Evaluation of PASI Before and After Combined Treatment in Mild to Moderate Psoriasis

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Article

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Abstract

Background. -

Plaque psoriasis is a disease of immunological origin that damages the skin, mucous membranes. Biological therapies combined with systemic medications are effective in treating plaque psoriasis. Our objective was to evaluate the treatment of Etanercept with methotrexate and to verify its response with the PASI index in its initial and control phase.

Methodology. -

The Universe of patient treated at the Military Hospital in Guayaquil was 2,620 corresponding from January until July 2020; the selected sample according to the inclusion criteria was 94 patients with plaque psoriasis. The method was retrospective, observational, descriptive, cross-sectional, correlational differential analytical.

Result. -

In this study, the prevalence was 3.58%, The BMI index was 28.13 corresponding to overweight and obesity. The PASI index in the initial stage before treatment showed 10.8% and in the control phase, it fell to 2.99%, showing a decrease in lesions and good improvement to the combined treatment. In Student´s T, the combination of Etanercept with Methotrexate was compared with the evolution of PASI index, in the initial and control phases, presenting a value lower than $0.001 < P = 0.05$, this response being very significant.

Discussion. -

In our study, the combination of Etanercept with Methotrexate has a favorable disease response in reducing this disease. It’s expected that, in Ecuador, the Health Authorities would implement the Biologics for the treatment of plaque psoriasis and including them in the basic list of medicines of the Public Health Ministry.

Introduction

Psoriasis is a chronic cutaneous disease of immunological affection that damages the skin, mucous membranes, scalp, and nails, with genetic predisposition, and can involve the joints. Environmental and psychosocial factors can aggravate the evolution of this disease that influences the quality and survival of these patients [1]. This pathology affects between 3% of the population worldwide, presenting variations depending on age, gender, ethnicity, and geographical area. It is estimated that, in the world, there are 175 million affected with psoriasis, according to WHO 2019 the prevalence ranges between 1 to
3% of the world population. At the 67th World Health Assembly, held from May 19–24, 2014, WHO describes psoriasis as "a chronic, non-contagious, painful, disfiguring and disabling disease for which there is no cure.”[2] The etiology is unknown.

The etiology is unknown, however, multiple studies link psoriasis to environmental, immunological, and genetic factors. It has also been linked to various histocompatibility antigens (HLA). The major susceptibility locus for the development of psoriasis is PSORS1, which is located on chromosome 6p21 and is a risk factor for type I psoriasis. [3]

In Ecuador, the prevalence of the disease is not known at the national level or by geographical areas, only reports of works of Health Units published in national journals, the information at the public level is general and this disease is not recorded within the picture of autoimmune diseases although Psoriasis is considered a multisystemic disease. [4]

Plaque psoriasis known as Vulgaris is the most typical form of this disease that can occur in mild, moderate, and severe forms, whose origin is presented as the most frequent desquamative type, these are composed of dead cells that are detached in the form of plaque, commonly located on the chest, abdomen, knees, elbow, scalp, hands and feet, presenting the Auspitz sign in most cases. At the beginning of the clinical picture, these lesions appear with redness, inflammation, desquamation, pain, itching, and cracking, the diagnosis is made by observation of the area of the lesion according to its intensity and extension, many times it is necessary to perform biopsies to confirm the diagnosis ruling out other pathologies that may share the appearance and associated symptoms. [5]

Due to the good response of drugs that act on T lymphocytes in their pro-inflammatory receptors, this disease is associated with other pathologies (comorbidities) endocrine, metabolic, osteoarticular, and psychosocial factors that aggravate the quality of life in this type of patient. [6]

In 2018, a study conducted by the Ecuadorian Psoriasis Foundation (FEPSO), determined that about 0.59% of the country’s population suffers from this condition, in addition to there being a marked trend toward an increase in cases; currently, there are approximately 100,000 Ecuadorians diagnosed with psoriasis, with a predilection for male patients, between 40–60 years of age[7].

Psoriasis can be classified according to its type, pathogenesis, and severity, using for the latter, the PASI scores scale, which assesses the severity of the lesions together with the percentage of body area affected [8].

As therapeutic strategies to manage this condition, we will have the use topical drugs such as emollients, corticosteroids, and vitamin D analogs, such as calcipotriol, Methotrexac, which is an anti-inflammatory drug, developed as an analog of folic acid [9] however, these alternatives only cause relief of the cutaneous symptoms of psoriasis, without causing any effect on the underlying causes of this dermatological condition. Despite all this, it is also necessary to have optimal family and psychological
support to ensure the effectiveness of all treatment strategies employed, in addition to making lifestyle changes to avoid comorbidities such as overweight, and obesity, among others [10].

