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ORAL JANUS KINASES IN PATIENTS WITH REFRACTORY MODERATE TO SEVERE ECZEMA

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ABSTRACT

Background: AD (eczema) has a complicated etiology that includes Th2 polarization, which is related with the cytokines IL-4, IL-5, and IL-13, as well as Th22, Th17, and Th1 cells in chronic lesions. Janus kinases suppress Th1, Th2, and Th17 cytokines by preferentially inhibiting JAK3 and JAK1 receptors.

Aim: The current research sought to investigate the safety and effectiveness of oral Janus kinases in patients with refractory moderate to severe eczema.

Methods: The trial included 32 adult individuals over the age of 18 with moderate to severe eczema who had previously received systemic medication but had not responded well. At baseline, quality of life scores with DLQI (Dermatology Life Quality Index), severity scores with SCORAD (SCORing Eczema), EASI (eczema area and severity index), past treatment history, and demographic data were collected. Blood tests at baseline include the interferon-gamma release assay for TB, lipid profile, renal function test, liver function test, and complete blood count. Subjects were evaluated every month for six months to determine any adverse events, DLQI, blood tests, and severity levels.

Result: Of the 32 participants, 10, 3, and 3 were treated with cyclosporine, methotrexate, or both. Mean EASI scores improved from 23.36±9.54 at baseline to 8.48±7.55 at 6 months. The mean SCORAD score improved from 41.23±8.67 to 14.91±7.80 after 6 months. The mean DLQI improved from 15.16±2.71 to 5.29±4.09 between baseline and 6 months, indicating an improvement in quality of life. There were no adverse events seen; however, 6 patients had dyslipidemia, and 4 had changed bleeding time.

Conclusion: The current study suggests that Janus kinases is an effective and safe treatment option for adult patients with moderate to severe eczema.

Keywords: refractory, severe eczema, Janus kinases .

INTRODUCTION

The characteristic indications of AD (eczema) include severe pruritus and persistent skin inflammation, both of which have a major impact on the individuals' quality of life. It is common in both children and adults, affecting around 15-20% of children and 2-10% of adults. The data on the prevalence of eczema in India is insufficient. Eczema has a complicated etiology, involving Th2 polarization linked with cytokines such as IL-4, IL-5, IL-13, and Th22, as well as Th17 and Th1 cells in chronic lesions. Treatment options for eczema include phototherapy, topical calcineurin inhibitors, topical corticosteroids, and emollients. However, moderate to severe cases are often resistant to these therapies.[1]

Immunomodulatory medications such as azathioprine, methotrexate, and cyclosporine have been used in refractory eczema with varying degrees of success; nevertheless, a greater knowledge of the etiology has led to the development of targeted and new therapy.[2]

JAK inhibitors have been tested in a variety of inflammatory skin disorders, including eczema, and have proven to be highly effective. Oclacitinib, a selective JAK1 inhibitor, was authorized in 2013 for eczema in dogs, while baricitinib was approved in November 2020 for eczema in humans. Other JAK inhibitors recently authorized by the USFDA include topically given ruxolitinib, oral qbrocitinib, and oral Upadacitinib.[3]

The topical application of Janus kinases citrate, a JAK 1/3 inhibitor used for systemic therapy of moderate to severe rheumatoid arthritis, is being investigated in people with eczema. Janus kinases primarily inhibits JAK1 and JAK3 receptors, specifically Th1, Th2, and Th17-associated cytokines. 4 The current research sought to investigate the safety and effectiveness of oral Janus kinases in participants with refractory moderate to severe eczema who had not responded well to systemic immunomodulators.

MATERIALS AND METHODS

The purpose of this retrospective analysis was to investigate the safety and effectiveness of oral Janus kinases in participants with refractory moderate to severe eczema who had not responded well to systemic immunomodulators. The research subjects were from the Institute's Department of Dermatology. All individuals provided verbal and written informed permission before participating in the study.

The research examined individuals admitted to the Institute with eczema. The trial comprised participants over the age of 18 who took oral Janus kinases for at least 6 months. Participants with moderate to severe eczema who had previously received at least one systemic immunomodulator with insufficient effectiveness were given oral Janus kinases . Inadequate effectiveness of prior treatment was defined as failure to reduce EASI scores to 7 or below after at least 8 weeks of treatment. All individuals received oral Janus kinases at a dose of one pill of 5mg twice daily.

Every month, SCORAD and EASI scores were collected from all individuals using a pre-designed structured proforma and compared to determine effectiveness at baseline, 1, 2, 3, 4, 5, and 6 months. Additionally, the DLQI questionnaire instrument was utilized to assess the impact of the subject's quality of life at baseline and 6 months. During the twice-weekly follow-up, any adverse events associated with the treatment were examined.

RESULTS

The purpose of this retrospective analysis was to investigate the safety and effectiveness of oral Janus kinases in participants with refractory moderate to severe eczema who had not responded well to systemic immunomodulators. The trial included 32 adults over the age of 18 who had moderate to severe eczema and had not responded well to prior systemic medication. At baseline, quality of life scores with DLQI (Dermatology Life Quality Index), severity scores with SCORAD (SCORing Eczema), EASI (eczema area and severity index), past treatment history, and demographic data were collected. The study included 56% (n=18) men and 44% (n=14) women.

The research individuals' mean age was 32.48±7.56 years, with a range of 22-45 years. Subjects have previously used at least one systemic immunomodulator with an accurate success rate. Among these participants, 20 received cyclosporin, 6 received methotrexate, and 6 had both methotrexate and cyclosporin therapy.

