A DOUBLE-BLIND PLACEBO-CONTROLLED STUDY OF AURANOFIN IN PATIENTS WITH PSORIATIC ARTHRITIS

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Two hundred thirty-eight patients with psoriatic arthritis were entered into a 6-month, multicenter, double-blind trial comparing auranofin and placebo. Polyarthritis (>5 tender joints) was present in 90% of the patients, and 94% were seronegative. Auranofin treatment was statistically superior to placebo treatment, according to physician's global assessment and functional scores. A trend in favor of auranofin treatment was seen for each of the other disease parameters studied. Psoriasis worsened in 6 auranofin-treated patients and in 3 placebo-treated patients. The incidence and nature of other side effects were similar to those observed in similar trials of patients with rheumatoid arthritis. Our observations suggest that the use of auranofin in the treatment of psoriatic arthritis is safe, although its therapeutic advantage over treatment with nonsteroidal antiinflammatory drugs alone is modest.

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Psoriatic arthritis is an inflammatory erosive joint disease characterized by its association with psoriasis and by the absence of serologic evidence of rheumatoid factor. Standard treatment for this condition includes salicylates and nonsteroidal antiinflammatory drugs (NSAIDs). When therapeutic response to this basic regimen is inadequate, disease-modifying agents, such as antimalarial drugs (1–4), gold salts (5–7), and methotrexate (8,9), have been used.

The efficacy of parenteral gold in the treatment of psoriatic arthritis has been evaluated in 3 studies (5–7). Although they were not placebo-controlled trials, they each concluded that injectable gold was efficacious in this condition. This apparent success of parenteral gold therapy in psoriatic arthritis, the comparable effects of oral and parenteral gold in treating seropositive rheumatoid arthritis (10–12), and the lower risk of toxic effects with oral gold strongly suggested that auranofin would be a safe and effective therapeutic option for treating patients with psoriatic arthritis.

We designed this multicenter, double-blind

study to evaluate the effectiveness, tolerability, and safety of auranofin (6–9 mg/day) versus placebo in the treatment of psoriatic arthritis. This study, with its enrollment of 238 patients, represents the largest prospective, double-blind, placebo-controlled trial assessing a pharmacologic agent in the treatment of psoriatic arthritis.

PATIENTS AND METHODS

Patient selection criteria. Patients eligible for entry into this 6-month double-blind parallel trial comparing auranofin and placebo therapy were age 18 years or older, and had been diagnosed as having psoriatic arthritis. Patients who had clinically apparent psoriasis or a documented history of psoriasis of the skin, scalp, or nails and active joint disease, which is defined as swelling and/or pain/tenderness in at least 3 joints and a total joint score of at least 10 using a grading system of 1 (mild) to 3 (severe) for each active joint, were entered into the study. The minimum duration of disease was 3 months. Twenty-seven centers participated. The study protocol was approved by each institution's review board, and each patient signed an informed consent form prior to entry into the study.

All patients had been treated with antiinflammatory doses of aspirin or other NSAID, which had not been adequately effective or toxic reactions to these agents had occurred. All patients were receiving stable doses of aspirin or NSAIDs and had not taken gold, D-penicillamine, levamisole, methotrexate, azathioprine, or antimalarial agents for at least 2 months. The decision not to exclude patients who had been treated with gold was based on the fact that parenteral gold and auranofin are basically different drugs and that the therapeutic response and/or toxic effects of one compound does not necessarily predict these outcomes with the other. Concomitant medications for conditions other than psoriatic arthritis were permitted. Concurrent treatment with 8-methoxypsoralen and ultraviolet A irradiation or treatment within 2 months of the initiation of the study medication, however, was a reason for exclusion from the study.

Patients were excluded if they had any of the following conditions: a diagnosis compatible with rheumatoid arthritis or evidence of lupus erythematosus, primary ankylosing spondylitis, polyarteritis nodosa, polymyositis/dermatomyositis, scleroderma, rheumatic fever, gouty arthritis, pseudogout, septic arthritis, Reiter's syndrome, hypertrophic osteoarthropathy, neuro-arthropathy, sarcoidosis, multiple myeloma, leukemia/lymphoma, or agammaglobulinemia. Patients with a history of exfoliative dermatitis or with clinically apparent psoriasis involving more than 60% of the total body area were also excluded.

