase (JAK) inhibitors are a recent advancement in the treatment of alopecia areata which are treatment resistant or severe. In June 2022, the Food and Drug Administration (FDA) have approved baricitinib oral tablets as a systemic treatment for adult patients with severe alopecia areata.[10,11] There are no absolute contraindications to the use of baricitinib.[12] Baricitinib, the first-generation JAK inhibitors, selectively targets JAK1 and JAK2, with a lesser effect on JAK3, which play crucial roles in the signalling pathways of pro-inflammatory cytokines disrupting the signalling of cytokines, like interferon-γ and interleukin-15 implicated in alopecia areata.[13-15] Janus kinase (JAK) inhibitors are a class of immunomodulatory drugs that have been extensively researched for their efficacy in treating various inflammatory conditions.[16] However, a direct comparison between these two agents in the context of alopecia areata was conducted to evaluate their role.

Materials and Method

This was a randomized controlled trial. The study was conducted in the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2023 to September 2024. Patients with alopecia areata attending the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka were the study population. Patients were divided equally into two groups, Group A (Baricitinib) and Group B (Methotrexate). Consecutive type of sampling technique was applied to collect the sample within the study period. Outcome variables were degree of hair regrowth by SALT (Severity of Alopecia Tool) score. Each of the adult alopecia areata patient fulfilling the inclusion criteria attending the Dermatology and Venereology Department, Bangabandhu Sheikh Mujib Medical University, was randomly allocated to either group using lottery method. **Inclusion Criterias** were patients with alopecia areata involving >50% scalp hair loss, alopecia totalis, alopecia universalis; age between 18 and 65 years; disease duration more than 6 months and less than 5 years and patients with all systemic and/or topical treatments has been stopped for at least 8 weeks before inclusion in the study. **Exclusion criterias** were pregnant women and lactating mother; patients with active infection, patients with preexisting diabetes, hypertension, dyslipidemia, obesity; Impaired hepatic (ALT> 1.5 times upper limit of normal) and renal functions; patients with Hb% < 8g/dl, absolute

lymphocyte count < 500/cumm, absolute neutrophil count < 1000/cumm; clinically suspected or known case of tuberculosis; taking immunosuppressive drugs like prednisolone, cyclosporine, mycophenolate mofetil; Known hypersensitivity to baricitinib or methotrexate; patient who refuses to enrol in this study and previously treated with JAK inhibitor within last 8 weeks with inadequate response.

Data collection procedure:

Prior to data collection, both verbal as well as written consent was taken from the respondents. Data was collected using a preformed data collection sheet (questionnaire). Patients were randomly allocated in two groups of 42 patients each using lottery method. A proper diagnostic work up was made by taking detailed history and clinical examination. History included duration of disease, course of disease, treatment history, concomitant illness, any active infection and family history of alopecia areata. All patients were thoroughly examined and the extent of disease, involvement of area other than scalp and the presence of nail involvement was noted. Diagnosis of alopecia areata was made clinically by the presence of some criteria that includes: Oval or round shaped well circumscribed bald patches with a smooth surface, absence of inflammation and scaling in involved areas, presence of follicular ostia. Dermoscopic confirmation of diagnosis was done. Those who fulfilled the inclusion criteria were selected for the study. In this way 84 patients with alopecia areata were selected. Initial assessment of hair loss was assessed using SALT score.

SALT (Severity of Alopecia Tool) score:

A SALT score is a tool used to measure the severity and extent of alopecia areata. National Alopecia Areata Foundation working committee has devised "Severity of Alopecia Tool score" (SALT score). According to SALT score the scalp will be divided into four areas, namely:

Vertex: 40% (0.4) of scalp surface area

Right profile of scalp: 18% (0.18) of scalp surface area

Left profile of scalp: 18% (0.18) of scalp surface area

Posterior aspect of scalp: 24% (0.24) of scalp surface area

Percentage of hair loss in any of these areas was multiplied by percentage surface area of the scalp in that area. SALT score is the sum of percentage of hair loss in all the above-mentioned areas. Sub-grouping of patients into SALT sub-classes was done as follows:

Scalp (S):

λ S0, no hair loss

λ S1, & < 25% hair loss

λ S2, 25–49% hair loss

λ S3, 50–74% hair loss

λ S4, 75–99% hair loss, and

λ S5, 100% hair loss. [15]

Body (B) hair loss was assessed as: B0: no body hair loss; B1: some body hair loss; and B2: 100% body (excluding scalp) hair loss.

