

Intra-articular (I/A) Methotrexate In Rheumatoid Arthritis.

M Taqweem, H Kan, A Takreem, I Alam

Citation

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Abstract

Objectives: To determine if I/A Methotrexate is effective in rheumatoid arthritis. **Material and methods:** this study was conducted in medical B unit of postgraduate medical institute, lady reading hospital and a private rheumatology clinic in Peshawar. A total of 40 rheumatoid arthritis patients who were resistant to patients who were I/A steroids were included in the study. At first visit 12.5 mg intra-articular Methotrexate with lignocaine was injected with aseptic technique. Twenty eight patients completed follow up and again 12.5 mg I/A Methotrexate was given. Clinical improvement was assessed with visual analogue scale (VAS) and parameter like pain, swelling, flexion and ESR. Patients with septic joints, sepsis around the joint, I/A steroids within last three months and bleeding disorders were excluded from the study. **Results:** A total of 28 patients completed twice follow up one for re-injection and other for response analysis. Eighteen (64.3%) were females and 10 (35.7%) males. The age range was from 40 to 50 years with mean age of 45.9643 +3.21 SD years. No response was received from 11 patients 6 females and 5 males with VAS 10/10 for pain and swelling, flexion up to 30 degree and ESR >60mm/hr. Partial response was recorded in 11 patients 7 females and 4 males, with VAS 5-10/10 for pain and swelling, flexion 30-90 degree and ESR 41-60mm/hr. Good response (VAS 0-4 /10 for pain and swelling) was noted in 6 patients with flexion >90 degree and ESR 20-40mm/hr. **Conclusion:** Our study response rate was 6/28 (21.42%) which is encouraging besides our patients received only two injections I/A MTX and is much better than as reported in very few studies from abroad. It is the first ever study on I/A Methotrexate from NWFP and probably from Pakistan.

INTRODUCTION

Based on visual observation, the ancients characterized inflammation by five cardinal signs, namely redness (rubor), swelling (tumour), heat (calor; only applicable to the body's extremities), pain (dolor) and loss of function (functio laesa). The first four of these signs were named by Celsus in ancient Rome (30–38 B.C.) and the last by Galen (A.D 130–200).

More recently, inflammation was described as “the succession of changes which occurs in a living tissue when it is injured provided that the injury is not of such a degree as to at once destroy its structure and vitality”, or “the reaction to injury of the living microcirculation and related tissues”¹.

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder that causes the immune system to attack the joints, where it causes inflammation (arthritis) and destruction. It can also damage some organs, such as the lungs and skin. It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility. It is diagnosed with blood tests (especially a test called rheumatoid factor) and X-rays². Diagnosis and long-term management are typically performed by a

rheumatologist, an expert in the diseases of joints and connective tissues³.

Various treatments are available. Non-pharmacological treatment includes physical therapy and occupational therapy. Analgesia (painkillers) and anti-inflammatory drugs, as well as steroids, are used to suppress the symptoms, while disease-modifying anti-rheumatic drugs (DMARDs) are often required to reverse the disease process and prevent long-term damage. In recent times, the newer group of biologics has increased treatment options³. I/A Steroid injections are commonly used for acute painful joints. A meta-analysis supports the recommendations of American and international authorities that I/A injection of corticosteroids provides short-term relief of the pain. I/A corticosteroids result in a clinically and statistically significant reduction in knee pain 1 week after injection that continues for 3 to 4 weeks^{4,5}. Cortisone therapy has offered relief in the past, but its long-term effects have been deemed undesirable⁶. However, cortisone injections can be valuable adjuncts to a long-term treatment plan, and using low dosages of daily cortisone (e.g., prednisone or prednisolone,

5-7.5 mg daily) can also have an important benefit if added to a proper specific anti-rheumatic treatment. Still

there are some cases that are resistant to intra-articular steroids and international recently Methotrexate has been tried intra-articularly and has shown its effectiveness as reported in various trials ⁷⁸⁹¹⁰.

Present study was a continuation of the recently conducted trial to see the effectiveness of I/A Methotrexate.

MATERIAL AND METHODS

A total of 40 rheumatoid arthritis patients who were resistant to patients who were I/A steroids were included in the study. Twenty eight patients completed twice follow up one for re injection and other for response analysis. Eighteen (64.3%) were females and 10 (35.7%) males. The age range was from 40 to 50 years with mean age of 45.9643 +3.21 SD years. Proper informed consent was taken from all the respondents.