Patients with proteinuria (>0.5 gm/24 hours), thrombocytopenia (platelet count <100,000 cells/mm^3), leukopenia (total white blood cell count <3,000 cells/mm^3 or polynuclear cell count <1,500 cells/mm^3), hematuria, or elevated levels of serum creatinine (>2 mg%) were excluded from the study Pregnancy was also a reason for exclusion, but female patients with childbearing potential were admitted if they practiced a clinically accepted method of contraception.

To assess eligibility, each patient was evaluated approximately 4 weeks before administration of the coded study medication. At this time, a medical history was taken and a physical examination was performed.

Drug administration. The randomization was done by computer-generated random numbers for patients at each clinic. Patients within each participating clinic were assigned in blocks of 10, at a 1:1 ratio, to receive either auranofin (3 mg/day) or placebo, initially administered in the form of 2 capsules/day. Uniform criteria were not used to define the lack of clinical improvement. Thus, if after 3 months there was no indication of clinical improvement (according to the investigator's judgment), the investigators had the option of increasing the dosage of the study medication to 3 capsules/day. The dosage could be reduced at any time because of intolerance.

Patients were instructed to maintain their pre-entry dosages of oral steroids (not to exceed 7.5 mg/day of prednisone or prednisone equivalent for women and 10 mg/day for men) and/or NSAIDs during the first 3 months of the study. Intraarticular injections of steroids were not permitted. Analgesic agents, such as propoxyphene or acetaminophen, could be taken as needed to treat pain.

Evaluations. Clinical assessments of disease activity were performed at baseline and monthly thereafter (except where noted).

Physician's evaluation. Physician's assessments included joint counts of tenderness and of swelling, evaluation of skin involvement, and a global assessment. For the joint tenderness count, 68 peripheral joints were evaluated, and a scale of 0–3 was used to score the assessment, as follows: 0 = no tenderness, 1 = positive response on questioning patient, 2 = spontaneous response elicited during examination of joint, and 3 = withdrawal by patient during examination of joint. For the joint swelling count, 66 joints were scored, using the following scale: 0 = no swelling, 1 = detectable synovial thickening without loss of bony contours, 2 = loss of distinctness of bony contours, and 3 = bulging synovial proliferation with cystic characteristics.

The skin was evaluated at baseline, 3 months, and 6 months of study. The area of psoriatic involvement, which was expressed as a percentage of the total body area, was recorded, and the "rule of nines" was used to divide body surface areas (head = 9%, upper extremity = 9% × 2, lower extremity = 18% × 2, upper trunk = 18%, lower trunk = 18%, and genitals = 1%). At each evaluation, the location of lesions was also noted on drawings of anterior and posterior views of the human body. The presence of fingernail dystrophy was noted, and any involved nail was identified.

The physician's global impression of the treatment results used the following qualifiers to describe the findings of the assessment: marked improvement = complete or nearly complete remission of disease activity, moderate improvement = partial remission of disease activity, minimal improvement = slight improvement that does not alter the status of the care of the patient, no change, and worsening of disease = exacerbation of disease activity.

Patient's evaluation. The patients assessed their conditions as well. Their evaluations included the duration

of morning stiffness (in minutes), the severity of pain (0 = no pain and 4 = excruciating pain), and an evaluation of skin discomfort caused by the psoriasis (0 = none and 3 = severe).

In addition, function scores both for activities of daily living and for occupational activities were arrived at using the following scale: 0 = no restriction of activities, 1 = able to carry out most activities, 2 = discomfort causing moderate restriction of activities, and 3 = unable to perform most of usual activities. The patients' global assessment of treatment results used the following undefined qualifiers: marked improvement, moderate improvement, minimal improvement, no change, and worsening of disease.