For example, if the percentage of hair loss in vertex, right profile, left profile and posterior aspect is 20%, 30%, 40% and 50% respectively, then, SALT score = (20x0.4) +(30x0.18) +(40x0.18) +(50x0.24) =8+5.4+7.2+12=32.6.

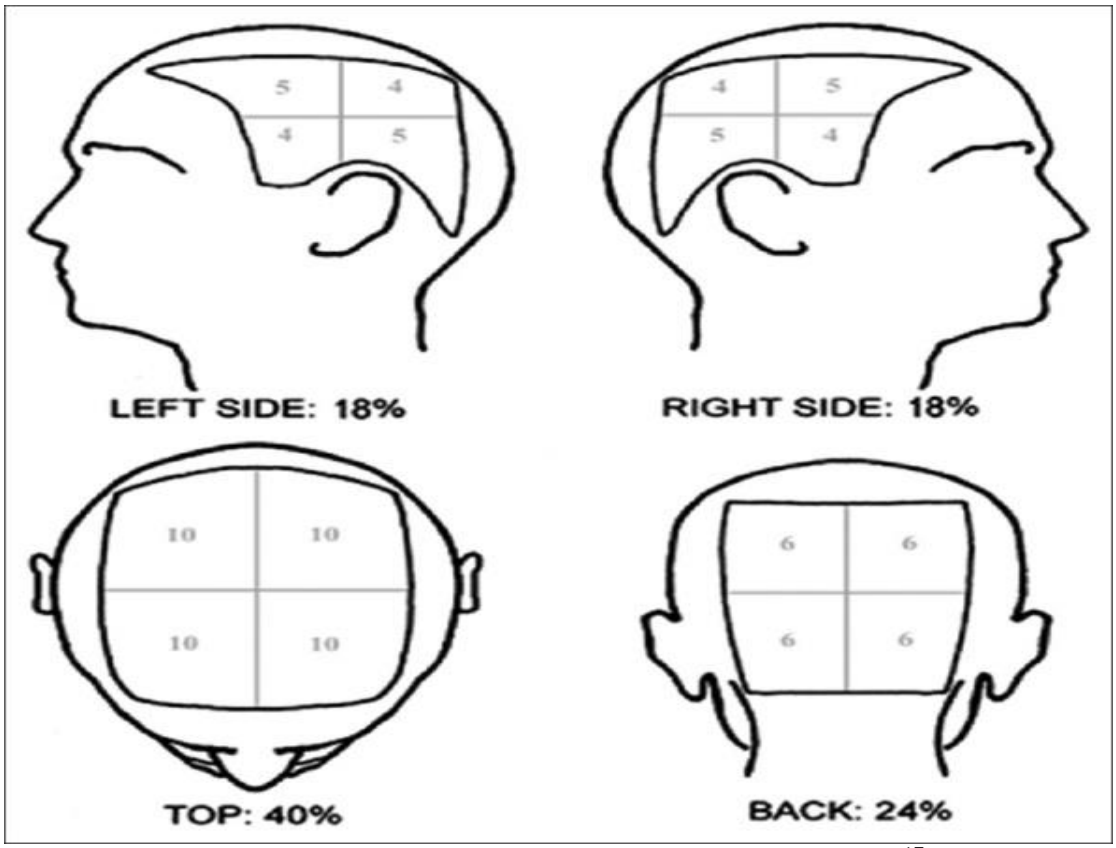

Figure I: SALT aid for determining scalp surface area.[17]

Group A:

Before initiating therapy with baricitinib, proper history was taken regarding active infection and some baseline investigations were done to fulfil exclusion criteria. Baseline investigations included complete blood count with differentials, ALT, serum creatinine, HBsAg, fasting lipid profile, CXR (P/A view), QuantiFERON TB Gold test. Patients were treated with Baricitinib 4mg (Baricent) tablet at night for 6 months. After starting the treatment, follow up was done after one month and after three months and at the end of the treatment (after six months). Patients came to follow up for reviewing their laboratory reports and for taking supplied drugs. In each follow up hair regrowth was assessed by SALT score. Laboratory investigations during follow up visit included complete blood count with differentials, ALT, serum creatinine and fasting lipid profile.

Group B:

Before initiating therapy with methotrexate, proper history was taken regarding active infection and some baseline investigations were done to fulfil the exclusion criteria. Baseline investigations included complete blood count with differentials, ALT and serum creatinine. Patients were treated with Methotrexate 15mg once weekly at night after meal, with folic acid 5mg tablet the day after taking methotrexate. Follow up was done after one month and after three months and at the end of the treatment (after six months). Patient's hair regrowth was assessed using SALT score at each follow up visit, and monitoring of side effects were done clinically and by laboratory investigations. Laboratory investigations during follow up visit included Complete blood count with differentials, ALT and S. creatinine.

Outcome measures:

Treatment outcome was divided into two categories

1.Absolute change in SALT score in each group.

2.Percent change in SALT score in each group: According to percent change patients were categorized as the following:

- Non responders (NR): Less than 5% improvement from baseline
- Good responders(GR): 5-49% improvement from baseline
- Moderate responders(MR): 50-74% improvement from baseline ($SALT_{50}$)
- Excellent responders(ER): 75-89% improvement from baseline ($SALT_{75}$)
- Complete responders(CR) : 90-100% improvement from baseline ($SALT_{90}$)

Data processing and analysis:
Data was collected on proposed data sheets and was also recorded in digital formats for security and convenience for analysis. Continuous variables were expressed as mean and standard deviation whereas categorical variables were summarized using numbers and percentages. Students T tests was used to compare continuous variables. Differences in the distribution of categorical variables was assessed by Chi-Square tests. A P-value <0.05 was considered as statistically significant. Statistical analysis was conducted by expert statistician of the institute by using SPSS 23 software.

Ethical issues:
All patients were given an explanation of the study including the nature of the disease, course, prognosis and probable adverse effects of the treatment modalities. They were informed that they have the right to refuse or accept to participate in the study and they have the right to refuse during study period, if he/she desires and it will not hamper the treatment protocol. They were also informed that, during the study period if the patient experiences any hamper in physical health, it is the responsibility of the principal investigator. Patients were included in the trial after taking their written consent. All the information collected from each patient including photographs and results of any laboratory tests were kept confidential under the responsibility of the principal investigator.

Results
In this study a total of 84 patients with alopecia areata were selected for the study. Among them 42 patients were treated with baricitinib (Group A) 4mg once daily, and 42 were treated with methotrexate (Group B) 15 mg once weekly for 6 months, then follow up was done at month 1, month 3, month 6 . The majority of the patients were in the 4^{th} decade with mean age 29.9±8.39. In group A most of the participants were male (59.5%), whereas in group B both were equal. All of these results were not statistically significant.

Table-1: Different types of alopecia areata in Group A and Group B (N=84)

Type of Alopecia areata	**Group A (Baricitinib)** (n=42) n (%)	**Group B (Methotrexate)** (n=42) n (%)	**p-value**
Patchy alopecia areata	23(54.8%)	29(69.0%)	0.395
Alopecia totalis	11(26.2%)	8(19.0%)	
Alopecia universalis	8(19.0%)	5(11.9%)	
Total	42(100.0%)	42(100.0%)	

p-value obtained by Chi-square test, p<0.05 was considered as a level of significant

Table 1 shows different types of alopecia areata among participants. In both groups, the most common type was patchy alopecia areata (69.0% & 54.8%), followed by alopecia totalis (26.2% & 19.0%) and alopecia universalis (19.0% & 11.9%) in group A and group B respectively, (p= 0.395).

