

Original Research Article

A Prospective Clinical Evaluation between Intra - Articular Injections of Methyl Prednisolone and Triamcinolone in Osteoarthritis of Knee Based On the Efficacy, Duration and Safety

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ABSTRACT

Keywords

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WOMAC
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SF-36 form;
Methylprednis
olone;
Triamcinolone

Osteoarthritis (OA) is a heterogeneous group of conditions that lead to joint symptoms which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins. OA is the most common joint disease of humans both in the western world as well as in India. Age, Major joint trauma and repetitive joint use (Anterior cruciate ligament insufficiency or meniscus damage and meniscectomy) obesity, genetic differences have been found as risk factors for development of OA. Intra-articular corticosteroids are widely used in the management of arthritic conditions for giving short term symptomatic relief from pain and stiffness. This study aimed to compare the efficacy of two intraarticular corticosteroid injections (Methylprednisolone and Triamcinolone) for providing symptomatic pain relief and improving the functional state and quality of life of the patients having osteoarthritis of knee. Long-term treatment of knee OA with repeated steroid injections at reasonable intervals appears to be clinically effective for the relief of symptoms of the disease. In the view of statistical data, we consider that Methylprednisolone may be first choice if early considerable symptomatic improvement is required. The results of the study can be extrapolated on patients who are co-operative and suffer from moderate to severe diseases.

Introduction

Osteoarthritis (OA), also erroneously called degenerative joint disease, represents failure of the diarthrodial

the American College of Rheumatology summarizes this idea: a heterogeneous group of conditions that lead to joint

symptoms and signs which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins (Altman *et al.*, 1986). OA can be classified as primary or secondary. Age is the most powerful risk factor for OA. Major joint trauma and repetitive joint use are also important risk factors for OA. Anterior cruciate ligament insufficiency or meniscus damage (and meniscectomy) may lead to knee OA. Racial differences exist in both prevalence of OA and in the pattern of joint involvement. The Chinese in Hong Kong have a lower incidence of hip OA than whites (Agarwal, 2007). Whether these differences are genetic or due to differences in joint usage related to lifestyle or occupation is unknown.

IA corticosteroid injection is recommended for patients with knee OA, particularly when signs of local inflammation with joint effusion (build-up of fluid within the joint) are present. Triamcinolone (THA) and methylprednisolone are the preferred agents for intra-articular use. It is evident that controversy still exists in the literature as to whether IA corticosteroids are beneficial in the long term or whether the response is measured only in days, and among methylprednisolone and triamcinolone which one gives early onset of symptomatic pain relief.

This study aimed to compare the efficacy of two intraarticular corticosteroid injections (Methylprednisolone and Triamcinolone) for providing symptomatic pain relief and improving the functional state of the patients having osteoarthritis of knee. Moreover, there is no data available on the comparative change in quality of life among steroid users. So this study was planned to get adequate data on

Indian population in terms of efficacy, safety, duration of action and change in quality of life in the OA of knee patients with the use of these two drugs.

Materials and Methods

The study was conducted in the Department of Orthopedics, Nova Speciality Surgery, Kailash Colony and Department of Orthopedics, Hindu Rao Hospital, New Delhi during the period of February 2013 to May 2013. A double blind, randomized, parallel, comparative model was designed for the study. A total of 80 subjects were screened from February 2013 to March 2013. Both male and female patients with 30-75 years of age, tibio-femoral OA of knee according to modified American College of Rheumatology (ACR) criteria, radiologically ascertained grade 2 and grade 3 of OA of knee on Kellgren-Lawrence scale, joint swelling and joint tenderness, pain on movement scored by patients at >40mm on a 100mm VAS, visible joint damage (i.e. bony growths), crepitus were included in the study. Female pre-menopausal patients were screened for pregnancy by urine pregnancy kit and were cautioned against getting pregnant during the study period. Patients with secondary OA, juvenile populations, accompanying hip OA, and patients on Paracetamol, Aspirin, NSAIDs or opioids for any other disease were excluded from the study.