Laboratory evaluation. A complete blood cell count (including differential cell count and platelet count) and blood chemistries profile were performed at baseline and every 4 weeks thereafter. The blood chemistries survey included levels of creatinine, serum glutamic oxaloacetic transaminase, alkaline phosphatase, total bilirubin, blood urea nitrogen, uric acid, total serum protein, and serum albumin. A complete urinalysis was also done at 4-week intervals. A multi-test reagent strip was used to detect urinary protein.

Adverse effects. Patients were interviewed monthly about untoward effects. The physician was asked to express an opinion concerning the severity (mild, moderate, or severe) of the symptom and its relationship to the study medication. Investigators were also asked to record the date the symptom first occurred and the date of its resolution.

Statistical analysis. Data were analyzed using the SAS software system. To compare treatment regimens, an analysis of covariance was used for continuous data, chi-square statistics were used for categorical data, and the CATMOD procedure was used for ordinal variables. Results were compiled for all patients who completed the 6 months of the trial. For patients who completed a minimum of 90 days of therapy with the study medication, a "last visit" analysis was made of the data from each patient's final visit of the study.

All 27 centers contributed "efficacy" data. Results were uniform across centers, and the data were therefore pooled for analysis.

RESULTS

Characteristics of the patient population. Two hundred thirty-eight patients were accepted into the study and randomized to the 2 coded medications (120 for auranofin and 118 for placebo). The demographic characteristics of these patients at study entry are shown in Table 1. More than 90% of the patients had presented with polyarticular arthritis (>5 affected joints). The patterns of peripheral joint involvement were similar for both treatment groups, and there were no between-group differences in tender or swollen joint counts or scores, duration of morning stiffness, pain scores, and functional scores. There were no between-group differences in the distribution of patients by the percentage of skin involved or the severity of the skin discomfort. Skin lesions affected 10% or less of the total body surface in 60% of the patients in each group, and most patients believed their skin discomfort was mild. Twenty-four patients in the auranofin treatment group and 21 in the placebo treatment group had previously taken gold. Seventeen (71%) of those in the auranofin treatment group had not responded to the drug, as compared with 13 (62%) of those in the placebo treatment group; all others had experienced toxic reactions.

Table 1. Demographics and clinical characteristics of study patients at baseline, by treatment group*

	Auranofin-treated group (n = 120)	Placebo-treated group (n = 118)
Age (years)		
Mean ± SEM	44 ± 1.1	45 ± 1.2
Range	20–79	19–80
Median	43	47
Sex		
Male	73 (61)	72 (61)
Female	47 (39)	46 (39)
Race		
White	120 (100)	113 (95)
Hispanic	–	3 (3)
Asian	–	2 (2)
Disease duration (months)		
Mean ± SEM	89 ± 8	89 ± 8
Range	3–408	3–360
Median	60	60
Disease severity		
Mild	37 (30)	33 (28)
Moderate	73 (62)	70 (59)
Severe	10 (8)	14 (12)
Not stated	–	1 (1)
Rheumatoid factor		
Positive (titer ≥1:80)	6 (5)	9 (8)
Negative	94 (78)	88 (75)
Not tested	20 (17)	21 (17)
Previous gold treatment (parenteral)	24 (20)	21 (18)
Taking corticosteroids	7 (6)	7 (6)

* Except where noted, values are number (%).

Withdrawal from the study. Of the 238 patients who entered the trial, 50 withdrew before completing the 6-month study (Table 2). Twelve patients taking auranofin and 8 patients taking placebo withdrew because of one or more adverse effects. With few exceptions, the symptom(s) that resulted in the patient's stopping therapy was judged by the investigator to be related to the use of the study medication (Table 3). Seven auranofin-treated patients (6%) and 10 placebo-treated patients (9%) stopped taking the medication because of insufficient therapeutic response. The average duration of treatment at the time of withdrawal was 116 days. An additional 13 patients withdrew from

Table 2. Reason for withdrawal from the study, by treatment group

	Auranofin-treated group	Placebo-treated group
No. entering trial	120	118
Reason for withdrawal		
Adverse effect	12	8
Insufficient therapeutic effect	7	10
Intercurrent illness	2	0
Pregnancy	0	1
Lost to followup	6	4
Total	27	23

the study because of reasons that were not related to the use of the study medication.