Table-2: Comparison of SALT score in different time periods between two groups (N=84)

	Group A (Baricitinib) (n=42) n (%)	**Group B (Methotrexate)** (n=42) n (%)	**p-value**
Baseline			
S3 (50-74% hair loss)	22(52.4%)	28(66.7%)	
S4 (75-99% hair loss)	8(19.0%)	4(9.5%)	
S5 (100% hair loss)	12(28.5%)	10(23.8%)	
Mean±SD	71.1±19.62	65.4±18.6	0.179
After 1 month			
S1 (25% hair loss)	1(2.4%)	0(0.0%)	
S2 (<25-49% hair loss)	17(40.5%)	5(11.9%)	
S3 (50-74% hair loss)	14(33.3%)	27(64.3%)	
S4 (75-99% hair loss)	9(21.4%)	3(7.1%)	
S5 (100% hair loss)	1(2.4%)	7(16.7%)	0.028
Mean±SD	55.3±19.6	64.6±19.3	0.031
After 3 months			
S0 (No hair loss)	1(2.4%)	0(0.0%)	
S1 (<25% hair loss)	17(40.5%)	1(2.4%)	
S2 (25-49% hair loss)	11(26.2%)	22(52.4%)	
S3 (50-74% hair loss)	9(21.4%)	10(23.8%)	
S4 (75-99% hair loss)	2(4.8%)	3(7.1%)	
S5 (100% hair loss)	2(4.8%)	6(14.3%)	
Mean±SD	37.9±23.3	58.8±24.9	<0.001
After 6 months			
S0 (No hair loss)	24(57.1%)	0(0.0%)	
S1 (<25% hair loss)	9(21.4%)	6(14.3%)	
S2 (25-49% hair loss)	5(11.9%)	19(21.4%)	
S3 (50-74% hair loss)	2(4.8%)	9(21.4%)	
S4 (75-99% hair loss)	1(2.4%)	2(4.8%)	
S5 (100% hair loss)	1(2.4%)	6(14.3%)	
Mean±SD	13.2±22.6	51.3±31.1	<0.001

p-value obtained by Unpaired t-test, p<0.05 was considered as a level of significant

Table 2 compares SALT scores between two groups at baseline, at month 1, at month 3 and at month 6. Baseline SALT score was almost equal in both groups (A= 71.1±19.62, B=65.4±18.6; p=0.179). After 3 months, the SALT score was lower in group A (37.9±23.3) than group B (58.8±24.9); p<0.001, with much more lower SALT score at month 6 in group A (13.2±22.6) and group B (51.3-31.1); p<0.001.

