E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2019; 5(2): 28-30

www.orthopaper.com
Received: 18-02-2019
Accepted: 27-03-2019

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A comparative study of CPH 82 and methotrexate in cases of rheumatoid arthritis

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DOI: https://doi.org/10.22271/ortho.2019.v5.i2a.2482

Abstract
Background: Rheumatoid arthritis is a chronic autoimmune condition that classically presents as a symmetrical polyarthritis of proximal small synovial joints. The present study was conducted to compare CPH 82 and methotrexate (MTX) in cases of rheumatoid arthritis.
Materials and methods: 58 patients with rheumatoid arthritis were divided into 2 groups of 29 each. Group I patients were given cap. 300 mg CPH 82 and group II were prescribed 10 mg methotrexate weekly. Swollen joints, number of tender joints, VAS, Health Assessment Questionnaire index and disease activity score was also recorded.
Results: Group I had 15 males and 14 females and group II had 13 males and 16 females. The mean disease duration was 11 months in group I and 10.4 months in group II, rheumatoid factor positive was seen in 34 in group I and 30 in group II, erosive disease was seen among 25 in group I and 29 group II, mean DAS was 4.48 in group I and 4.82 in group II, HAQ was 1.20 in group I and 1.21 in group II. The difference was non- significant ($P > 0.05$).
Conclusion: Authors found that MTX more effective than CPH 82. The safety profile of CPH 82 was more favourable than MTX.

Keywords: Autoimmune, rheumatoid arthritis, methotrexate

Introduction
Rheumatoid arthritis is a chronic autoimmune condition that classically presents as a symmetrical polyarthritis of proximal small synovial joints. It has a prevalence of 0.46% in the Australasian region, and affects women more frequently than men. The onset is usually between 35 and 60 years, however the majority of the disease burden in Australia is in people over 65 years. The cause of rheumatoid arthritis remains unknown, although our understanding of the pathological processes has advanced greatly in the last 20 years. Many pro-inflammatory cytokines are involved and some of these are therapeutic targets for the development of new drugs.
The cytokine milieu in rheumatoid arthritis influences a multitude of physiological processes. These include promoting the influx of immune effector cells into the joint synovium, and activation of osteoclasts, chondrocytes and fibroblasts. There is a positive feedback loop that reinforces the inflammatory process. Unabated, this process results in joint pain and destruction, ultimately causing deformity and disability. CPH 82, a semi-synthetic podophyllotoxin glycoside with anti-rheumatic properties, has been shown to be more effective than placebo in the treatment of established active rheumatoid arthritis (RA). Other data suggest that it is as effective as sulphasalazine and has a more rapid onset of action than auranofin. Korpela *et al.* reported that CPH 82 was as effective as azathioprine in the treatment of RA with amyloidosis and was also better tolerated. The present study was conducted to compare CPH 82 and methotrexate (MTX) in cases of rheumatoid arthritis.

Materials and Methods
The present study was conducted among 58 patients with rheumatoid arthritis of both genders. All were informed regarding the study and their consent was obtained.
Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 29 each. Group I patients were given cap. 300 mg CPH 82 and group II were prescribed 10 mg

methotrexate weekly. A thorough clinical examination was performed in all patients. Swollen joints, number of tender joints, VAS, Health Assessment Questionnaire index and disease activity score was also recorded. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

Groups	Group I	Group II
Drug	Cap. 300 mg CPH 82	10 mg methotrexate
M:F	15:14	13:16

Table 1 shows that group I had 15 males and 14 females and group II had 13 males and 16 females.

Table 2: Assessment of parameters

Parameters	Group I	Group II	P value
Mean disease duration (months)	11	10.4	0.12
Rheumatoid factor positive	34	30	0.23
Erosive disease	25	29	0.14
DAS	4.48	4.82	0.92
HAQ	1.20	1.21	0.98

Table 2, Figure 1 shows that mean disease duration was 11 months in group I and 10.4 months in group II, rheumatoid factor positive was seen in 34 in group I and 30 in group II, erosive disease was seen among 25 in group I and 29 group II, mean DAS was 4.48 in group I and 4.82 in group II, HAQ was 1.20 in group I and 1.21 in group II. The difference was non- significant (*P*> 0.05).