Patients were asked to come to the OPD every 15 days for the next 16 weeks. Simple randomization was done manually and equal numbers of patients were allotted to both the groups (50 patients/group). Group 1 received Methylprednisolone 40-80mg/mL and group 2 received Triamcinolone

40mg/mL. Treatment was given for 12 weeks following which patients were followed up for another 4 weeks. After every 4 weeks, patients underwent evaluation of symptomatology and physical examination during each visit. They were asked to fill up VAS Scale, WOMAC score and Knee Society Score. At the end of 12 weeks of treatment, patient in addition was asked to fill up SF-36 form. After 3 months the treatment was stopped and patients were observed for 1 month.

Apart from these scores, patients were assessed for presence or absence of joint swelling, tenderness and crepitations. In case the patient had bilateral painful knee joints, then the joint which was more painful was taken as the test joint and all measurements and questions were asked regarding that particular knee joint.

Assessment criteria

A total of score obtained after completion of the interview with the patients was calculated by adding individual scores of each question and the total score generated was considered as the final value which was then assessed according to the standard criteria mentioned in all the questionnaires.

Statistical analysis

SPSS 16 program for Windows was used for statistical evaluation. Student's "t" test (Unpaired) was used to evaluate inter group homogeneity and statistical difference in the outcomes. $P < 0.05$ value was considered as significant.

Result and Discussion

A total of 80 subjects were screened from February 2013 to March 2013. Twenty subjects were excluded as they did not

meet inclusion criteria or fell in the exclusion criteria. Two subjects did not give consent for enrollment in the study and eight withdrew as they expressed their inability to come for regular follow up every 2 weeks.

The remaining 50 subjects completed the study with 25 in methyl prednisolone group and 25 in triamcinolone group. None of the subjects enrolled suffered from serious adverse event. All the 50 subjects completed the efficacy analysis. Since in all the above cases, our p value is greater than 0.05 therefore we accept H_0 (null hypothesis), i.e., there's no significant difference between the two study groups with respect to age, height, sex, weight and BMI. It means that the two sample groups are homogeneous.

Primary END-POINT: 100mm VAS after 20 meters walk

100mm VAS score was taken at baseline and after every 4 week interval for 12 weeks. No statistical significant difference was observed at the baseline score as well as at the end of 8th and 12th week between the two groups. But there was statistical significant difference when inter group comparison was done between the two groups at the end of 4th week.

Secondary end points

WOMAC Score

WOMAC has 3 sub scores which add up to make the overall score.

1a. In the WOMAC Pain sub score, inter group comparison revealed that there was no statistical significant difference at baseline but as the study progresses significant statistical difference was seen at the end of 4th and 8th week. At the end of 12th week again there was no statistical

Table.1 Baseline demography of study groups

| Particulars | Mean | | Standard deviation | | P value |
|-------------------------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| Age(yrs) | 53.8 | 59.72 | 9.51 | 11.94 | .239>.05 accept null hypothesis |
| Sex | 1.36 | 1.4 | .49 | .50 | .574>.05 accept null hypothesis |
| Weight(Kg) | 72.6 | 73.52 | 7.31 | 10.63 | .2>.05 accept null hypothesis |
| Height(m) | 1.62 | 1.66 | .08 | .07 | .72>.05 accept null hypothesis |
| BMI(Kg/m ²) | 27.88 | 28.13 | 0.69 | 1.01 | .96>.05 accept null hypothesis |