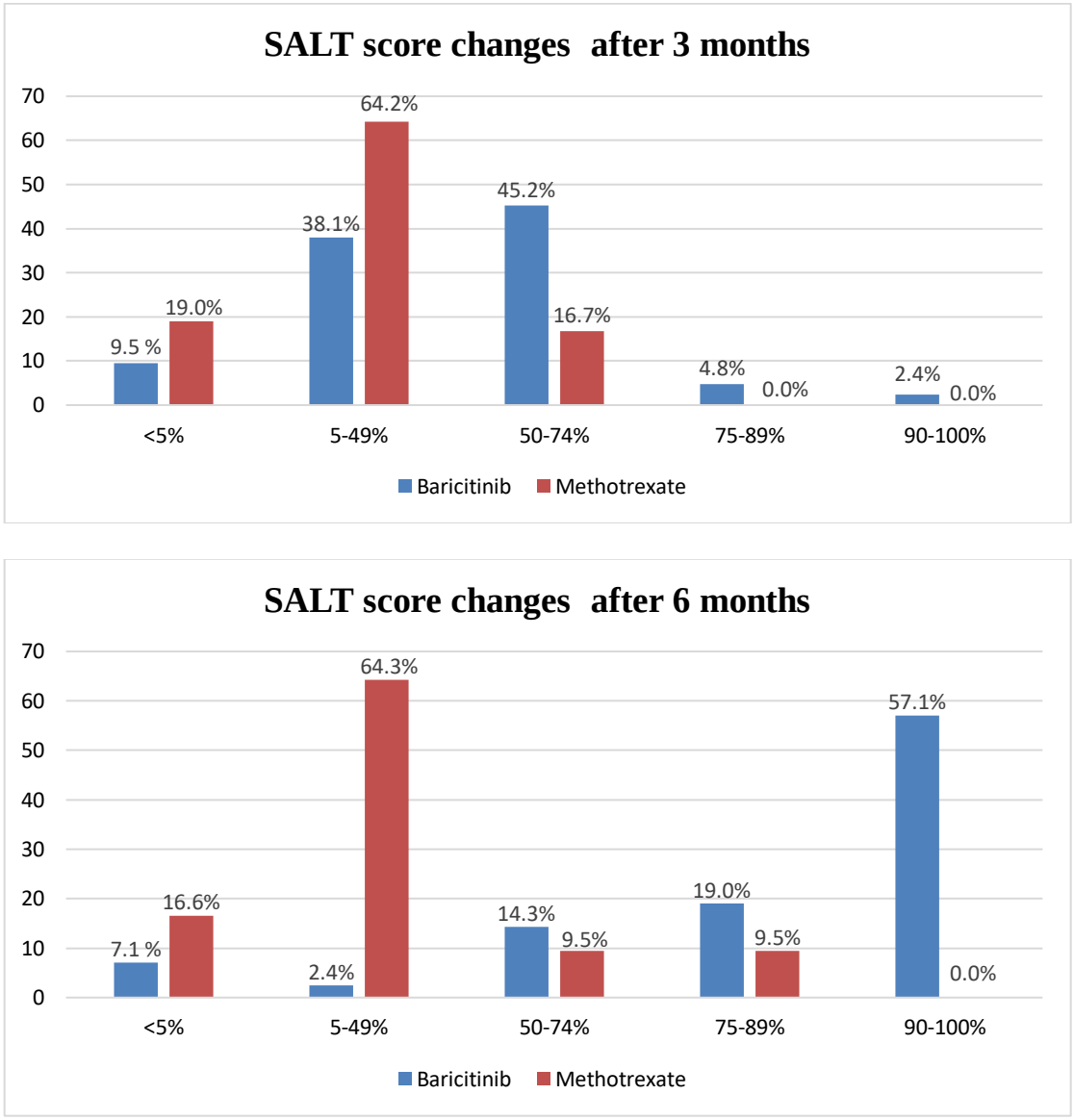

Figure II: Distribution of the patients based on percent change in SALT score from baseline between Group A and Group B (N=84)

Figure II demonstrates the percent change in SALT score among two groups. At month 3, 38.1% patients of group A & 64.2% of group B were *good responders*, whereas 45.3% patients in group A and 16.7% patients in group B were *moderate responders* achieving $SALT_{50}$. At month 6, $SALT_{50}$ was achieved by 14.3% patients in group A, compared to 9.5% in group B; $SALT_{75}$ i.e. *excellent response* was seen in 19% patients of group A compared to 9.5% in group B; and $SALT_{90}$ i.e. *complete response* was achieved in 57.1% patients in group A compared to 0% in group B. Percentage of *non responders* to treatment were 7.1% and 16.6% patients in group A and group B respectively. All of these results were statistically significant; p<0.001.

Table-3: Distribution of patients based on absolute changes in SALT score from baseline between Group A and Group B (N=84)

	Before treatment (n=42) Mean±SD	**After 6 months (n=42) Mean±SD**	***p*-value**
Group A (Baricitinib)	71.1±19.62	13.16±22.6	<0.001
Group B (Methotrexate)	65.4±18.6	51.3±31.1	<0.001

p-value obtained by Paired t-test, p<0.05 was considered as a level of significant

