Methotrexate in Psoriatic Arthritis: A Retrospective Study

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Received June 21, 1982

Abstract. The response of psoriatic arthritis to methotrexate was evaluated retrospectively in 59 consecutive patients. Initially almost all received 15 mg weekly. When clinical improvement occurred, the dose was gradually reduced. In 7 patients methotrexate had to be discontinued within a year due to adverse reactions. The remaining 52 patients were treated from 1 to 11 years, median 3 years. Among these a modest improvement was seen in 21, while in 22 the signs of inflammatory joint disease almost disappeared. The favourable response was related to the short duration of arthritis, but unrelated to the severity of the disease.

Key words: Methotrexate; Psoriatic arthritis

Methotrexate (MTX) has been used in psoriatic arthritis since 1964, when Black and co-workers (1) in a double-blind study of 21 patients found the drug effective in suppressing both skin and joint manifestations. Later other small trials have indicated a beneficial effect (2, 3), but no large follow-up studies have appeared. Nyfors in a survey on effects and side effects of MTX therapy of psoriasis (5), however, declared that 15 of 41 MTX-treated patients with psoriatic arthritis were relieved of pain, and that in another 15 the pain had been appreciably mitigated. The present report concerns a retrospective analysis of a 11-year material of 59 consecutive patients suffering from psoriatic arthritis and treated with MTX in our departments.

MATERIAL AND METHODS

The response of psoriatic arthritis to MTX was evaluated in 59 consecutive patients. All had classical sero-negative psoriatic arthritis (9) and manifest psoriasis. Only patients with polyarthritis not responding favourably to therapy with non-steroid anti-inflammatory drugs were considered as candidates for MTX treatment. Excluded from this therapy were patients who had severe renal and liver disease, or a hematological disorder, such as severe anemia, neutropenia or thrombocytopenia. Pregnancy was also a cause for exclusion.

MTX was administered weekly on a divided dose intermittent oral dosage schedule over a 36-hour period (8). In case of troublesome dyspepsia the intramuscular route of administration was used. Initially most patients received 15 mg MTX weekly. When clinical improvement occurred the dose of MTX was gradually reduced.

Before treatment, clinical and roentgenographic studies were made on the joints. All patients were questioned about age at onset of their arthritis and about their analgesic consumption. The erythrocyte sedimentation rate (ESR) was determined and sera were analysed by Rose-Waaler sheep-cell agglutination test, latex-fixation test (RAT), and antinuclear factor. Patients having a positive sheep-cell agglutination test or RAT were not included in the study.

During treatment, joint involvement (pain on motion, tenderness, and swelling), analgesic consumption and ESR were estimated. These parameters were graded as −1 (worsened), 0 (unchanged), 1 (improved) and 3 (normalized). By adding these scores an improvement score (range −3 to 9) was obtained for each patient. Statistical significance was assessed using Wilcoxon's test for two samples. A p-value below 0.05 was considered significant.

RESULTS

In 7 (8%) of the 59 patients MTX had to be discontinued within one year. The adverse reactions that caused discontinuation of the drug were nausea (1), vertigo (1), dyspepsia (1), duodenal ulcer (1), incipient or manifest liver cirrhosis (2), and persistent elevation of serum glutamic pyruvic transaminase (1).

The influence of MTX on psoriatic arthritis was evaluated in the remaining 52 patients (28 females and 24 males). The median age at onset of arthritis was 37 years (range 10 to 73 years). 47 (90%) of these patients had distal interphalangeal joint involvement, 33 (63%) had sacro-iliitis, and 9 (17%) had roentgenographic signs of spinal involvement. 46 had psoriasis vulgaris and 6 pustular psoriasis.

The response to MTX was favourable in most instances (Table I), and in 22 (42%) patients the signs of inflammatory joint disease nearly disappeared. Also, Table I shows that statistically this favourable response was related to a short duration of arthritis, but unrelated to sex, age, initial ESR and number of joints affected.

The duration of MTX treatment varied from 1 to 11 years (median 3 years). However, the improvement of psoriatic arthritis was not related to duration of MTX treatment (Table I).

Table 1. *Response of psoriatic arthritis to MTX treatment*
Values are medians. The 95% confidence limits are indicated in parentheses

Improvement[a] score	*n*	Female/male	Age (yrs)	Duration of arthritis (years)	Initial ESR	Number of joint-groups affected before therapy	Duration of therapy (years)
−3 to 0	9	5/4	45 (26–52)	8 (4–20)	48 (15–61)	4 (3–8)	4 (2–11)
1 to 3	10	7/2	44 (36–63)	11 (4–15)	41 (10–75)	6 (4–8)	5 (2–9)
4 to 6	11	4/7	55 (41–69)	10 (2–13)	26 (10–41)	4 (3–5)	3 (2–4)
7 to 9	22	11/11	57 (29–68)	2[b] (1–4)	36 (25–45)	3 (2–4)	3 (2–4)

[a] Combined "clinical response score" including parameters: pain on motion, tenderness, swelling, analgesic consumption and ESR, parameters were graded −1 (worsened), 0 (unchanged), 1 (improved) and 3 (normalized).
[b] $p<0.01$.

When the status of arthritis was investigated, MTX had been withdrawn in 9 of the 52 patients, showing no relapse of their arthritis. After drug withdrawal, these patients were observed for 9 to 22 months. The other 43 patients were maintained on a median MTX dose of 10 mg (range 2.5 to 15 mg) weekly.

