Factors affecting response to psoriasis treatment

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Abstract

Psoriasis is a common chronic, recurrent, immune mediated disease of the skin and joints. It can have a significant negative impact on the physical, emotional, and, psychosocial wellbeing of affected patients. Psoriasis is found worldwide but the prevalence varies among different ethnic groups. It has a strong genetic component but environmental factors such as infections can play an important role in the presentation of disease. There are several clinical cutaneous manifestations of psoriasis but most commonly the disease presents as chronic, symmetrical, erythematous, scaling papules and plaques. Methotrexate (MTX) has remained the backbone of the treatment for moderate to severe psoriasis ever since its first use nearly half a century ago. Over the years, its high efficacy, low cost, relative ease of administration and usefulness in concomitant psoriatic arthritis have contributed in making MTX the drug of choice in managing severe psoriasis. Although the majority of patients achieve remission of disease activity with MTX, a significant proportion may experience mild and transient adverse effects. In this study, it was aimed to evaluate the factors which affecting response to psoriasis treatment. The study included 28 patients suffering from psoriasis and 30 healthy control subjects of different age, sex, disease duration and PASI score.

Keywords: Methotrexate, Prognosis, Psoriasis.

1. Introduction

Psoriasis is a chronic inflammatory skin disease with a strong genetic predisposition and autoimmune pathogenic traits. The worldwide prevalence is about 2%, but varies according to regions. [1]

Psoriasis can appear at any time of life. There are 2 common ages for the onset of psoriasis: the first is at around 20 years and the second is at approximately 50 years. However, other studies suggest that the mean age of onset for psoriasis vulgaris was estimated at 33 years with 75% of cases occurring before 46 years of age. Others suggest that the onset is bimodal, with peaks between 16 years and 22 years and later at 57–60 years. The age of onset seems to be slightly earlier in women than in men without sex predilection [2]

About 90% of psoriasis cases correspond to chronic plaque-type psoriasis. The classical clinical manifestations are sharply demarcated, erythematous, pruritic plaques covered in silvery scales. The plaques can coalesce and cover large areas of skin. Common locations include the trunk, the extensor surfaces of the limbs, and the scalp [3]

Psoriatic arthritis (PsA) is an inflammatory arthritis occurring either during the course of cutaneous psoriasis or without cutaneous psoriasis and characterized by negative rheumatoid factor. PsA may develop in up to 30% of psoriatic patients [4]

Pustular psoriasis is classified into two main groups

A. Generalized pustular psoriasis (Von Zumbusch):

This form is characterized by the rapid development of widespread tender erythema followed by an eruption of 1-2 mm pustules. The skin eruption is preceded by fever and malaise. It is associated with leucocytosis and elevated ESR. This severe form carries an increased morbidity and mortality and rarely acute respiratory distress syndrome [5]

B. Localized pustular psoriasis:

Two types of localized forms are palmar/plantar pustulosis and Acrodermatitis continua of hallopeau [6].

Psoriasis Vulgaris is the best-understood and most accessible human disease that is mediated by T cells and dendritic cells. Inflammatory myeloid dendritic cells release various interleukines (IL) such as: IL-23 and IL-12 to activate IL-17-producing T cells, Th1 cells, and Th22 cells to produce abundant psoriatic cytokines IL-17, interferone-γ (IFN-γ), tumor necrosis factor (TNF), and IL-22. These cytokines mediate effects on keratinocytes to amplify psoriatic inflammation. [7]

Methotrexate (MTX) is a derivative of aminopterin, an analogue and antimetabolite of folic acid. The substance inhibits dihydrofolate reductase – an enzyme responsible for the reduction of dihydrofolic acid to tetrahydrofolic acid. Methotrexate is indicated for the treatment of practically all forms of moderate or severe psoriasis, including psoriatic arthritis [8]

The mechanism of action is centered around the anti-proliferative effects of methotrexate on DNA synthesis in epidermal cells, immunosuppressive and anti-inflammatory properties [9]

The general recommendation dose in psoriasis is to start at 5–15 mg once weekly, with dose acceleration up to 25–30 mg weekly, depending on the clinical response. Folic acid, 1 mg daily, protects against some of the common side effects seen with low-dose methotrexate such as stomatitis, nausea and vomiting [10]

Monitoring for bone marrow suppression and hepatotoxicity are necessary during therapy. Concurrent use of other medications that interfere with

folic acid metabolism, such as sulfa antibiotics, can increase the toxicity of methotrexate [11]

2. Subjects and methods

This prospective case-control study included 58 participants. 28 patients suffering from psoriasis vulgaris (moderate and severe forms) in addition to 30 apparently healthy as control subjects of matched age and sex. All patients were selected from the outpatient clinic of Dermatology, Venereology and Andrology Department of Benha University Hospitals, Benha, Egypt.

Participants gave their informed written consent before enrollment and the study was approved by the Research Ethics Committee in Faculty of Medicine, Benha University.

All patients included in the study have psoriasis.

Subjects suffering from any of these conditions were excluded from the study:

1. Erythrodermic, pustular or active guttate psoriasis.
2. Psoriatic arthritis.
3. Coexisting serious medical conditions such as malignancy, diabetes mellitus, hepatic, renal or cardiovascular diseases.
4. Other infectious, inflammatory or autoimmune systemic or cutaneous disease.
5. Undergone treatment with any systemic antipsoriatic therapy or phototherapy within one month or applied topical antipsoriatic therapy within 2 weeks prior to the study initiation.
6. Pregnancy and lactation.
7. Contraindication of methotrexate for example: infections, liver disease, renal failure, conception.

