Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15468
DOI URL: http://dx.doi.org/10.21474/IJAR01/15468

RESEARCH ARTICLE

"OUTCOME OF DOUBLE BLIND COMPARATIVE STUDY OF SULFASALAZINE AND HYDROXYCHLOROQUINE IN EARLY UNDIFFERENTIATED INFLAMMATORY ARTHRITIS"

Dr. Akash[1], Dr. Suryakanth K.[2], Dr. C.V Mudagal[3], Dr. Madhuchandra[4] and Dr. A.A Hosangadi[5]

1. Postgraduate,Dept Of Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.
2. Professor And Hod Dept Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.
3. Professor, Dept Of Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.
4. Associate, Professor, Dept Of Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.
5. Associate, Professor, Dept Of Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.

Manuscript Info

Manuscript History
Received: 05 August 2022
Final Accepted: 09 September 2022
Published: October 2022

Abstract

Objective: Undifferentiated inflammatory arthritis is one of the requirements for being diagnosed in the patient doesn't meet the classical criteria for recognized arthritis. which no approved treatment algorithm exist. Sulfasalazine and hydroxychloroquine used in this trial for early Undifferentiated inflammatory arthritis.

Methods: A six-month, double-blind, randomized experiment was conducted. Undifferentiated arthritis in 100 consecutive patients. ESR, morning stiffness, number of swollen joints, and a pain score are all measured on a monthly basis. Patients with certain rheumatological diagnoses were excluded..

Results: The trial was completed by 74 patients.The sulfasalazine group patient responds better and more promptly. There have been respond in terms of grip strength, pain score, and the duration of morning stiffness compared to hydroxychloroquine.The 26 withdrawal from the research prematurely owing to side effects, with gastrointestinal symptoms being the primary cause in the actively treated group.

Conclusions: Our statistics lead us to the conclusion that sulfasalazine provides an earlier and better response than hydroxychloroquine. The earlier Response to sulfasalazine is a significant benefit for patients' quality of life.

Introduction:-

Undifferentiated inflammatory arthritis affects an estimated 30%-50%(1,2) of patients who visit the rheumatology department. Undifferentiated arthritis has been characterized in a variety of ways, but the diagnosis is typically one of exclusion since it does not meet the categorization criteria for another well-known rheumatic illness, such as psoriatic arthritis or rheumatoid arthritis (RA). Patients with undifferentiated arthritis are often those who have the potential to develop as persistent inflammatory arthritis in those who have no recognizable clinical patterns. While in many cases the illness regresses, in some of these people it develops into other rheumatic disorders. Most instances are minor(2). It is inherently difficult to diagnose a patient who has early inflammatory arthritis since the characteristic symptoms of RA might not be present. Classification standards might not be helpful (3.4). Early

Corresponding Author:- Dr. Akash
Address:- Postgraduate,Dept Of Orthopaedics, Karnataka Institute Of Medical Sciences, Hubli.

research using these criteria, however, has revealed that 25–30% of patients initially stratifying their criteria, have persistent disease 3-5 years later (5.6). Early outcome studies may offer a better potential for a qualitative improvement before it established for persistence synovitis since it has been hypothesised that very early inflammatory disease symptoms for less than 12 weeks may differ immunologically from illness of longer duration. Effective RA care has been shown to reduce long-term damage and disability (7–9), but little study has been done on how to handle the very early undifferentiated arthritis.This study has a research goal. Whether therapy for undifferentiated inflammatory arthritis was preferable to that with sulfasalazine and hydroxychloroquine.According two significant meta-analyses ,felson et al. (10, 11), sulfasalazine was much more successful than hydroxychloroquine compared oral gold in terms of ESR, Tendon joint count, and grip strength. It was also comparable to injectable gold, penicillamine, and methotrexate.Sulfasalazine was shown by Pullar et al. (12) to greatly outperform hydroxychloroquine in reducing erosion. Sulfasalazine and hydroxychloroquine have not yet been compared in studies of undifferentiated inflammatory arthritis. According to lotteau v et (13) hydroxychloroquine inhibition of MHC 2 expression,antigen presentation . van den borne et al (14) study hydroxychloroquine inhibition of various cytokines like IL-1,IFN alpha,and TNF which can protect against cytokine mediated cartilage resorption.Smedegard g et al (15) study Sulfasalazine suppression of production of the cytokine and by inhibition of receptor binding and potent inhibitor of transcription factor nf-kb.

