Effectiveness and Safety of Tofacitinib in Patients With Recalcitrant Frontal Fibrosing Alopecia : A Pilot Study

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Introduction

Frontal fibrosing alopecia (FFA) was first described in 1994 and predominantly affects women aged 50–60 years. It can be observed in up to 13% of women of reproductive age and 4% of men of color. Among women of reproductive age, FFA is more prevalent in black ethnic groups compared to Caucasian women. Clinically, patients with FFA typically present with symmetrical bandlike hairline recession in the frontotemporal region, often accompanied by scaling and redness around the hair follicles. FFA manifests in three patterns: linear, diffuse, and pseudo-"fringe signs." Hairline recession can progress to involve the posterior ear hairline and occipital area. Moreover, prolonged sun exposure can lead to lighter and glossier skin in the affected area compared to normal skin. The presence of “lonely hairs sign”, where terminal hairs remain in the original 3–7 cm hairline, is a characteristic diagnostic clue found in over 50% of FFA cases. Currently, there are no standardized guidelines for treating FFA. Treatment options include 5-alpha reductase inhibitors, corticosteroids (oral and topical), hydroxychloroquine, isotretinoin, antibiotics, pioglitazone, and JAK inhibitors. These treatments yield variable outcomes, with no definitive information on the effectiveness of individual drugs. Systemic treatments generally aim to slow disease progression. JAK inhibitors are believed to reduce interferon-gamma and interleukin 15, thereby suppressing white blood cell activity in FFA remains unstudied in Thailand and inhibiting hair follicle growth. However, the use of tofacitinib in FFA has not yet been studied in Thailand. High treatment costs, including travel expenses and time constraints, may limit patient access. Further research is necessary to evaluate the effectiveness and safety of tofacitinib in treating FFA and to determine its potential benefits for patients with this challenging condition.

Objective

The objective is to study the effectiveness and safety of oral tofacitinib in treating recalcitrant FFA.

Research Methodology

The research procedure involved a pilot single-arm before-and-after clinical trial at the Institute of Dermatology in Bangkok, Thailand. The study protocol was approved by the Institutional Review Board, Institute of Dermatology, Bangkok, Thailand.

Population of study

Our study focused on patients diagnosed with recalcitrant FFA who were treated at The Hair and Nails Center, Institute of Dermatology, between November 2023 and March 2024. The

aim was to assess the effectiveness and safety of treatment through a pilot study as no prior studies conducted in Thailand, with only case series published worldwide.

Inclusion criteria included Thai individuals aged 18 or older diagnosed with FFA, who had failed treatment with at least one drug for more than three months, maintained medication adherence, and possessed relevant medical records. Exclusion criteria involved recent diagnoses of hair growth-affecting conditions, pregnancy, contraindications to oral tofacitinib, recent use of strong CYP3A4 medications, and positive tests for Hepatitis B and C.

Research procedure

Eleven eligible patients with recalcitrant FFA, who had been on at least one systemic medication for a minimum of six months, were enrolled based on inclusion and exclusion criteria. Demographic information, including disease duration, medical and medication history, symptoms, diagnoses, type of FFA, comorbidities, and family history, was collected from each patient. Baseline laboratory tests were performed, encompassing Complete Blood Count (CBC), liver function tests, lipid profile, fasting blood sugar, renal function tests, hepatitis B and C screening, chest X-ray, and urine pregnancy tests for women of reproductive age. Photography and dermoscopy were utilized for comprehensive evaluation.

Patients received oral tofacitinib 5 mg twice daily for 12 weeks, with scheduled follow-up visits and assessments conducted throughout the treatment and post-treatment phases, totaling 16 weeks. The effectiveness of treatment was evaluated using various assessments and evaluations, culminating in data collection and statistical analysis at the end of the study.

Evaluations

The Frontal Fibrosing Alopecia Severity Index (FFASI) is a scoring system designed to assess the severity of FFA. It focuses primarily on evaluating the recession of the frontal and temporal hairlines, assigning 80 out of 100 points to this criterion. Additional points are allocated based on factors such as inflammation, eyebrow loss, face papules, cutaneous lichen planus (LP), oral or genital LP lesions, and nail involvement.

The construct validity of the Frontal Fibrosing Alopecia Severity Score (FFASS) was established through its correlation with other severity measures, clinical features, the Lichen Planopilaris Activity Index (LPPAI) and the Investigator's Global Assessment. Intra-observer and interobserver reliability tests were also carried out.

The Lichen Planopilaris Activity Index (LPPAI) is a numerical scoring system used to quantify the signs and symptoms of FFA and LPP for statistical analysis. Prior to the development of FFASI and FFASS, hair specialists commonly relied on the LPPAI to evaluate these conditions. The LPPAI assigns weights to subjective and objective measurements, resulting in a score ranging from 0 to 10. Symptoms and indicators are assessed on a 4-point scale from absent to severe. The anagen pull test, which involves pulling hair shafts to assess for anagen hairs, is used to gauge

local disease activity and is recorded as a binary value and as the ratio of anagen hairs to total hairs pulled.

Data analysis

For this research investigation, data collection adheres to a specific format with discrete entries to uphold participant anonymity and confidentiality. Patient-specific data remains confidential, accessible only to authorized personnel, and is not included in any public records.

The data analysis process involved using descriptive statistics for qualitative data and the median with interquartile range for quantitative data. Statistical tests were applied to evaluate the effectiveness and safety of oral tofacinib before and after treatment in patients with recalcitrant FFA. A p-value of ≤ 0.05 was considered statistically significant, indicating a meaningful difference between pre- and post-treatment outcomes.