Inclusion criteria were all rheumatoid arthritis patients with single knee joint involvement, not responding to I/A steroids. While exclusion criteria were all patients with septic joints, sepsis around the joint, I/A steroids within last three months and bleeding disorders. After proper selection of patients, at first visit 12.5 mg intra-articular Methotrexate with lignocaine was injected with aseptic technique. Twenty eight patients completed follow up and again 12.5 mg I/A Methotrexate was given. Combination with lignocaine was aimed to increase the volume of the drug to cover more joint space. Twenty eight patients completed follow up and again 12.5 mg I/A Methotrexate alone was given. Clinical improvement was assessed with parameter of pain, swelling, flexion and ESR. Visual analogue scale was used for pain analysis. A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain. Just asking the patient how much is sever your pain right now as shown in the figure 1.

Figure 1
Figure 1

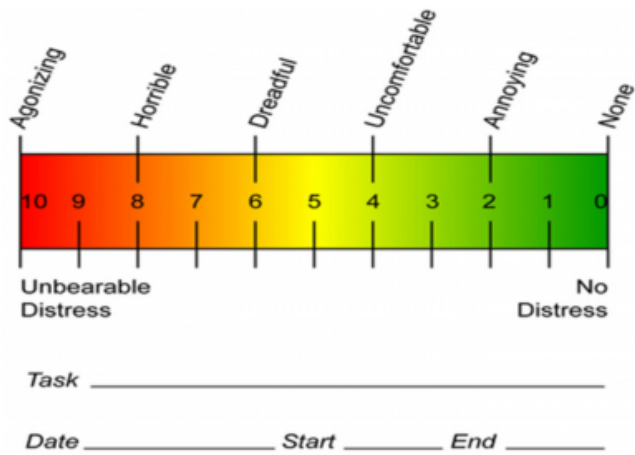


Figure 1.

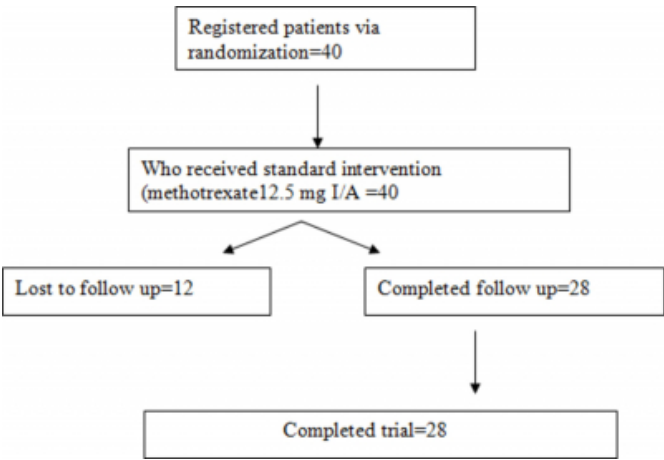
No pain _____ agonizing pain ¹¹.

Swelling and joint flexion was clinically assessed as well as swelling was also weighted on VAS. ESR was done in all visits and compared together. Both readings noted on a specially designed proforma prepared in accordance with the objective of the study.

Further more our trial was in accordance with CONSORT (consolidated standard of reporting trials) trial guidelines and its flow chart was as follow,

Flow chart of the trial based on CONSORT trial guidelines ¹²:

Figure 2
Figure 2



Finally data collected was entered in SPSS 11 version and was analyzed in frequency, median mode statistics for age and sex parameters and cross tabulation analysis was done

for pain, swelling, flexion and ESR.

RESULTS

A total of 28 patients completed twice follow up one for re-injection and other for response analysis. Eighteen were females and 10 males (table 1). The age range was from 40 to 50 years with mean age of 45.96 +3.21 SD years (table 2). Visual analogue scale (VAS) analysis was used to see the response along with clinical examination and ESR. No response was received from 11 patients 6 females and 5 males with VAS 10/10 for pain and swelling, flexion up to 30 degree and ESR>60mm/hr. Partial response was recorded in 11 patients 7 females and 4 males, with VAS 5-10/10 for pain and swelling, flexion 30-90 degree and ESR 41-60mm/hr. Good response (VAS 0-4 /10 for pain and swelling) was noted in 6 patients with flexion >90 degree and ESR 20-40mm/hr. Flexion, swelling and sex cross tabulation clinically elicited response analysis of patients are shown in table 3. Reduction in ESR improvement in pain that was orally explained by patient and recorded in terms of percentage improvement is shown in table 4.

Figure 3

Table 1: Sex wise distribution of patients

Sex	Number of patients	Percentage %
Males	10	35.71
Females	18	64.28

Figure 4

Table 2: Age Statistics of patients

Total number of the respondents	28
Mean	45.9643
Median	46.0000
Mode	50.00
Std. Deviation	3.21434
Range	10.00
Minimum	40.00
Maximum	50.00

RESPONSE ANALYSIS IN PATIENTS SUBJECTED TO I/A METHOTREXATE INJECTIONS

Figure 5

Table 3: Flexion, swelling and sex cross tabulation clinically elicited response analysis of patients.