Patient And Methods:-

From July 2021 to June 2022. one hundred Patients who have had undifferentiated inflammatory arthritis for less than a year duration . The study was a 6months, parallel, double-blind comparison of patients treated with hydroxychloroquine vs. sulfasalazine. were assigned to get one of the two. Using a blocked randomization approach, 100 undifferentiated inflammatory patients were given hydroxychloroquine and sulfasalazine,Patients with undifferentiated arthritis had symptoms, such as a history, physical, and test results suggesting the presence of an inflammatory condition, but they lacked a definitive diagnosis of a particular rheumatic disease(2). Patients meeting the criteria for spondylarthropathy as defined by the European Spondylarthropathy Study Group and the American College of Rheumatology were excluded from the study. Table no;1 participants ages 18 to 75 included the research. Corticosteroid use was prohibited during the study in patients with major complicating illnesses or prior allergic reactions to salicylates or sulfonamides. Active illness was defined by stiffness lasting for at least an hour in the morning, swollen joints, and painful joints that were tender to motion. More than 28 mm/hr for ESR. functional impairment. The health evaluation Questionnaire was used to evaluate it. (HAQ)(16), with lab evaluations included, CRP, RF, ESR, and plain radiography of the hands, foot, and other joints are all evaluated. Obtained. on a professionally recommended follow-up.patient assessments were carried out at each monthly clinically visit to asses any suspected adverse drugs reactions,drug overdose/withdrawal or sensitivity.Inflammation of new joint or a new extraskeletal manifestration,abnormalities in physiological testing and laboratory abnormalities.

Tab 1:- Baseline characteristic and clinical characteristic of the study.

characteristic	Sulfasalazine (n=50)	Hydroxychloroquine(n=50)
Mean age	36.3	38.6
Peripheral arthritis	40	34
Mean (SD) number of swollen joints	6.4	7.8
enthesitis	32	26

Drug administration:

Non-steroidal anti-inflammatory medication concomitant therapy a steady doge for one month prior to continuing included,Throughout. as much as possible was studied. Both additional concurrent medication therapy and intra-articular steroids were not permitted. For the first six months, patient received 200 mg of hydroxychloroquine twice daily. The patient receiving sulfasalazine got a daily 500mg dosage, not more than 2gm/day. This was increased by 500 mg after four days. All patients receiving HCQ were screened at the beginning by an ophthalmologist and after every six months.Patient was asked about her any new symptoms(17) and the relationship between trial medication therapy are explored.

Statistical analysis.

Wilcoxon's Rank Sum Test(parametric) or the Student's T-test (Non parametric) were used to compare the treatment group at baseline as (18) deviates from the starting point. These changes were compared across treatment groups using a two sample t-test for each patient. They were determined as the Score after treatment minus the ball

line score. Using the paired t test, p values 0.05 were used to determine if changes within the groups were statistically significant. The duration of the symptoms and the presence of RF were independent variables. At baseline, three months, and In the past six months, there have been synovitis, CRP levels, aching joints, sensitive joints, and swollen joints.

Results:-

A total of 26 patients out of the 100 patients enrolled were lost to follow-up, the majority of which (8 patients) occurred after the baseline demographic data for 74 patients (12 weeks). Statistics for patients whose follow-up visits were based on the most recent observation are shown in for study participants. Improvement from the baseline was statistically (fig 1,2,&3) in the sulfasalazine-treated group after 4 weeks for morning stiffness, grip strength, after & wells for ESR and CRP, and after 12 weeks for Ritchie articular index number of swollen joints. And following 20 weeks,for the quantity of tender joints. 24 weeks later, all clinical and laboratory reports improved Except for haemoglobin, abortive measures of disease activity were significantly improved. Reducing the rate at which new bone degradation.Hydroxychloroquine treated group the improvement from baseline for the number of swollen joints, involved after 12 weeks treated group approached statistical significance.After 24 weeks,Duration of morning stiffness and ESR dropped.34 patients received hydroxychloroquine tab 1 and 40 patients continued to take sulfasalazine. unfavourable effects experienced by patients.In tab 2 There were 10 withdrawals from the sulfasalazine group, of these3 were due to non-drug related causes, 3 were due to lack of efficacy, and 4 were due to adverse events. The most serious adverse responses were agranulocytes, a little abnormal in the liver function test, and bitter taste. One patient had nausea, and 16 people were in the hydroxychloroquine group are withdrawal.Six were for non drug related reason, nine because of lack of effects, and one due to diarrhea. No ophthalmological side effects to the treatment were seen.