Changes in medication dosages. Changes in NSAID therapy during the study were minimal. Eight patients (4 in each treatment group) decreased the daily dosage of NSAID, and 12 patients (6 in each treatment group) increased the daily dosage. Seven patients in the auranofin treatment group were taking steroids; 2 of these patients decreased the dosage. None of the placebo-treated patients who were taking steroids decreased the dosage. Thirty-two auranofin-treated patients (27%) and 39 placebo-treated patients (33%) increased the dosage of the study medication to 3 capsules per day. Most of the patients (57 of 71, 80%) tolerated the increased dosage and continued to take the higher dosage until the end of the study.

Table 3. Adverse effects leading to withdrawal from the study, by treatment group*

	Auranofin-treated group	Placebo-treated group
Diarrhea/loose stools	6	3
Abdominal distress/cramps	2	2
Worsening psoriasis	2	1
Proteinuria	2	1
Rash	1	1
Stomatitis	1	–
Dizziness	1	–
Weakness	1	–
Shingles	1†	–
Hives	1†	–
Microscopic hematuria	1†	–
Rectal bleeding	1	–
Skin infection	1	–
Bladder pressure	–	1
Light sensitivity/blurred vision	–	1
Flu-like symptoms	–	1†
Fever	–	1
Nausea	–	1
Perianal itching	–	1
Gastroenteritis/pseudomembranous colitis	–	1
Leukopenia	–	1

* Some patients withdrew because of more than 1 symptom.
† Symptom was not related to the study medication.

Response to treatment. Data from 93 auranofin-treated patients and 95 placebo-treated patients were available for analysis at study end (6 months). For both groups of patients, there was a significant decrease in the number of tender and swollen joints at 6 months compared with baseline values (Table 4). The reductions were slightly higher for auranofin-treated patients, but no statistically significant difference between regimens was observed. Similarly, there was a significant decrease in joint tenderness scores, joint swelling scores, and duration of morning stiffness, but comparisons between treatment groups showed no statistically significant differences.

"Last visit" data were available for 105 auranofin-treated patients and 109 placebo-treated patients. The findings were similar to those of the 6-month data analysis. There was a significant decrease from baseline values of the number of tender joints (-3.7 ± 1.0 mean $\pm$ SEM in auranofin-treated patients and -3.5 ± 1.1 in placebo-treated patients), and the number of swollen joints (-2.5 ± 0.6 in auranofin-treated patients and -1.8 ± 0.8 in placebo-treated patients), but there were no statistically significant differences between regimens.

Important improvement (defined as a reduction in joint count >50% of the baseline value) was seen in 33 patients taking auranofin (36%) and in 24 patients taking placebo (25%). Worsening (defined as a 50% increase from baseline) was seen in 2 patients taking auranofin (2%) and in 6 taking placebo (6%).

Because the global assessments, pain scores, and scales measuring the disease effects on patients' activities were discrete categories, we analyzed changes in grades relative to the baseline scores, using the SAS CATMOD procedure. This analysis compares the distribution of the magnitude of change (e.g., improvement by 1 grade, worsening by 2 grades, etc.) between the 2 treatment groups. For brevity, Figure 1 shows only the 2 broad categories of improvement and worsening. For the global assessments data, improvement was defined as a rating of marked or moderate improvement; for the pain and disability scales, improvement was defined as a decrease in the score by 1 grade. Worsening was defined as a global rating of worsening of disease and an increase by 1 grade in the pain or function (disability) score. The probability statements were calculated on the magnitude of change.