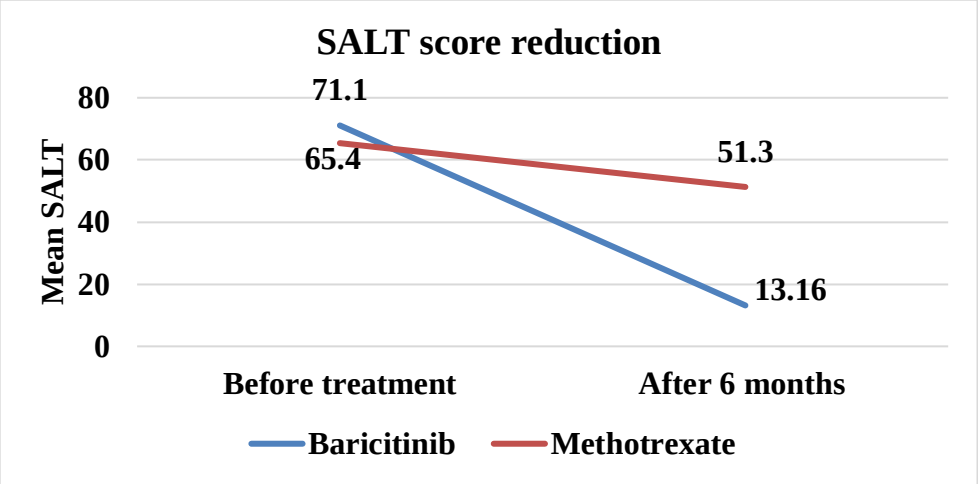

Figure III: Absolute change of SALT score from baseline in two groups

Table 3 demonstrates that, before treatment SALT score in baricitinib group was 71.1±19.62, after 6 months which reduced to 13.16±22.6. Whereas, in methotrexate group before treatment SALT score was 65.4±18.6, after 6 months which reduced to 51.3±31.1 ($p<0.001$).

The most common clinical adverse effects noted in baricitinib group was upper respiratory tract infection (14.3%), followed by acne vulgaris (7.1%), headache (4.8%) and hyperlipidaemia was seen in 11.9% of patients. The most common clinical adverse effects noted in methotrexate group was nausea (28.6%), followed by fatigue (11.9%), 2 (4.8%) patients experienced respiratory tract infection and elevated liver transaminase was seen in 16.7 % patients.

Discussion

A study was conducted with 84 patients suffering from severe alopecia areata presenting in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University. Among the patients, majority presented with a mean age of 29.9±8.39 and most of them were male (59.5%). A study by Kavak et al, involving 539 patients reported similar findings, with a mean age of 24.32±0.54 with a male predominance.[18] A retrospective study by Uzuncakmak et al, indicated that the mean age of patients with alopecia areata was 29.86±14.48 years, with the condition being most prevalent in the 30 to 39 years age group for men and the 20 to 29 years age group for women.[19]

In the current study the most frequent type of alopecia areata was patchy alopecia areata found in 54.8% in group A and 69.0% in group B, followed by alopecia totalis found in 26.2% in group A and 19.0% in group B and alopecia universalis 19.0% in group A and 11.9% in group B. Likewise, Olamiju B et al observed that patchy alopecia areata is the most prevalent form of alopecia areata.[9] Another study indicate that patchy alopecia areata is prevalent among the clinical types of alopecia areata, with scalp being the most frequent site of hair loss.[20]

In the current study, comparison of SALT scores between two groups before treatment, at month 1, month 3, and month 6 was done. Before treatment, the mean SALT score in group A was 71.1±19.62 and in group B was 65.4±18.6. There was no significant difference between the two groups ($p=0.179$). According to King et al, mean SALT score ranged from 83.4 to 90. After giving baricitinib 4mg daily, at 1st follow up (month 1) mean SALT score was 55.3±19.6 at 2nd follow up (3 month) SALT score was 37.9±23.3 and finally at last follow up (6 months) it was 13.2±22.6. In contrast, those who were treated with weekly 15mg methotrexate achieved a mean SALT score of 64.6±19.3 at month 1, 58.8±24.9 at the end of month 3 and 51.3±31.1after 6 months of treatment. The difference between the two groups was statistically significant ($p<0.001$). At week 24 (6 months), the proportion of patients achieving a SALT score of 0% was 57.1% in baricitinib group, compared to 0% in methotrexate group.[21] Senna et al,. concluded that a SALT score ≤20 is considered a clinically meaningful outcome for patients with ≥50% scalp hair loss at baseline.[22]