Currently, the use of biologic agents that seek to attenuate the inflammatory cascade that triggers psoriasis is a highly effective alternative for the management of this pathology, since, in this way, one of the main underlying causes of the disease is modified, improving the quality of life of patients. [11] A study conducted with 1,187 patients treated with 50 or 100 mg per week of etanercept found a better response in patients with normal weight. [12]

In this study, most of these patients received combined treatments with topical and oral urea, topical calcipotriol, local Betamethasone, Loratadine tablets, Methotrexate, and Etanercept among others. For this reason, our objective is to evaluate the response of treatments with Etanercept and Methotrexate in patients with plaque psoriasis, its pathogenic basis concerning BMI, and PASI evaluation at the beginning and control of its administration.

**Materials And Methods**

The data universe was 2820 active and passive duty military patients and their families who were treated at the Military Hospital of the city of Guayaquil from July 2020 to July 2021, of which 262 had various skin diseases and annexes, of which 94 patients with a confirmatory diagnosis of mild and moderate psoriasis, belonging to the outpatient clinic of the Department of Dermatology of the hospital. The database was obtained from the electronic medical records of each patient. The treatments used were monotherapy or combined therapy for the management of plaque psoriasis, topical, oral drugs, injectable, and biologics.

The 94 patients, all adults confirmed with mild and moderate psoriasis, received the following treatment: Initial dose of Methotrexate 5 mg increasing in intervals of 2.5 to 5 mg weekly (maximum dose 20 mg). In addition, 5 mg per day of folic acid was included. At the evaluation of the patient, the following laboratory parameters were checked: hemogram, urea, creatinine, electrolytes, and liver enzymes, with no adverse reactions or hepatotoxicity.

The dose of etanercept was 25 mg subcutaneously, twice a week. Locally, moisturizers and keratolytic were used: urea 20–40%, calcipotriol/betamethasone cream, and Loratadine 1 tablet daily. The duration of treatment was variable depending on the response of each patient, resulting in satisfaction in most of them where the intensity of skin involvement was evaluated by PASI before and after treatment.

The variables used were age, weight, height, BMI, personal and family pathological history, PASI index at the beginning and end of treatment, and laboratory parameters. Only complete clinical histories were included using the international classification ICD-10 L40, excluding patients with other types of dermatological pathology. The method used was retrospective, observational, descriptive, cross-sectional, correlational, and differential analytical. The SPSS V26.0 program (IBM Corporation, Armonk, NY, USA)
was used for data analysis. The comparison of percentages, prevalence, and ranges of the variables were determined using differential analytical statistical tests \( p < 0.05 \).

**Results**

A prevalence of 3.33% (94/2820 x 100) with mild and moderate psoriasis was obtained (Table1). The mean age was 52.2 years (with a range from 1 to 88), with a standard deviation of 17.9 years. The percentage of male patients was 71.35% (67) and 27.7% female (27), with male patients predominating. Based on height and weight, the Body Mass Index (BMI) was calculated and the average was 28.13, which according to the WHO classification table would be between the overweight and pre-obesity ranges.

In personal pathological antecedents, 35 patients presented various pathologies such as hypertension (15), type II diabetes (8), allergic rhinitis (6), hypothyroidism, hepatic steatosis, breast cancer, atopic dermatitis, rheumatoid arthritis, vitiligo, among others. Regarding family pathological history, only 2 patients reported having relatives with plaque psoriasis.

The average PASI index in the initial stage before treatment registered 10.8% corresponding to mild psoriasis and in the control phase of treatment, there was a very significant decrease of 2.99%. (Table2)

In the Pearson's Correlation in its initial stage, the age/IMC and PASI results were 0.334 and 0.381 \( >P=0.05 \) being not significant even though most of these patients were young adults with overweight and pre-obesity (Table3).

In the Student's t-test comparing the Etanercept - Methotrexac treatment with the evolution of PASI, in its initial phase and then in the control, a value of less than 0.001\( <P=0.05 \) was obtained demonstrating a very significant response, previously referred to in the evaluation of PASI, where the scaly and erythematous lesions had an excellent response to this type of biological treatment (Table 4).

In the cross-test of risk estimation, we see that, when Glycemia values exceed the normal limit \( >120\text{mg/dl} \), it constitutes a risk factor when administering Etanercept (2.231\( >\text{RR}=1 \)) and Methotrexate (2.008\( >\text{RR}=1 \) (Table 5 and 6). Most of these patients were overweight and pre-obese; however, the response to treatment with these two biologics was very significant, which was proven by the PASI index values before and after treatment.

