ORIGINAL RESEARCH

Comparison of intra-articular glucocorticoid injections with dmards versus dmard alone in rheumatoid arthritis

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ABSTRACT
"Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder which is characterised by synovial inflammation and joint destruction, as well as extraarticular manifestations". A crucial part of the pathophysiology of this synovial inflammation is played by cytokines. One of the predominant cytokines is tumour necrosis factor a (TNFa). In conclusion, it can be said that for patients with early RA, a combination of intra-articular steroids and DMARDs is substantially more effective at controlling disease activity than DMARDs alone.

INTRODUCTION

"Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder which is characterised by synovial inflammation and joint destruction, as well as extraarticular manifestations".[1] A crucial part of the pathophysiology of this synovial inflammation is played by cytokines. One of the predominant cytokines is tumour necrosis factor a (TNFa).[2] Numerous investigations have demonstrated that RA synovial tissue and fluids contain biologically significant levels of TNFa, and that these levels appear to be correlated with the degree of inflammation and bone erosion.[2,3] "RA is the rheumatic condition that most severely affects the joints. Pannus, the hyper-trophic and hyperplasic synovial membrane formed, is an aggressive tissue that damages articular and periarticular structures, whether through the release of metalo-proteinases or its mechanical invasion of the surrounding joint space" [4-6]. "Even though RA treatment has evolved in recent decades with the advent of immunobiological therapy allied with disease-modifying antirheumatic drugs (DMARDs), [7] patients with mono or oligoarticular synovitis may persist". "In these cases, intra articular corticosteroid injection can be a useful therapeutic tool. "Even though RA treatment has evolved in recent decades with the advent of immunobiological therapy allied with disease-modifying antirheumatic drugs (DMARDs), [7] patients with mono or oligoarticular synovitis may persist". "In these cases, intra articular corticosteroid injection can be a useful therapeutic tool. It is known that triamcinolone acetonide (TH) is the drug of choice for intra-articular treatment of RA, given its synovial atrophying properties and slow absorption from the injection site" [8-9]. Biologic DMARDs and intra-articular steroids are the only two agents acting on the RANKL/ OPGL and MMP systems, leading to greater bone and cartilage preserving effects.

This study aims to compare intra-articular glucocorticoid injections with DMARDS versus DMARD alone in rheumatoid arthritis

METHODOLOGY

This study was carried out in the department of orthopaedics, Narayan Medical College and Hospital, Jamuhar in patients diagnosed as RA based on American Rheumatology Association (ACR) criteria (2010) with disease duration less than two years.This is a hospital based prospective study. Inclusion criteria for this study were 1)Patient above 18 years of age 2)Patients diagnosed with RA according to ACR criteria (2010) 3)Willing to participate in the study.

Exclusion criteria were 1)Contraindications to steroids like Diabetes, acute infections, peptic ulcer disease

and renal disease, joint deformity or erosions. 2)Treatment with oral or intra-articular steroids in the last one year. 3)Treatment with any other DMARD combination 4)Pregnant and lactating women.

50 patients were selected and divided into two groups. Study group received oral Methotrexate (MTX) 15mg per week, oral Folic Acid 5 mg per day, (except on day of MTX administration) oral Sulfasalazine (SSZ) 2gm per day and intra-articular injections of Triamcinolone acetonide (40mg per ml) in each of the swollen joints (small joints of hand = 0.2 ml, wrist, elbow and ankle joints = 0.5 ml and knee and shoulder = 1 ml each) and Control group received oral MTX (15mg per week), oral folic acid (5mg per day, except on the day of MTX intake) and oral SSZ (2gm daily). Disease Activity Score (DAS-28) and ACR20/50/70 score at 12 weeks was considered as primary outcome measures. In addition, ESR, EMS, HAQ scores, TJC, SJC, general health status (patient reported on VAS scale 0 to 100, 0=best, 100=worst) and number of rescue medication tablets used were considered as secondary outcome variables. Data was managed on Microsoft Excel© and tested on SPSS for windows version 15 software. Independent T test, Chi-Square test and Wilcoxon rank sum was used for data analysis. Results were considered significant at $p<0.05$.

RESULTS

50 patients were selected and divided into two groups. Study group and control group with 25 patients each.

The mean age of patients in the study group was 37 years (range=18 to 64 years) and the control group was 36 years (range=18 to 62 years) with a female to male ratio of 20:5 in both groups. Five patients in the study group (20%) and 2 patients in the control group (8%) were smokers. The mean disease duration was 13.24 months in the study group (range=3 to 24 months) and 14.44 months (range=3 to 24 months) in the control group. Twenty patients (80%) were rheumatoid factor positive in the study group while it was 15 patients (60%) in the control group. Both groups were comparable in all baseline characteristics. At the end of 6 and 12 weeks, significant reduction in all disease parameters was seen in the study group. (Table 2 and 3) Patients who received steroid injections with DMARDs showed an initial quick fall in all parameters which improved further at 12 weeks. Patients who were treated with only DMARDs also improved in all parameters but did so, slowly in comparison to the study group across the duration of the study.