Table.2 Baseline assessment scores using various scales

| Particulars | Methylprednisolone | | Triamcinolone | | P Value |
|----------------------|--------------------|-------|--------------------|-------|--------------------------------------------|
| | MEAN | | STANDARD DEVIATION | | |
| 100mm VAS Score | 6.56 | 6.73 | 1.01 | 1.2 | 0.275>.05 accept null hypothesis |
| WOMAC | | | | | |
| Pain Score | 30.95 | 33.74 | 6.56 | 5.42 | 0.247>.05 accept null hypothesis |
| Stiffness Score | 11.53 | 13.04 | 3.97 | 3.00 | 0.108>.05 accept null hypothesis |
| Function Score | 100.8 | 108.2 | 19 | 10.9 | 0.061>.05 accept null hypothesis |
| Total WOMAC | 143.3 | 148.7 | 27.67 | 14.9 | 0.096<.05 accept null hypothesis |
| KSS | 41.48 | 38.56 | 13.37 | 12.78 | 0.54>.05 accept null hypothesis |
| SF-36 QOL | | | | | |
| SF-36 Physical Score | 44.05 | 44.36 | 9.19 | 8.45 | 0.526>.05 accept null hypothesis |
| SF-36 Mental Score | 37.8 | 34.88 | 6.56 | 7.04 | 0.222>.05 accept null hypothesis |
| SF-36 Overall | 116.72 | 112.8 | 13.46 | 13.99 | 0.318>.05 accept null hypothesis |

Table.3 Primary END-POINT: 100mm VAS after 20 meters walk

| WEEK | MEAN | | STANDARD DEVIATION | | P VALUE |
|------|--------------------|---------------|--------------------|---------------|------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 6.56 | 6.73 | 1.01 | 1.2 | .275 >.05 accept null hypothesis |
| 4 | 5.35 | 6 | 1.01 | 1.57 | .016 <.05 reject null hypothesis |
| 8 | 4.32 | 4.54 | 1.2 | 1.32 | .746 > .05 accept null hypothesis |
| 12 | 3.00 | 3.58 | 1.27 | 1.12 | .718 > .05 accept null hypothesis |

Figure.1 Womac pain subscore trend from baseline to 12th week

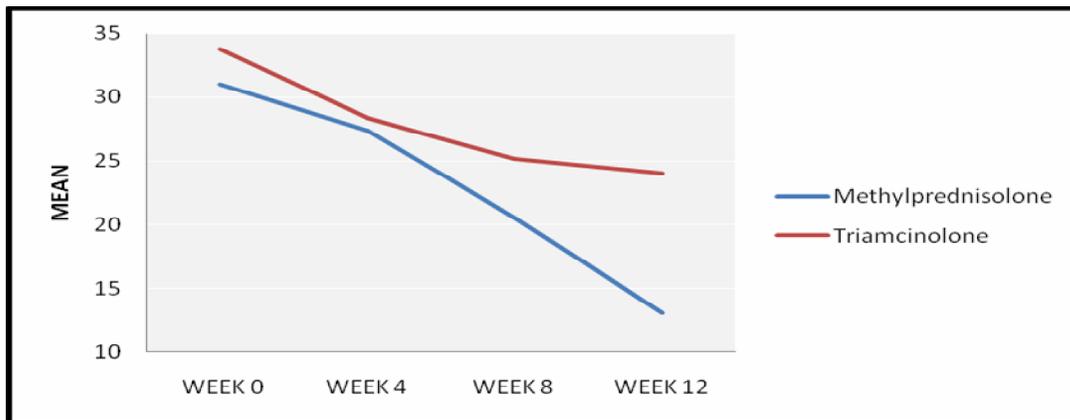
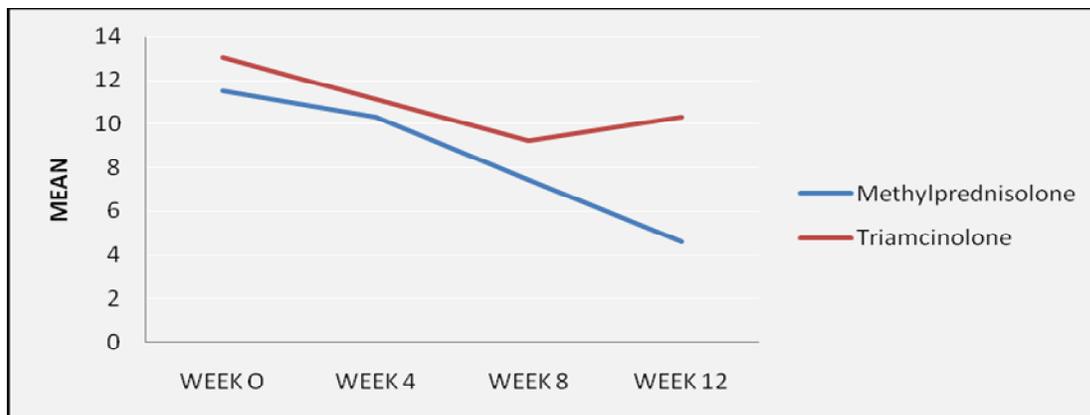