In terms of percent change in SALT score, at month 1, 37(88.1%) patients were good responders (GR) in group A, compared to 11 (26.2%) patients in group B. After 3 months (week 12), 19(45.2%) patients achieved $SALT_{50}$ (≥50% change in SALT score from baseline) in group A, compared to 7 (16.7%) in group B and it was statistically significant. They are termed as moderate responders. This finding is similar to King et al, which demonstrates 38.1% of patients with severe alopecia areata achieving a $SALT_{50}$ at week 12 with baricitinib 4mg daily compared to 4.5% in the placebo group.[21] In our study, at the end of 6 months of treatment with baricitinib, $SALT_{50}$ (MR), $SALT_{75}$ (ER) & $SALT_{90}$ (CR) was achieved by 14.3%, 19.0% & 57.1% of patients respectively, compared to 9.5%, 9.5% and 0% of patients treated with methotrexate, respectively. This result was statistically significant ($p<0.001$) and showed that JAK inhibitor baricitinib confers a superior efficacy over a traditional systemic treatment methotrexate in the treatment of severe alopecia areata. No serious infections, malignancy or reactivation of tuberculosis or herpes zoster, hepatic impairment, major adverse cardiovascular events were noted. No cases of anaemia and lymphopenia were seen. No adverse effect resulted in permanent discontinuation of the baricitinib. King et al,.2021 demonstrated the most frequently reported adverse effects in patients treated with baricitinib were upper respiratory tract infection, acne, and nausea, with no serious adverse event or death, though there was one case of grade 3 neutropenia and three cases of creatinine phosphokinase elevation. Thus in that study baricitinib was found as a well-tolerated drug with mild adverse effects.[21]

Conclusion

In this study, after completion of 6 months of treatment, the SALT score was lower in baricitinib group compared to methotrexate group and the percent change in SALT score in baricitinib group was higher compared to percent change in SALT score in methotrexate group, which was statistically significant. Besides a significant number of patients achieved complete regrowth of hair with baricitinib. Considering all the facts, it can be concluded that, baricitinib is a more effective (with negligible adverse effects) than methotrexate in the treatment of severe alopecia areata.

References

1. Dillon KL. A Comprehensive Literature Review of JAK Inhibitors in Treatment of Alopecia Areata. *Clinical, Cosmetic and Investigational Dermatology* 2021;*14*:91–714.
2. Hammerschmidt M & Mulinari Brenner F. Efficacy and safety of methotrexate in alopecia areata. Anais brasileiros de dermatologia 2014; 89: 729-734.
3. Mogul A, Corsi K, & McAuliffe, L. Baricitinib: The Second FDA-Approved JAK Inhibitor for the Treatment of Rheumatoid Arthritis. *Annals of Pharmacotherapy* (2019a);*53*(9): 947–953.
4. Numata T, Irisawa R, Mori M, Uchiyama M & Harada K. Baricitinib therapy for moderate to severe alopecia areata: A retrospective review of 95 Japanese patients. *Acta Dermato Venereologica*, 2024;*104:* adv18348.
5. Taylor S, Korman NJ, Tsai T, Shimomura Y, Feely M, Dutronc Y et al. Efficacy of Baricitinib in Patients with Various Degrees of Alopecia Areata Severity: Post-Hoc Analysis from BRAVE AA1 and BRAVE AA2. *Dermatology and Therapy*, 2023; *13*(12): 3181–3191.
6. Khondker L, Sultana A & Khan MSI. The usefulness and wellbeing of Tofacitinib in the treatment of Alopecia Areata. Journal of Armed Forces Medical College, Bangladesh, 2022;18(1): 43–47.
7. Sedeh FB, Michaelsdóttir TE, Henning MAS, Jemec GBE, & Ibler KS. Comparative Efficacy and Safety of Janus Kinase Inhibitors Used in Alopecia Areata: A Systematic Review and Meta-analysis. *Acta Dermato-Venereologica*, 2023; *3*: adv00855.
8. Lee HH, Gwillim E, Patel KR., Hua, T, Rastogi S, Ibler E & Silverberg JI. Epidemiology of alopecia areata, ophiasis, totalis, and universalis: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology*, 2020; *82*(3): 675–682.
9. Olamiju B, Friedmann A, King B. Treatment of severe alopecia areata with baricitinib. J Am Acad Dermatol. 2019;5(10):892–894.