Table 1

Parameters	At 6 weeks			At 12 weeks		
	control	study	p-value	control	study	p-value
ESR(mm/hour)	38.66(±12.57)	26.74(±13.57)	0.001	30.32(±12.57)	22(±13.57)	0.002
Tender joint count	12.28(±5.57)	4.3(±3.57)	0.001	8(±3.57)	4(±3.57)	0.001
Swollen joint count	6(±1.5)	1(±1.03)	0.001	3(±1.03)	0.3(±1.03)	0.001
VAS 0 to 100	52.6(±12.57)	32(±14.57)	0.001	40(±12.57)	29(±12.57)	0.001
DAS 28 scores	6.12(±0.57)	3(±1.07)	0.001	4.8(±1.07)	2.48(±1.07)	0.001

$p < 0.05$ taken as statistically significant

Table 2

Parameters	Control group	Study group	p-value
Early Morning Stiffness (minutes)	42(±15.07)	13(±14.07)	0.001
Fall in HAQ scores	0.45(±0.31)	0.69(±0.31)	0.009
ACR 20	20(80%)	25(100%)	0.004
ACR 50	7(28%)	15(60%)	0.001
ACR 70	0	10(40%)	0.001

$p <0.05$ taken as statistically significant

DISCUSSION

A state of low disease activity, or remission, is the aim of treatment for rheumatoid arthritis.

In order to achieve this goal, the "reverse pyramid" concept—which starts with a combination of DMARDs with or without steroids—is preferred in modern treatment approaches. This involves either using biologic agents or tapering to maintenance levels.

Both the groups in our study were comparable at baseline in all parameters. At the end of 6 weeks, the study group showed a significant improvement in both the primary and secondary outcome measures as compared to the control group. This effect was carried over till 12 weeks. This result is in agreement with a number of studies which showed significantly more improvement when a combination of DMARDs was used with local and oral steroids.

The study group's ESR improved, and this improvement was significant at six weeks but not at twelve. This is because ESR is a poor predictor of a patient's long-term prognosis and has low discriminatory power. Therefore, rather than focusing on ESR's absolute value, an improvement should be sought after.

At 12 weeks the DAS-28 score was 2.48 which indicates moderate disease activity. This is close to the low disease activity score (2.6 to 3.1) which is the aim of treatment. Although significantly more patients achieved the ACR 20 and ACR 50 criteria in the study group, greater achievement of ACR 70 criteria in the study group (40% in the study group compared to 0% in the control group) was considered as a highly desirable goal in the management of patients with RA. All the secondary end-points, that is tender joint count, swollen joint count, general health status scores and early morning stiffness showed significantly more improvement in the study group signifying across the board improvement when DMARDs were used with intra-articular steroids. Our study also showed significantly lower HAQ scores in the study group which entails a better functional outcome in these patients. We have used a validated modified HAQ for Indian population which focuses on tasks specific to our population.[19] At the end of 12 weeks, the study group required significantly lesser rescue medication tablets thus lessening the cost of therapy and minimising potential risk of added side-effects.

We have come across several studies which have used various combinations of oral and/or intra- articular steroids in RA but we have not come across any study with intra-articular triamcinolone acetonide. Triamcinolone was used in our study because of its property of staying in the joint for long periods and thus producing more local effects. The ideal agent to be used would be triamcinolone hexacetonide but it is not available in India and both the acetonide and hexacetonide compounds have similar fractions of systemic absorption.

CONCLUSION

In summary, it can be said that for patients with early RA, a combination of intra-articular steroids and DMARDs is substantially more effective at controlling disease activity than DMARDs alone. They may also prove to be a useful substitute for more costly options, such as biologic agents, in achieving the intended level of disease control. Additional research is necessary, particularly comparing biologics to DMARDs plus intra-articular steroids.

REFERENCE

1. Valentini G, Black C. Systemic sclerosis. Best Pract Res Clin Rheumatol. 2002;16:807–16.
2. Farrell RJ, Kelly CP. Celiac sprue. N Engl J Med. 2002;346:180–8.
3. Cooper T, Holmes GKT, Cooke WT. Coeliac disease, and immunological disorders. BMJ. 1978;1:537–9.
4. Lee DM, Weinblatt ME. Rheumatoid arthritis. Lancet. 2001;358:903–11.
5. Firestein GS. Evolving concepts of rheumatoid arthritis. Nature. 2003;423:356–61.
6. Bartok B, Firestein GS. Fibroblast-like synoviocytes: key effector cells in rheumatoid arthritis. Immunol Rev [Review]. 2010;233:233–55.
7. Nam JL, Winthrop KL, van Vollenhoven RF, Pavelka K, ValesiniG, Hensor EM, et al. Current evidence for the management of rheumatoid arthritis with biological disease-modifying antirheumatic drugs: a systematic literature review informing the EULAR recommendations for the management of RA. AnnRheum Dis. 2010;69:976–86.
8. Lopes RV, Furtado RN, Parmigiani L, Rosenfeld A, FernandesAR, Natour J. Accuracy of intra-articular injections in peripheral joints performed blindly in patients with rheumatoid arthritis. Rheumatology (Oxford). 2008; 47:1792–4.
9. Santos MF, Furtado RN, Konai MS, Castiglioni ML, MarchettiRR, Natour J. Effectiveness of radiation synovectomy withsamarium-153 particulate hydroxyapatite in rheumatoid arthritis patients with knee synovitis: a controlled randomized double-blind trial. Clinics (São Paulo). 2009;64:1187–93.