Figure.2 Womac stiffness subscore trend from baseline to 12th week



significant difference which proves methyl prednisolone gave early onset of symptomatic pain relief but by the end of 12th week both the drugs have similar pain related efficacy

1b. In the WOMAC Stiffness sub score, inter-group analysis between both the groups revealed that there was no statistically significant difference in the score at baseline but as the study progresses there is statistical significant difference in the scores of week 4 and week 12. This indicates that Methyl prednisolone is supposed to be longer acting and better than Triamcinolone in giving relief from stiffness.

1c. The WOMAC function sub score inter group analysis between both the groups revealed that there was no significant difference in the score at the baseline but as the treatment progresses the score of both the drugs decreases and there was statistically significant difference in the week 8 and week 12 values. So Methyl prednisolone is proved to be more effective in the week 12 than Triamcinolone and increases movement of the OA knee joint.

In the TOTAL WOMAC SCORE, inter-group analysis between both the groups revealed that there was no statistical significant difference at the baseline values but with the progress of the treatment the values of both the drugs decreases. Starting from week 8 till the end of week 12 there is statistically significant difference in the scores of two groups which proves Methyl prednisolone is more effective in giving relief from pain, stiffness and increases the function of the OA knee joint in comparison to Triamcinolone.

Knee Society Score

The intra-group analysis of the scores between the two groups revealed that there was no significant difference statistically at baseline but with the progress of the treatment the Methyl Prednisolone showed better results than Triamcinolone and there was statistically significant difference in the scores calculated at week 12.

SF-36 Quality of Life Questionnaire

It has 2 categories which add up to make the overall score.

SF-36 Physical Health Score

Inter group analysis between both the groups revealed that there was no significant difference in the score at the baseline but as the treatment progresses the score of both the drugs decreases and there was statistically significant difference in the week 12 values.

SF-36 TOTAL Health Score

Inter group analysis between both the groups revealed that there was no significant difference in the score at the baseline but as the treatment progresses the score of both the drugs decreases and there was statistically significant difference in the week 12 values. This shows that subjects physical and mental quality of life in Methyl prednisolone group is better than those in Triamcinolone group.

Swelling, Tenderness and Crepitations in knee joint

At the starting of the study there was no statistical significant difference when inter group comparison was done between the