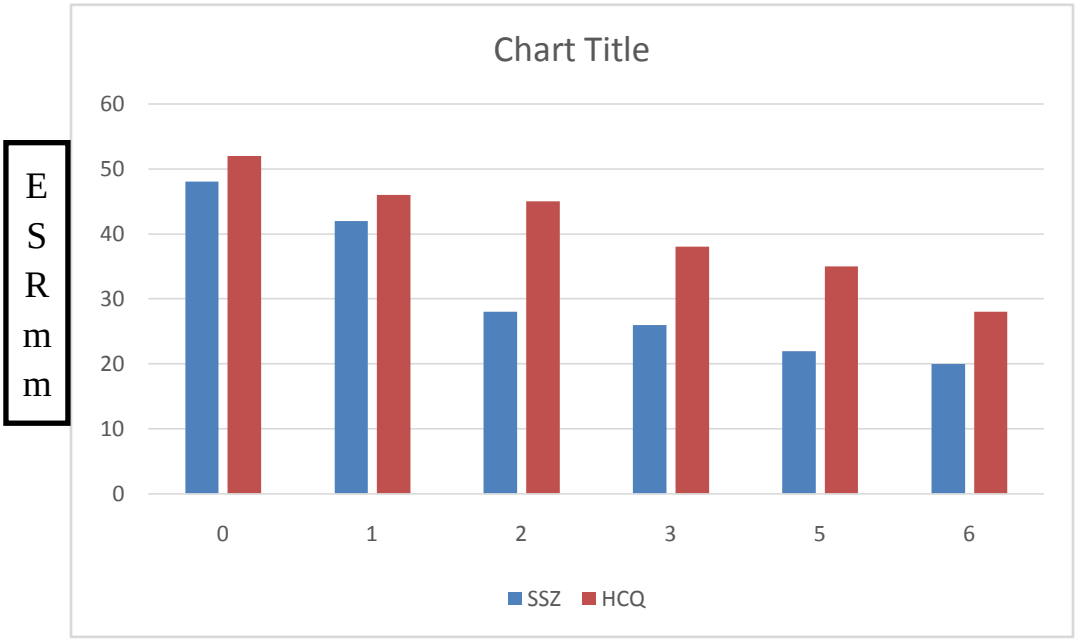

Fig no 1:- Months of treatment.

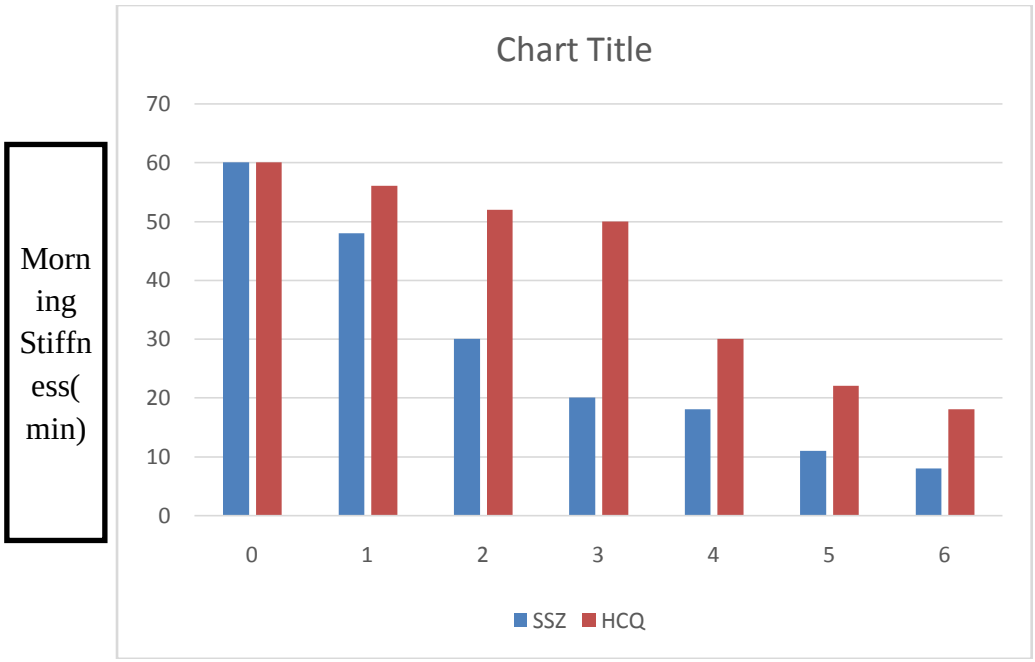

Fig no 2:- Months of treatment.