The study found that at baseline, the EASI for oral Janus kinases was 23.36±9.54, increased to 19.67±9.61 at 1 month, and decreased to 16.17±9.03, 13.98±8.97, 11.04±8.35, 9.54±7.53, and 8.48±7.55 at 2, 3, 4, 5, and 6 months (p=0.0001). SCORAD dropped significantly from baseline (41.23±8.67) to 34.91±8.90, 29.86±8.98, 25.73±8.62, 22.29±8.32, 19.48±7.81, and 14.92±7.80 at 1, 2, 3, 4, 5, and 6 months (p=0.0001). The research individuals' DLQI scores decreased significantly from baseline to 6 months, from 15.17±2.71 to 5.29±4.09 (p=0.0001) (Table 1).

After 6 months of therapy, the average EASI score improved by 8.48±7.55. 62.5% (n=20) of participants showed at least 75% improvement from baseline to 6 months following therapy. In 25% of individuals (n=8), EASI response improved by ≥50% compared to baseline data. After 6 months of therapy, the average SCORAD score improved to 14.92±7.82, demonstrating effectiveness.

The study results also indicated that when SCORAD and EASI scores were compared before and after administration of oral Janus kinases in study patients using a paired t-test, there was a very significant improvement, with the two-tailed p-value of both scores being less than 0.001.

A paired t-test analysis compared DLQI values before and after treatment (15.17±2.71 and 5.29±4.09, respectively) to assess treatment effects on quality of life in these subjects. A two-tailed p-value of 0.0001 was found, indicating a significant improvement in quality of life for those treated with Janus kinases .

DISCUSSION

The current trial included 32 adult individuals over the age of 18 who had moderate to severe eczema and had not responded well to previous systemic treatment.

At baseline, quality of life scores with DLQI (Dermatology Life Quality Index), severity scores with SCORAD (SCORing Eczema), EASI (eczema area and severity index), past treatment history, and demographic data were collected. The study included 56% (n=18) men and 44% (n=14) women. The research respondents had a mean age of 32.48±7.56 years and ranged in age from 22 to 45 years. Subjects have previously used at least one systemic immunomodulator with an accurate success rate. Among these participants, 20 received cyclosporin, 6 received methotrexate, and 6 had both methotrexate and cyclosporin therapy.

These findings were similar to those of Ytterberg SR et al5 in 2022 and Bissonnette R et al6 in 2016, who evaluated participants with eczema and demographic data similar to the current investigation in their separate studies. The EASI for oral Janus kinases was 23.36±9.54 at baseline, rose to 19.67±9.61 at 1 month, and declined to 16.17±9.03, 13.98±8.97, 11.04±8.35, 9.54±7.53, and 8.48±7.55 at 2, 3, 4, 5, and 6 months (p=0.0001). SCORAD dropped significantly from baseline (41.23±8.67) to 34.91±8.90, 29.86±8.98, 25.73±8.62, 22.29±8.32, 19.48±7.81, and 14.92±7.80 at 1, 2, 3, 4, 5, and 6 months (p=0.0001).

DLQI scores in study patients decreased significantly from baseline to 6 months, from 15.17±2.71 to 5.29±4.09 (p=0.0001). These findings were congruent with those of Shalabi MMK et al7 in 2022 and Levy LL et al8 in 2015, who found comparable outcomes for quality of life in study individuals as the current investigation.

The study found that after 6 months of therapy, the mean EASI improved by 8.48±7.55. 62.5% (n=20) of participants showed at least 75% improvement from baseline to 6 months following therapy. In 25% of individuals (n=8), EASI response improved by ≥50% compared to baseline data.

After 6 months of therapy, the average SCORAD score improved to 14.92±7.82, demonstrating effectiveness. These findings were consistent with the findings of Fardos MI et al9 in 2022 and Alves C et al10 in 2022, who found EASI and SCORAD improvements similar to those described in the current research. It was also discovered that when the SCORAD and EASI scores of research individuals were compared before and after oral Janus kinases administration using a paired t-test, a very significant improvement was seen, with the two-tailed p-value of both scores being less than 0.001.

These findings were consistent with the findings of Feldman SR et al11 in 2016 and Zhang J et al12 in 2017, who indicated that the comparison of SCORAD and EASI scores before and after oral Janus kinases administration was equivalent to the results of the current research. The study found a significant improvement in quality of life for subjects treated with Janus kinases , with paired t-test results of 15.17±2.71 and 5.29±4.09, respectively. These findings were consistent with the findings of Bachelez H et al13 in 2015 and Le M et al14 in 2021, in which the authors reported DLQI levels similar to those in the current investigation.

CONCLUSIONS

The present study, considering its limitations, concludes that Janus kinases is an effective and safe management option in adult subjects with moderate to severe eczema. However, the study had a few limitations including a smaller sample size with smaller monitoring and assessing subjects from a single-institutional set-up. Hence, further clinical studies are needed to prospectively assess a larger number of subjects with longer monitoring periods and from a multi-institutional set-up.

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	Baseline	1 month	2 months	3 months	4 months	5 months	6 months	p-value
EASI	23.36±9.54	19.67±9.61	16.17±9.03	13.98±8.97	11.04±8.35	9.54±7.53	8.48±7.55	**0.0001**
SCORAD	41.23±8.67	34.91±8.90	29.86±8.98	25.73±8.62	22.29±8.32	19.48±7.81	14.92±7.80	**0.0001**
DLQI	15.17±2.71						5.29±4.09	**0.0001**

Table 4: Assessment of oral Janus kinases at six months in study subjects