Table 4. Findings at 6 months, versus baseline data, in 188 patients who completed the study, by treatment group*

Variable	Auranofin-treated group (n = 93)			Placebo-treated group (n = 95)		
	Baseline	6 months	Change	Baseline	6 months	Change
No. tender joints						
Mean ± SEM	18.2 ± 1.4	14.2 ± 1.4	−4.0 ± 1.1	18.8 ± 1.3	15.1 ± 1.4	−3.7 ± 1.2
Range	2–62	0–60	−35–32	0–58	0–67	−36–46
Joint tenderness score						
Mean ± SEM	27.7 ± 2.3	20.1 ± 2.3	−7.7 ± 1.7	27.3 ± 2.3	21.2 ± 2.4	−6.1 ± 1.8
Range	2–105	0–116	−56–58	0–155	0–122	−55–97
No. swollen joints						
Mean ± SEM	13.2 ± 1.1	10.8 ± 1.1	−2.5 ± 0.7	14.3 ± 1.3	12.3 ± 1.3	−2.0 ± 0.8
Range	0–44	0–49	−23–12	0–52	0–50	−24–46
Joint swelling score						
Mean ± SEM	19.0 ± 1.6	13.6 ± 1.5	−5.4 ± 1.1	20.5 ± 2.1	15.9 ± 1.7	−4.6 ± 1.6
Range	0–75	0–71	−44–34	0–113	0–85	−82–79
Pain score						
Mean ± SEM	2.1 ± 0.06	1.6 ± 0.09	−0.5 ± 0.10	1.9 ± 0.09	1.7 ± 0.09	−0.2 ± 0.10
Range	1–3	0–3	−3–2	0–4	0–4	−2–2
Morning stiffness (minutes)						
Mean ± SEM	100.7 ± 12.1	58.5 ± 9.3	−42.1 ± 13.6	97.1 ± 11.1	80.0 ± 11.1	−17.2 ± 8.2
Range	0–780	0–600	−780–360	0–780	0–780	−360–240
Daily activities function score						
Mean ± SEM	1.3 ± 0.09	0.8 ± 0.09	−0.5 ± 0.09	1.2 ± 0.08	1.0 ± 0.08	−0.2 ± 0.08
Range	0–3	0–3	−2–2	0–3	0–3	−2–3
Occupational activities function score						
Mean ± SEM	1.2 ± 0.09	0.7 ± 0.09	−0.5 ± 0.09	1.1 ± 0.1	1.0 ± 0.9	−0.1 ± 0.09
Range	0–3	0–3	−2–2	0–3	0–3	−3–2

* All changes from baseline values were statistically significant ($P < 0.05$ by Student's paired t-test), except for the occupational activities function scores in the placebo-treated group. See Patients and Methods for explanation of scoring systems used.

The auranofin-treated group demonstrated significantly greater improvement than the placebo-treated group in terms of the physician's global assessment and changes in occupational and daily activity scores. There was a trend in favor of auranofin treatment for improvements in pain score and patient's global assessment.

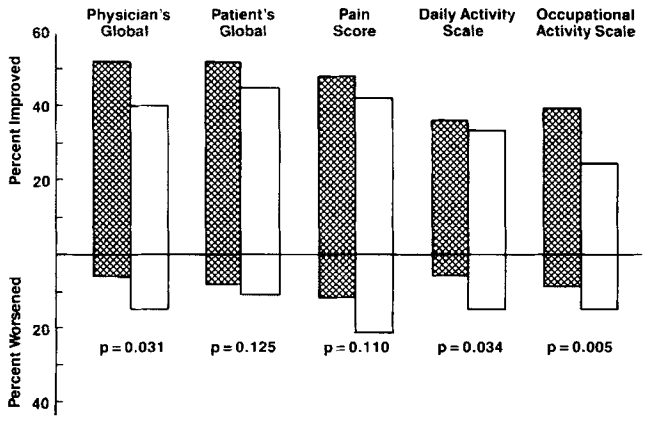

Figure 1. Proportion of patients whose psoriatic arthritis symptoms improved or worsened while taking auranofin (hatched bars) or placebo (open bars). See Patients and Methods for definitions and scoring systems used. P values indicate differences between the 2 treatment groups (CATMOD procedure).

For both treatment groups, the percentage of the total body area affected by psoriasis decreased during therapy, with a slightly larger mean (±SEM) decrease in those treated with auranofin (−1.6 ± 0.7 versus −0.7 ± 1.0). In addition, equal proportions of both groups reported a reduction in the degree of skin discomfort.