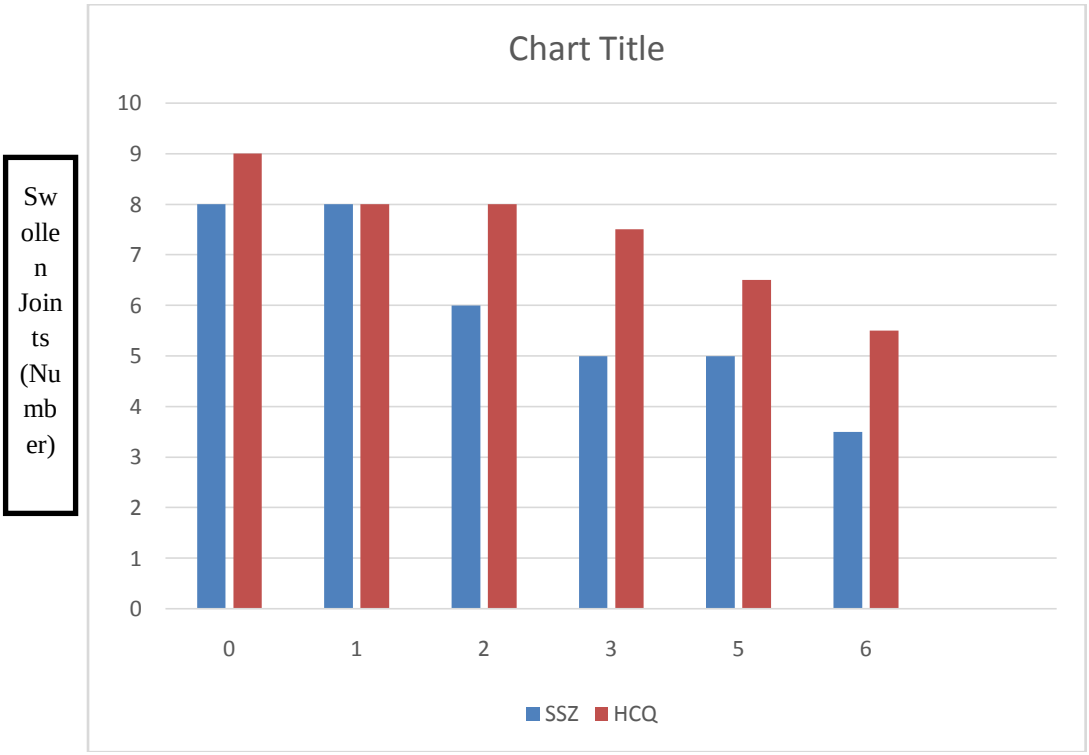

Fig no 3:- Months of treatment

TAB 2:- Reasons for withdrawal from study (no. Of patients).

	Sulfasalazine	Hydroxychloroquine
Gastrointestinal symptoms	4	1
Non compliance	3	9
Non drug related	3	6
Total	10	16