DISCUSSION

The purpose of the present study was to evaluate retrospectively the use of MTX in a larger group of patients suffering from psoriatic arthritis. Our data argue that MTX may continue to play an important role in the medical management of the more severe forms of the disease. The results of treatment seem to be most favourable, the shorter the duration of the disease. Our data agree closely with previous works on smaller materials of psoriatic arthritis (1, 2, 3), and it may also be noted that methotrexate has recently been reported successful in rheumatoid arthritis (4) as well as in Reiter's disease (6).

Methotrexate should be given with caution and monitored carefully, as adverse reactions are not uncommon (5, 7). In long-term studies special attention should be given to liver toxicity. Liver biopsies should be performed at least in all patients in whom a cumulative dosage of MTX exceeds 1.5 g (10). Also alcohol intake should be limited in patients on MTX. In our study only 7 patients discontinued MTX treatment due to side effects. Liver cirrhosis was observed in 2 but was found only to be of mild nature (10), and apart from transient increases in serum pyruvic transaminases no other abnormalities were found in laboratory data for evaluating liver damage.

It is also mandatory that patients be aware of drug interactions. Salicylates, i.e. common analgetics, displace MTX from plasma protein binding and increase the risk of toxicity. On the other hand the effect of MTX may be reduced with concurrent administration of Trimethoprim, also a folic acid antagonist (5). Several articles have dealt with the management of psoriasis by MTX (7, 8, 10). These articles are in general also valid for the control of MTX treatment in psoriatic arthritis. If adequate precautionary measures are taken, patients with psoriatic arthritis—as other psoriatics—may be treated safely and beneficially for years with MTX (5). Naturally, however, one should try to reduce the dosage gradually, when sufficient clinical improvement has occurred. In our study in 9 of 52 patients MTX were withdrawn without recurrence of the arthritis.

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Segmental Pigmentation Disorder

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Received April 14, 1982

Abstract. Pigmentary changes with a dermatomal distribution are described in 30 children. The disorder, up to now unrecognized as an entity, is apparently caused by an embryological determination. It is more obvious in children with darker skin, and seems to fade very slowly over the years. In our experience the incidence is 0.35%. No relation to other anomalies could be established.

Various pigmentary disorders are known to be associated with lesions of the nervous system.

Segmental pigmentation disorder (SPD) is a rather common hypo- or hyperpigmented lesion, having a dermatomal distribution or being sharply delineated along the midline and thus related to a neurogenic distribution.

Occasional case reports of this condition have appeared, but it has not been thoroughly discussed. The purpose of this communication is to report on our experience with this entity.

MATERIAL AND RESULTS

Thirty cases corresponding to the description of SPD were seen in our pediatric dermatology clinic between 1977 and 1981, giving an incidence of 0.35%.

The children were referred because of various dermatological lesions, but only a few of them were related to this specific disorder. In no case was attention drawn by the referring physician to the neurological distribution.

The ages of our patients ranged between 2 months and 17 years. There were 16 males and 14 females.

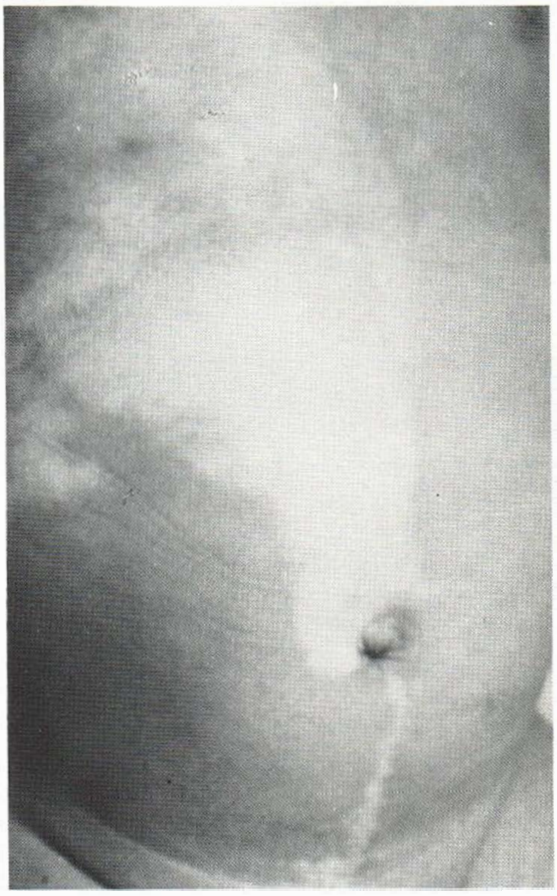

Fig. 1. Depigmentation on abdomen wall with a sharp midline demarcation.

All the children examined were Jewish. The majority (21 out of 30) were of oriental origin (who tend to have a darker skin complexion). The parents of 3 children were of mixed origin, and only 6 children had parents of Ashkenazi origin.

In 23 the lesion was noticed by the parents before the age of 1 year, in 25 before the age of 5 years. In most cases the parents did not seem to be concerned and only 5 children had been brought previously to medical attention because of this pigmentation disorder.

Skin characteristics: 15 cases presented with hyperpigmentation, 15 with hypopigmentation. The distribution varied as follows: over the back (9), the chest (12), and the abdomen (16), with a sharply demarcated border over the midline in the linea alba, but not along its whole length. The lateral border was not sharply delineated. In 7 cases the pigmentation disorder had a dermatomal distribution over an upper extremity (3) or lower extremity (4), in 2 cases over the face. Occasionally it was difficult to determine whether the disorder was hypopigmentation of one side or hyperpigmentation on the neighbouring area.