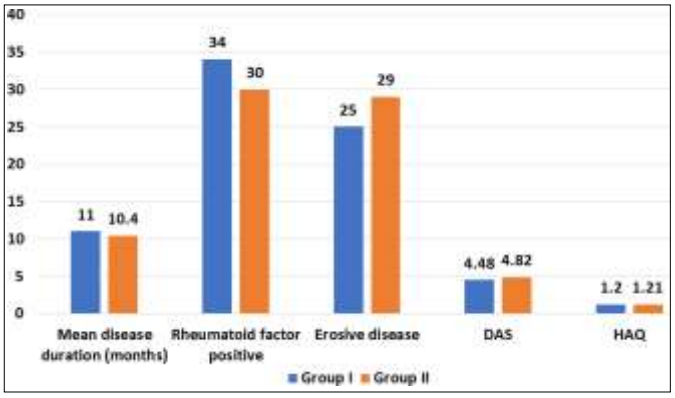

Fig 1: Assessment of parameters

Table 3: Outcome variables

Parameters	Group I		Group II		P value
	0 week	24 weeks	0 week	24 weeks	
RAI	12.4	6.1	14.3	5.2	0.15
Swollen joints	20.3	9.2	21.5	8.5	0.28
Patient's global score	52.3	23.2	54.2	28.6	0.05
Physician's global score	51.0	26.7	55.4	23.1	0.02

Table 3, Figure 2 shows that mean RAI was 12.4 and 6.1 in group I and 14.3 and 5.2 in group II at 0 week and 24 weeks respectively, mean swollen joints were 20.3 and 9.2 in group I, 21.5 and 8.5 in group II at 0 week and 24 weeks respectively, patient's global score was 52.3 and 23.2 in group I and 54.2 and 28.6 in group II at 0 week and 24 weeks respectively, physician's global score was 51.0 and 26.7 in group I and 55.4 and 23.1 in group II at 0 week and 24 weeks respectively. The difference was non- significant (*P*> 0.05).

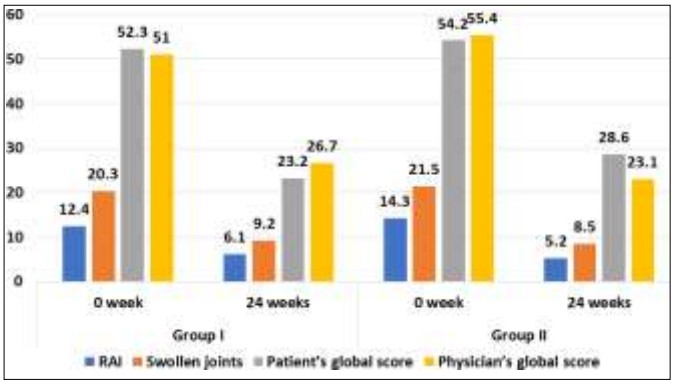

Fig 2: Outcome variables

Discussion

Methotrexate is the backbone of rheumatoid arthritis treatment. Monotherapy consistently reduces radiographic progression and improves quality of life [6] Approximately 40% of patients will respond to monotherapy [7] Limited comparative data suggest that other conventional DMARD monotherapies are as effective as methotrexate [8] However, its demonstrated long-term benefits, cost, acceptable safety profile and synergy with other DMARDs make methotrexate the recommended first choice for monotherapy in the guidelines of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) [9]. The present study was conducted to compare CPH 82 and methotrexate (MTX) in cases of rheumatoid arthritis.

In present study, group I had 15 males and 14 females and group II had 13 males and 16 females. Lerndal *et al.* [10] evaluated the therapeutic efficacy of CPH 82 in comparison with methotrexate (MTX) in adult patients with early, active rheumatoid arthritis (RA). 100 patients with active RA, with a disease duration of less than 2 yr at the start of treatment, which consisted of either CPH 82 300 mg/day or MTX 10 mg/week. There was a significant improvement for both drugs in all variables. Significant differences between the drugs in favour of MTX were found only in patient's pain score, CRP and ESR. By the EULAR criteria, 76% and 86% were judged to be responders in the CPH 82 and MTX groups, respectively. By the ACR criteria, the corresponding figures were 58% and 64%. The most common side-effects were gastrointestinal, which were similar in both groups. The numbers of treatment failures due to adverse events were two with CPH 82 and 14 with MTX. Conclusions. The clinical effect of CPH 82 in this study was comparable to that of MTX at a dose of 10 mg/week. Both drugs reduced acute-phase reactants, MTX more effectively than CPH 82. The safety profile of CPH 82 was more favourable than that of MTX without folic acid supplementation.

We found that mean disease duration was 11 months in group I and 10.4 months in group II, rheumatoid factor positive was seen in 34 in group I and 30 in group II, erosive disease was seen among 25 in group I and 29 group II, mean DAS was 4.48 in group I and 4.82 in group II, HAQ was 1.20 in group I and 1.21 in group II.

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group II at 0 week and 24 weeks respectively.

Patients with rheumatoid arthritis have an increased incidence of infection compared to the general population, in particular those with higher disease severity, corticosteroid use and other comorbidities [11] Combination DMARD regimens, especially those that include a biologic drug, are associated with a markedly increased risk of serious infections. This risk is highest in the first six months of therapy. These infections are of concern, in particular reactivation of tuberculosis. The risk of reactivation of latent tuberculosis is high with DMARD use, particularly with biologic DMARDs and tofacitinib [12].

The limitation of the study is small sample size.

Conclusion

Authors found that MTX more effective than CPH 82. The safety profile of CPH 82 was more favourable than MTX.

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