Adverse effects. During the course of the trial, 80 auranofin-treated patients (67% of total) and 68 placebo-treated patients (58% of total) experienced at least 1 adverse reaction that was judged to be related, probably related, or possibly related to the use of the study medication. The clinically important adverse reactions, defined as those occurring in >5% of patients in either treatment group, are listed in Table 5. The most common symptom was diarrhea, which occurred in approximately 50% of the auranofin-treated patients, a rate that is similar to that reported in worldwide clinical trials of auranofin (13).

Psoriasis symptoms worsened in 5% and 3% of

Table 5. Clinically significant adverse reactions related to the study medication, by treatment group*

	Auranofin-treated group (n = 120)	Placebo-treated group (n = 118)
Diarrhea/loose stools	61 (51)†	29 (25)
Nausea/vomiting	11 (9)	10 (9)
Abdominal distress/cramps	10 (8)	11 (9)
Stomatitis	10 (8)	5 (4)
Rash	5 (4)	10 (9)
Exacerbation of psoriasis	6 (5)	3 (3)
Proteinuria	5 (4)	9 (8)

* Values are number (%).
† $P < 0.001$ versus placebo-treated group, by Student's t-test.

the auranofin-treated and placebo-treated patients, respectively. Most of the exacerbations were mild. Two patients in the auranofin group were successfully treated with topical administration of betamethasone, but withdrawal of the study medication was necessary for 2 patients in the auranofin group and 1 in the placebo group.

Effects on laboratory variables. Except in the 3 patients who were withdrawn from the study because of proteinuria (2 in the auranofin group and 1 in the placebo group), there were no statistically significant or clinically important changes in the laboratory variables.

DISCUSSION

Clinical practice, as reflected in most textbooks (14,15), acknowledges the importance of the use of NSAIDs in treating the joint symptoms of psoriatic arthritis. But for patients with significant joint disease or for patients with symptoms that persist despite NSAID therapy, other remittive therapies are required. Antimalarial agents, gold salts, D-penicillamine, azathioprine, 6-mercaptopurine, and methotrexate have thus far been used as remittive agents in patients with psoriatic arthritis. However, the evidence supporting the efficacy of any of these drugs in treating this disease is based mainly on observations in studies not using controls (1–7,16,17).

We are aware of only 3 controlled trials in patients with psoriatic arthritis; 1 of them involved azathioprine (18), and the other 2 involved methotrexate (8,9). The first was a cross over study in which azathioprine treatment was evaluated in 6 patients (18). Assessment of joint changes after 6 months revealed a mean decrease of 11 tender joints compared with baseline values. No improvement was noted during placebo treatment. The second trial was a double-blind cross over study reported by Black et al (8), in which 21 patients were treated with methotrexate at a dosage of 1–3 mg/kg, parenterally, every 10 days for 1 month. A significant reduction in the joint index, erythrocyte sedimentation rate, and percentage of skin area affected was observed in the patients when they were taking methotrexate. In the third study, 37 patients were randomized to methotrexate treatment (7.5–15 mg/week) or placebo treatment for 12 weeks (9). Results showed that methotrexate was superior to placebo only in the physician's assessment of arthritis activity and in improvement of the amount of skin surface area involved. There were no significant between-group differences in the reduction of the number of tender and swollen joints, grip strength, or erythrocyte sedimentation rate. Although the sample size was small, the investigators concluded that there was no objective evidence that methotrexate was effective in controlling the joint symptoms of psoriatic arthritis.

In the present study, in which 238 psoriatic arthritis patients were initially enrolled, we found no statistically significant evidence that auranofin was superior to placebo in reducing the number or severity of joints affected with arthritis. The reduction in the number of affected joints at 6 months, compared with baseline scores, was larger for auranofin-treated patients than for placebo-treated patients, by 0.7 tender joints and 0.5 swollen joints. Based on the error term in the model, a true difference of 5.2 tender joints and 3.3 swollen joints would provide a statistically significant observed difference, with a type I error of 5%.