Discussion:-

There are Studying undifferentiated inflammatory arthritis is challenging. based on the exclusion of other conditions, Patients were disqualified from the trial at the baseline stage if a definite rheumatic diagnosis could be made.Patients who had a history that suggested inflammatory arthritis were eligible to participate in the trial. By concealing synovitis and using NSAIDs, individuals with early inflammatory illness may present differently (19). We compared the efficacy and toxicity of sulfasalazine. It should be noted that this selection process was similar to that described by Wolfe et al. early undifferentiated inflammatory arthritis therapy. Both medications have been demonstrated to be early placebos. controlled trials for a disease-modifying drug effects (20 -24) According to the Quicken response, we discovered that sulfasalazine medication appears to have certain advantages over the use of hydroxychloroquine. Improvement from inside the sulfasalazine group. After 4 weeks of therapy, the duration of morning stiffness, grip strength, and pain score were recorded. Since hydroxychloroquine was not reduced until week 12, it would seem that the commencement of the reaction had already begun. About 8 weeks sooner than the hydroxychloroquine group was the sulfasalazine group. Retinopathy The major toxic symptoms of hydroxychloroquine treatment did not occur in our study. All side effects were mild and reversible. In studies, a dosage of 3g(6,20) of sulfasalazine produced a comparable early response.The same observation has been made regarding her gastrointestinal side effects in patients treated with sulfasalazine for inflammatory bowel disease. Sulfasalazine considerably outperformed hydroxychloroquine in a trial with early RA (16, 17) in terms of reducing the rate of new bone erosion. both at age one to three. Sulfasalazine is also shown to be Reduces ESR, the number of painful joints, and grip strength in two sizable meta-analyses by felson et al. (10,11). In a similar research, sulfasalazine outperformed oral gold, hydroxychloroquine, and antimalarial drugs by a wide margin. No evidence of teratogenicity has been obtained from either maternal or paternal sulfasalazine usage, according to Pullar et al. (12). Capell et al.(22) recently recorded seven cases of leucopenia, all of which occurred in the first three months of therapy and all of which shown fast recovery within three weeks after treatment discontinuation. Salphasalazine was found to be significantly better than hydroxychloroquine at 8 weeks for pain score and grip strength in a double-blind, intention-to-treat 48-week trial in a total of 60 patients (30 per group) by nuver-zvart et al.(23). This study and other published series have some similarities(24–26); however, a notable difference in remission rate is apparently (57.9% in the cohort described by wolfe et al) despite the use of similar definations.karan et al(27) A patient with undifferentiated arthritis has a more broad inflammatory disease than is clinically apparent, as evidenced by the considerable microscopic and macroscopic synovitis that was reported in the knees of RA patients whose clinical examinations were normal. In early oligoarthritis patients, Wake Field et al. found that ultrasound identifies synovitis in much more joints than clinical evaluation, and that patients with ultrasound detectable synovitis had a higher likelihood of persistent infections (28).

Conclusion:-

Based on the information we have, When treating early undifferentiated inflammatory arthritis, sulfasalazine produces a response that is both sooner and somewhat better than that of hydroxychloroquine. Sulfasalazine early response in particular may be a significant benefit for patients' quality of life. In comparison to hydroxychloroquine, it reduces the onset of fresh bone erosion.

References:-

1 Van der Horst-Bruinsma 1. Speyer 1. Visser H. Breedveld FC. Hazes JM. Diagnosis and course of carly-onset arthritis: results of special early arthritis clinic compared to routine patient care. Br J Rheumatol 1998:37:1084-8.

2 Wolle F. Ross K. Hawley F. Roberts F. Cathey M. The prognosis of theumatoid arthritis and undifferentiated polyarthritis syn drome in the clinic: a study of 1141 patients. J Rheumatol
1993:20:2005-9.

[8:06 pm, 30/09/2022] Akash K: 3. Green M. Marzo-Ortega H. McGonagle D. Wakefield R. Proud man S, Conaghan P, et al. Persistence of mild, early inflammatory arthritis: the importance of disease duration, rheumatoid factor. and the shared epitope. Arthritis Rheum 1999;42:2184-8.

4. Harrison BJ. Symmons DPM, Barrett EM, Silman AJ, The performance of the 1987 ARA classification criteria for Rheumatoid arthritis in a population based cohort of patients with carly inflammatory arthritis. J Rheumatol 1998;25:2324-30.

5. O'Sullivan JB, Catheart ES. The prevalence of theumatoid arthri tis: follow-up evaluation of the effect of criteria on rates in Sudbury, Massachusetts. Ann Intern Med 1972;76:573-7.

6. Mikkelen WM. Dodge H. A four year follow-up of suspected rheumatoid arthritis: the Tecumseh, Michigan, Community Health Study. Arthritis Rheum 1969:12:87-91.