Sex	SWELLING (clinically assessed and then presented on VAS)					Total
			VAS score 10/10	VAS score 5-10/10	VAS score 0-4/8	
Males	FLEXION	Flexion up to 30 degree	5			5
		Flexion 30-90 degree		4		4
		Flexion more than 90 degree			1	1
		Total	5	4	1	10
Females	FLEXION	Flexion up to 30 degree	6			6
		Flexion 30-90 degree		8		8
		Flexion more than 90 degree			4	4
		Total	6	8	4	18

Figure 6

Table 4: ESR * Pain * Sex -Cross Tabulation response analysis

SEX	PAIN					Total
			VAS score 10/10	VAS score 5-10/10	VAS score 0-4/8	
Males	ESR	20-40 mm/hr			1	1
		41-60mm/hr		4		4
		>60mm/hr	5			5
		Total	5	4	1	10
Females	ESR	20-40 mm/hr			4	4
		41-60mm/hr		8		8
		>60mm/hr	6			6
		Total	6	8	4	18

DISCUSSION

There is no cure for rheumatoid arthritis. Treatment for rheumatoid arthritis aims to reduce inflammation in your joints in order to relieve pain and prevent or slow joint damage. Clinical results from trials conducted on I/A Methotrexate support the hypothesis that Methotrexate may be used intra-articularly as an immuno-suppressor rather than at the heavily toxic doses required for a cytostatic effect. Further more repeated intra-articular injections of MTX results in a decrease of local as well as systemic inflammatory signs in RA₈₁₃. Intra articular MTX therapy results in a strong decrease of SF-granulocyte counts. This effect may be due to the impairment of IL-8 mediated chemotaxis by decreased IL-8 synthesis in synovial fluid mononuclear cells₁₄. Our patients received two injections in a dose of 12.5mg of MTX one month apart but still the response was satisfactory. In another study in patients with definite RA and knee effusions under constant doses of DMARD therapy were treated with up to 6 intra-articular injections of 10 mg Methotrexate (MTX) every 3 to 7 days₁₄. Iagnocco A, et al₉ treated his patients with intra-articular injections of MTX 10 mg every 7 days for 8 weeks. Hence

with a disciplined dosage and proper follow up the much better response can be achieved. But as it was first ever attempt here so was as properly not arranged. In present study visual analogue scale (VAS) analysis was used to see the response along with clinical examination and ESR. Iagnocco A, et al, also assessed the response of MTX I/A therapy through clinical evaluation measuring maximal knee flexion angle, visual analog scale (VAS) and erythrocyte sedimentation rate (ESR). Ultrasonographic examination of the involved knee was performed to see synovial thickness in the suprapatellar bursa and the presence of joint effusion and Baker's cyst. We observed that no response was received from 11 patients 6 females and 5 males with VAS 10/10 for pain and swelling, flexion up to 30 degree and ESR>60mm/hr. Partial response was recorded in 11 patients 7 females and 4 males, with VAS 5-10/10 for pain and swelling, flexion 30-50 degree and ESR 41-60mm/hr. Good response (VAS 0-4 /10 for pain and swelling) was noted in 6 patients with flexion >50 degree and ESR 20-40mm/hr. Iagnocco A et al, also concluded that repeated intra-articular injections of MTX resulted in a decrease of local as well as systemic inflammatory signs. But Gao IK et al₁₄ reported that repeated intra articular MTX therapy results in a worse 13 week outcome than I/A. steroid treatment measured in an intention-to-treat analysis. As far as we know, this is the first study reported from NWFP that explores the effects of intra-articular MTX in RA clinically. Further studies are encouraged to prove effects of intra-articular MTX in RA by ultrasonography of joints. Our study has reported 28 cases with I/A MTX which are far greater than many trials that have reported IA Methotrexate in the world around [[8, 9, 10, 14 etc.]]

CONCLUSION

Our study response rate was 6/28 (21.42%) which is encouraging besides our patients received only two injections I/A MTX and is much better than as reported in very few studies from abroad.

It is the first ever study on I/A Methotrexate from NWFP and probably from Pakistan as so far we have searched on pubmed, pakmedinet, and Google search. Further more we reported maximum number of cases that so far has been published in literature.

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Author Information

Mohammad Amjad Taqweem

Medical B Unit, Department of Medicine, Post-Graduate Medical Institute, Lady Reading Hospital

Hamzullah Kan

Medical B Unit, Department of Medicine, Post-Graduate Medical Institute, Lady Reading Hospital

Amera Takreem

Medical B Unit, Department of Medicine, Post-Graduate Medical Institute, Lady Reading Hospital

Intekhab Alam

Medical B Unit, Department of Medicine, Post-Graduate Medical Institute, Lady Reading Hospital