2.1. Methods
1) Before Starting the Treatment Course
Patients were subjected to

A. Full history taking

Including personal history, family history, psoriasis history and past history.

B. Clinical examination

Complete general examination; including the body mass index and complete cutaneous examination; to evaluate the clinical type and severity of psoriasis using Psoriasis Area and Severity Index (PASI score

C. Laboratory examination

-Pregnancy for female patients in child bearing period.
-Liver function test.
- Kidney function test .
-Complete blood count .
-ESR
-Antinuclear antibodies , HCV antibodies .

2)Laboratory follow up of patients

Complete blood count , liver function test and kidney function test were repeated one week after the test doses then monthly.

3)After 12 weeks therapy: PASI score

2.2. Statistical analysis

The collected data was analyzed using Statistical package for Social Science (**IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).**
Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

3. Results
Demographic data

There was insignificant difference between patients and controls regarding age (p=0.267), sex (p=0.272) and BMI (p= 0.998) Table (1).

Clinical data

The mean age of onset was 31.1±10.1 years old, the mean disease duration was 9.9±3.1 years. The disease course was stationary in 42.9% and progressive in 57.1%. Eight patients had positive family history (28.6%) of psoriasis. The mean baseline PASI score was 20.7±.6.6 Table (2).

Table (1) Demographic and anthropometric data of the studied groups.

		Control N=30	Psoriasis N=28	P
Age (years)	**mean±SD**	37±12.1	41±12.9	0.267
Males	**N (%)**	15 (50)	18 (64.3)	0.272
Females	**N(%)**	15 (50)	10 (35.7)	
BMI (kg/cm^2)	**mean±SD**	24.3±3.7	24.3±4.1	0.998

N: number,SD: standard deviation; student t test was used for numerical parameters; Chi square test was

**Table (2)** Baseline clinical data in the studied cases

			Psoriasis N=28
Age of onset (years)		**mean±SD**	31.1±10.1
Disease duration (years)		**mean±SD**	9.9±3.1
Course	**Stationary**	**N %**	12 (42.9)
	Progressive	**N %**	16 (57.1)
Positive family history		**N %**	8 (28.6)
PASI		**mean±SD**	20.7±6.6

N:number, SD:standard deviation.

Table (3) PASI scores before and after treatment in all studied cases.

	Psoriasis					N=28	
	Before mean	**±SD**	**After Mean**	**±SD**	**P**	**PASI improvement (%)** Mean	**±SD**
PASI	20.7±6.6		5.9±1.7		<0.001	71.1±9.1	

N:number, SD:standard deviation.
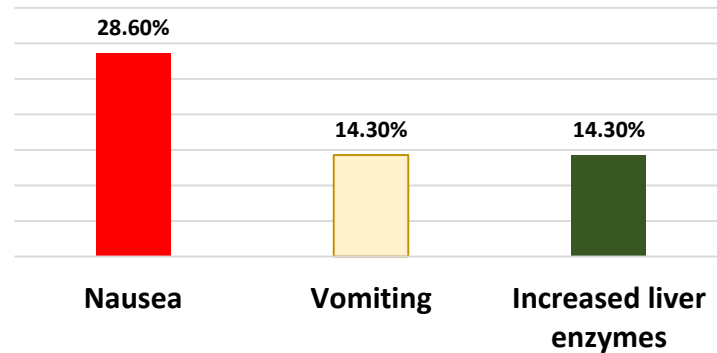
Fig. (1) Treatment side effects in the studied cases.

Table (4) Correlation between the percentage of improvement and the study variables.

	PASI improvement	
	R	**P**
Age	-0.090	0.650
BMI	0.001	0.998
Onset	-0.266	0.172
Duration	0.309	0.110
Baseline PASI	-0.645	**<0.001**

Clinical Improvement

There was significant reduction in PASI scores after treatment (p<0.001). The mean percentage of improvement (reduction in PASI scores) after treatment was 71.1% Table (3).

Safety of Psoriasis Therapy

Methotrexate was generally well tolerated by the patients. The reported side effects were nausea (28.6%), vomiting (14.3%) and increased liver enzymes (14.3%) Fig. (1).

Factors affecting the improvement percentage

PASI improvement showed significant negative correlation with baseline PASI, PASI improvement had no significant correlation with age, BMI, onset, and duration Table (4).

4. Discussion

Psoriasis is a common chronic inflammatory disease of the skin and joints affecting approximately 2–3% of the world's population. Many studies have reported various factors contributing to the pathogenesis of psoriasis including genetic factors, the immune system and environmental conditions [12].

The hallmark of psoriasis is the sustained inflammation that leads to an uncontrolled keratinocytes proliferation and dysfunctional differentiation. The histology of the psoriatic plaque shows acanthosis (epidermal hyperplasia), which overlies inflammatory infiltrates composed of dermal dendritic cells, macrophages, T cells, and neutrophils [13].

Methotrexate is still the backbone of the treatment for moderate to severe psoriasis. Over the years, its high efficacy, low cost, relative ease of administration and usefulness in concomitant psoriatic arthritis have contributed in making MTX the drug of choice in managing severe psoriasis, so it is considered as the first-line systemic agent in moderate to severe psoriasis as recommended by evidence based guidelines in Europe and North America [14]

In our study there was insignificant difference between patients and controls regarding age, sex and BMI . This was in agreement with [15]

There was significant reduction in PASI scores after treatment in this study which approved with [16]

There was no significant correlation between PASI improvement and age, quality of life, BMI, onset, and duration in our study, but in [17] they found that there was relation between PASI improvement and quality of life, onset and duration of disease.

5. Conclusion

The most important factor that effect on response to psoriasis treatment on patients is PASI score

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