7. . Pinals R S. Kaplan S B, Lawson J G, Hepburn B. Sulfasalazine The first in rheumatoid arthritis: a double-blind, placebo-controlled trial. Arthritis Rheum 1986; 29: 1427-34.
8. [8:09 pm, 30/09/2022] Akash K: 8. Van der Heide A. Jacobs JW, Bijlsma JW. Heurkens AH, van Booma-Frankfort C, van der Veen MJ, et al. The effectiveness of early treatment with "second-line" anti-rheumatic drugs: a ran domised controlled trial. Ann Intern Med 1996;124:699-707,
9. . Fries JF, Williams CA, Morfeld D, Singh G, Sibley J. Reduction in Long-term disability in patients with rheumatoid arthritis by disecase-modifying antirheumatic drug-based treatment strategies Arthritis Rheum 1996:39:616-22 10.
10. Abu-Shakra M. Toker R. Flusser D. Flusser G, Friger M. Sukenik S. et al. Clinical and radiographic outcomes of theumatoid arthritis patients not treated with disease-modifying drugs. Arthritis Rheum 1998:41:1190-5. 11.
11. .Felson DT, Anderson JJ, Meenan RF. The comparative efficacy and toxicity of second line drugs in rheumatoid arthritis. Arthritis Rheum 1990;33:1449-61.
12. Pullar T, Hunter JA, Capell HA. Effect of sulphasalazine on the radiological progression of rheumatoid arthritis. Ann Rheum Dis 1987;46:398-402.
13. Lotteau, V. et al. Intracellular transport of class II MHC molecules directed by invariant chain. Nature 348, 600-605 (1990).
14. van den Borne, B. E. et al. Chloroquine and hydroxychloroquine equally affect tumor necrosis factor-alpha, interleukin 6, and interferon-gamma production by peripheral blood mononuclear cells. J rheumatol 21.375-376(1994)
15. Smedegard G, Bjork J. Sulphasalazine: Mechanism of action in arthritis. Br J Rheumatol 1995;34(suppl. 2):7-15.
16. van der Heijde DMFM, Van Riel PCLM, Nuver-Zvart IH, Gribnau FWJ, Van De Putte LBA. Effects of hydroxychloroquine and sulphasalazine on progression of joint damage in rheumatoid arthritis. Lancet 1989;1:570-3.
17 van der Heijde DMFM, van Riel PCLM, Nuver-Zvart HH, van de Putte LBA. Sulphasalazine versus hydroxy chloroquine in rheumatoid arthritis: 3-year follow-up. Lancet 1990;335:539.
18.Felson DT, Anderson JJ, Meenan RF. The comparative efficacy and toxicity of second line drugs in rheumatoid arthritis. Arthritis Rheum 1990;33:1449-61.
19.Felson DT, Anderson JJ, Meenan RF. Use of short term efficacy/toxicity trade offs to select second line drugs in rheumatoid arthritis. A meta analysis of published clinical trials. Arthritis Rheum 1992;35:1117-25.
20 Mogadam M, Dobbins WO, Korelitz BI, Ahmed SW. Pregnancy in inflammatory bowel disease: Effect of sulphasalazine and corticosteroid on fetal outcome. Gastroenterology 1981;80:72-6.
21 Pullar T. Adverse effects of sulphasalazine. Adverse Drug React Toxicol Rev 1992;11:93-109. 63.
22 Capell HA, Maraban M, Madhok R et al. Degree and extent of response to sulphasalazine or penicillamine therapy for rheumatoid arthritis: results from a routine clinical environment over a 2 year period. Q J Med 1990;75:335-44.
23 . Nuver-Zvart IH, van Riel PL, van den Putte LB et al. A double blind comparative study of sulphasalazine and hydroxychloroquine in rheumatoid arthritis: evidence of an earlier effect with sulphasalazine. Ann Rheum Dis 1989;48:389-95.
24. Pinals RS, Kaplan SB, Lawson JG, Hepburn B. Sulphasalazine in rheumatoid arthritis. A double blind placebo controlled trial. Arthritis Rheum 1986;29: 1427-34.
25. Williams HJ, Ward JR, Dahl SL et al. A controlled trial comparing sulphasalazine, gold thiomalate and placebo in rheumatoid arthritis. Arthritis Rheum 1988;31:702 13.
1. Ebringer R, Ahern M, Thomas D et al. Sulphasalazine in early rheumatoid arthritis. J Rheumatol 1992;19:1672
2. Kraan MC. Versendaal H. Junker M. Bresnihan B. Post WJ. 1 Hart BA, et al. Asymptomatic synovitis precedes clinically manifest arthritis Arthritis Rheum 1998:41:1481-8. 24.
3. , Wakefield RJ, Green MJ, Gibbon WW, Proudman S, Marzo H, O'Connor P, et al. High resolution ultrasound (HRUS) defined subclinical synovitis: a predictor of outcome in early oligoarthritis? Arthritis Rheum 1998:41 Suppl 9:5246.