In double-blind studies comparing oral gold and placebo in patients with rheumatoid arthritis (10–12), the absolute difference in response ranged from 1.9 to 9 for the joint variables (tenderness and swelling). Although the response to placebo was higher in the present study, these prior studies provide evidence that a positive effect of auranofin in psoriatic arthritis is less than that in rheumatoid arthritis.

Despite the lack of statistically significant differences between the 2 treatment groups with respect to the joint variables, there were many trends to suggest that auranofin plus NSAID treatment was more effective in controlling the disease than was NSAID therapy alone. Thus, in every parameter studied, auranofin was "numerically superior" to placebo. If there was no difference between treatment regimens, then one might expect that placebo would have

been "numerically superior" to auranofin in at least 1 or 2 variables that defined improvement. Placebo, however, was superior only in parameters that suggested that the disease activity had worsened.

In clinical trials assessing chronic multifaceted diseases such as rheumatoid or psoriatic arthritis, there is no 1 objective parameter to adequately describe the results of treatment. Nevertheless, global impressions are often used as a single indicator to measure the success of medical intervention in any given patient. In this study, a patient was considered to have been treated successfully if the global rating given by the treating physician was that the patient's condition was either markedly or moderately improved. Similar to the results of the objective disease factors analysis, there was a trend to suggest that auranofin was superior to placebo. In fact, the largest difference distinguishing treatment groups in this study is found here. Fifty-two percent (47 of 91) of auranofin-treated patients who completed 6 months of therapy were considered to have been successfully treated, in contrast to 40% (38 of 95) of the placebo-treated group. When one includes in the analysis of the global impressions that a greater proportion of placebo-treated patients worsened, statistical significance is achieved.

Is the modest advantage of auranofin treatment clinically meaningful? When controlled for the slight differences between treatment groups at baseline, the observed difference between auranofin and placebo treatment in the reduction of tender and swollen joints was, as mentioned before, less than a single joint—an unimpressive result. Of course, larger differences were seen in duration of morning stiffness and in joint tenderness and swelling scores. Perhaps the combination of these variables or some variable not included in the study could explain why investigators, when making their global assessment of treatment, judged over half of the auranofin-treated patients to have shown a moderate or marked improvement—a more impressive result.

We explored the possibility that in the global assessments the support for auranofin was a result of a combination of response variables that could only be detected by a multivariate statistic. Therefore, although not defined by our study protocol, we performed a multivariate analysis. We designed the comparison between treatment regimens to include 2 dependent variables: 1) the sum of all 4 joint criteria as 1 factor, and 2) the sum of the pain scores, morning stiffness, and the activity scores (daily and occupational) as a second factor. Because the degree of skin involvement is not related to the arthritis symptoms, this variable was omitted. The analysis considered each factor separately (univariate) and in combination (multivariate).

The results of the univariate analysis for the joint factor showed a favorable trend for the auranofin response, but again, one that was not statistically significant ($P = 0.416$). The univariate analysis for the second factor, however, was significant ($P = 0.014$), and the multivariate analysis of the combined factors also showed statistical significance ($P = 0.046$).

Since the multivariate analysis includes the joint count data, we interpret the positive finding as confirmation that the trend favoring auranofin represents not just a few patients who experienced a large change, but rather, many patients who experienced some improvement on many (but, perhaps, not all) of the efficacy criteria. The positive finding is also evidence that a favorable global impression reflects a favorable clinical improvement.

In conclusion, the results of this study suggest that auranofin is a therapeutic option for psoriatic arthritis. Since exacerbations of the skin condition occur infrequently if at all, and since the nature of adverse events is similar to that in rheumatoid arthritis patients, auranofin can be safely used in the psoriatic arthritis population, with the same monitoring that is recommended for its use in rheumatoid arthritis. Based on the articular indices, the value of auranofin in managing joint disease is less in psoriatic arthritis than in rheumatoid arthritis, but the addition of auranofin to NSAID therapy may produce benefits to the psoriatic arthritis patients that are above those offered by NSAID therapy alone.

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