Limitation: In the Hospital there are no genetic or molecular tests that would have allowed us to compare the type of circulating IL, they are active and passive service military patients with a diagnosis of mild and moderate Psoriasis that during the time of confinement due to the Covid19 Pandemic many were infected, there was a restriction in the number of patients seen in outpatient consultation, however, some were seen by teleconference as well as post-treatment control.
Discussion

In the Military Hospital of Guayaquil, combined drug and biological therapies were used in 94 patients whose mean age was 52 years, being these treatments topical and oral urea, topical calcipotriol, local Betamethasone, Loratadine tablets, Methotrexate and Etanercept among others. Methotrexate was used as systemic anti-inflammatory therapy mainly in moderate Psoriasis, in single doses of 0.2-0.4 mg/kg per week. Patients had to be carefully monitored for side effects such as bone marrow suppression or hepatotoxicity. [13] Etanercept which is a biologic was administered orally at 50 mg 2/week subcutaneously for 12 weeks, followed by 50 mg subcutaneously, 1/week, this biologic aids in blocking inflammatory cytokine activity. Analyzing the combination of Methotrexac with Etanercept, gave us a highly significant result in the improvement, although most patients were overweight and pre-obesity, when evaluating the PASI at the beginning at 10.8% and control at 2.99%, the response to treatment decreased their clinical picture characteristic of mild and moderate plaque psoriasis. This study corroborates a work conducted at the Hospital "Carlos Andrade Marín de Quito, Ecuador from 2010 to 2017 Treatment using infliximab had an improvement of 76.4% (± 21.7), etanercept 65.88%, adalimumab 86.2 (± 13.6) and secukinumab 94.1% (± 5. 3), concluding that biologic therapy in moderate, severe and refractory psoriasis, achieves a high percentage of improvement in most patients, regardless of the selection of the biologic drug that was not influenced by the demographic characteristics of the population, but by its availability, without modifying the final clinical response. [14]

In the management of comorbidities, the average BMI was 28.13 which corresponds to overweight and pre-obesity, some are referred to as Hypertension, Diabetes type2, rheumatoid arthritis, allergic rhinitis, breast cancer, vitiligo among others. In a study carried out in Mexico on comorbidities in plaque psoriasis, 76.31% of the population was overweight and obese, with a prevalence of 4.3% [15], which is similar to that shown in our study with a prevalence of 3.33%.

This type of comorbidity often has implications for the types of drug and biological treatments. In numerous studies, which have been published, the effectiveness of different therapies, has been negatively affected by increased BMI. [16]

In recent years, the introduction of new biologic agents has demonstrated efficacy in moderate and severe stages, with a secondary literature review highlighting the biologics as the most scientific evidence. Systemic treatments can reduce the severity of symptoms and prevent further damage so timely therapy should be initiated, to stop the progression of cutaneous symptoms and possibly reduce systemic ones. [17-18]

In our study, the combination of etanercept with methotrexate had a significant response in reducing the clinical symptoms of this disease. In a published study of a radiographic, efficacy, safety, double-blind, randomized, radiographic clinical trial in 686 patients with active rheumatoid arthritis who were randomized to treatment with etanercept 25 mg (subcutaneously twice weekly) and oral methotrexate (up
to 20 mg per week), an improvement in functional disability and delayed radiographic progression was demonstrated in this combination compared to methotrexate or etanercept alone. These findings bring us closer to achieving remission and repair of structural damage in rheumatoid arthritis[19].

It is expected that, in Ecuador, the biologics used for the treatment of mild, moderate, and severe psoriasis will be included in the basic drug list of the Ministry of Public Health, having endocrine, metabolic, osteoarticular, and psychosocial factors as comorbidities. It is for this reason that Psoriasis is considered a multisystemic disease and is at risk of presenting complications that may affect the quality of life of these patients at a personal, family, and work level.

**Declarations**

**Additional contribution:** The authors are grateful for the collaboration of the Military Hospital in obtaining the database. Special thanks to Miquel Blasco PHD. Ing, César Pincay, Dr. Mario Paredes MSc, of the Catholic University of Guayaquil and Dr. José Moleón of the Granada University of Spain, for helping us in the critical revision of the manuscript.

**References**


Tables
Tables 1-6 are in the supplementary files section.

**Figures**

## Plaque psoriasis therapy

1. **Where**
   Naval Hospital in Guayaquil, Ecuador

2. **Patients**
   94 patients with plaque psoriasis

3. **Treatment**
   Methotrexate, Etanercept

4. **Method**
   Retrospective, observational, descriptive, cross-sectional.

### Results

- **PASI index**
  - Before treatment: 10.8%
  - Control phase: 2.99%
  - P value < 0.05

The combination of Etanercept with Methotrexate has a favorable response in reducing this disease.

**Figure 1**

Combination therapy of Etanercept with Methotrexate in patients with mild and moderate Psoriasis.

**Supplementary Files**

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- Table.docx