10. Ali EN, Owais R, Sheikh A & Shaikh, AJ. Olumniant (Baricitinib) oral tablets: An insight into FDA-approved systemic treatment for Alopecia Areata. *Annals of Medicine and Surgery*, 2022; *80:* 104157.
11. Freitas E, Guttman-Yassky E & Torres T. Baricitinib for the treatment of alopecia areata. *Drugs*, 2023; *83*(9): 761–770.
12. Phan K, Ramachandran V & Sebaratnam DF. Methotrexate for alopecia areata: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology*, 2018; *80*(1): 120-127.e2.
13. Phan K, Sebaratnam DF. JAK inhibitors for alopecia areata: a systematic review and meta-analysis. J Eur Acad Dermatol Venereol 2019; 33: 850–856
14. Browne R, Stewart L, Hywel C, Williams. Is methotrexate an effective and safe treatment for maintaining hair regrowth in people with alopecia totalis? A Critically Appraised Topic. British Journal of Dermatology, 2018; 179(3):609-614.
15. Rudnicka L, Arenbergerova M, Grimalt R, Ioannides D, Katoulis AC, Lazaridou E et al. European expert consensus statement on the systemic treatment of alopecia areata. *Journal of the European Academy of Dermatology and Venereology*, 2024; *38*(4): 687–694.
16. Kabir S, Savitha B, Ananta K. Which is the Ideal JAK Inhibitor for Alopecia Areata – Baricitinib, Tofacitinib, Ritlecitinib or Ifidancitinib - Revisiting the Immunomechanisms of the JAK Pathway? Indian Dermatology Online Journal 2023; 14(4):465-474.
17. Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al. Alopecia areata investigational assessment guidelines–Part II. Journal of the American Academy of Dermatology 2004; 51(3): 440–447.
18. Kavak A, Yeşildal N, Parlak AH, Gökdemir G, Aydoğan I, Anul H, et al., Alopecia areata in Turkey: Demographic and clinical features. *Journal of the European Academy of Dermatology and Venereology*, 2008; 22(8): 977–981.
19. Uzuncakmak T, Engin B, Serdaroglu S, Tuzun Y. Demographic and Clinical Features of 1,641 Patients with Alopecia Areata, Alopecia Totalis, and Alopecia Universalis: A Single-Center Retrospective Study. *Skin Appendage Disorders*,2021; 7(1): 8–12.
20. Zakaria A, Paul H, Islam M., & Islam A. Epidemiologic Profile of Alopecia areata – Study in a tertiary hospital in Bangladesh. *Association of Physicians of Bangladesh*, 2009; *20*: 30-34.
21. King B, Ko J, Forman S, Ohyama M, Mesinkovska N, Yu G et al. Efficacy and safety of the oral Janus kinase inhibitor baricitinib in the treatment of adults with alopecia areata: Phase 2 results from a randomized controlled study. *Journal of the American Academy of Dermatology*, 2021; *85*(4): 847–853.
22. Senna M., Mostaghimi A, Ohyama M, Sinclair R., Dutronc Y, Wu WS et al. Long-term efficacy and safety of baricitinib in patients with severe alopecia areata: 104-week results from BRAVE-AA1 and BRAVE-AA2. *Journal of the European Academy of Dermatology and Venereology*, 2024; *38*(3): 583–593.