Figure.3 Womac function subscore trend from baseline to 12th week

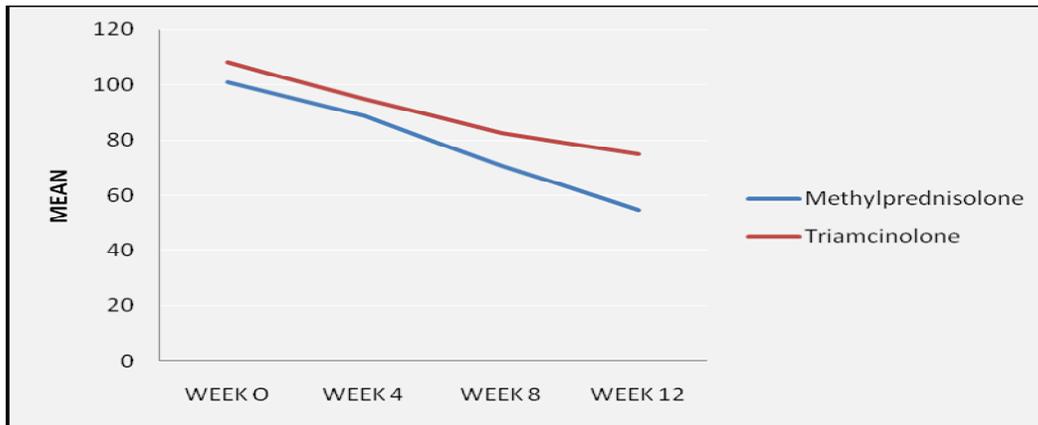


Table.4 Total Womac Score

| WEEK | MEAN | | STANDARD DEVIATION | | P VALUE |
|------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 143.3 | 155 | 27.67 | 17.26 | .096<.05 accept null hypothesis |
| 4 | 126.4 | 134.5 | 32.2 | 17.7 | .102>.05 accept null hypothesis |
| 8 | 98.5 | 117.01 | 30.03 | 17.67 | .011<.05 reject null hypothesis |
| 12 | 76.21 | 105.37 | 24.9 | 16.27 | .02<.05 reject null hypothesis |

Table.5 Knee Society Score

| Week | MEAN | | Standard deviation | | P value |
|------|--------------------|---------------|--------------------|---------------|-------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 41.48 | 25.56 | 13.37 | 12.78 | .54>.05 accept null hypothesis |
| 4 | 58.3 | 42.8 | 18.3 | 13.3 | .06> .05 accept null hypothesis |
| 8 | 65.9 | 54.8 | 14.63 | 10.75 | .36> .05 accept null hypothesis |
| 12 | 83.52 | 60.24 | 6.92 | 10.6 | .004<.05 reject null hypothesis |

Table.6 SF-36 Physical Health Score

| WEEK | MEAN | | STANDARD DEVIATION | | P VALUE |
|------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 44.05 | 44.36 | 9.19 | 8.45 | .526>.05 accept null hypothesis |
| 12 | 71.08 | 40.08 | 5.09 | 11.36 | .011<.05 reject null hypothesis |

Table.7. 3b. SF-36 Mental Health Score

| Week | MEAN | | Standard deviation | | P value |
|------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 37.8 | 34.88 | 6.56 | 7.04 | .222>.05 reject null hypothesis |
| 12 | 42.4 | 37.12 | 2.06 | 6.96 | .000<.05 accept null hypothesis |

Table.7 3b. SF-36 Mental Health Score

| Week | MEAN | | Standard deviation | | P value |
|------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 37.8 | 34.88 | 6.56 | 7.04 | .222>.05 reject null hypothesis |
| 12 | 42.4 | 37.12 | 2.06 | 6.96 | .000<.05 accept null hypothesis |

Table.8 SF-36 TOTAL Health Score

| WEEK | MEAN | | STANDARD DEVIATION | | P VALUE |
|------|--------------------|---------------|--------------------|---------------|----------------------------------------------|
| | Methylprednisolone | Triamcinolone | Methylprednisolone | Triamcinolone | |
| 0 | 116.72 | 107.8 | 13.46 | 13.99 | .618>.05 accept null hypothesis |
| 12 | 89.4 | 89.92 | 7.75 | 12.18 | .046<.05 reject null hypothesis |

two groups ($p= 0.09$). But methyl prednisolone showed great decrease in the swelling by the end of 12th week and there was a significant difference statistically ($p = 0.00$) as compared to triamcinolone. Statistical analysis showed no significant difference in the value of tenderness present in the patients at baseline ($p= 0.173$) but there was significant statistical difference by the end of 12th week ($p= 0.00$). Methylprednisolone showed better results than triamcinolone in decreasing the tenderness. In the values of crepitations there was no significant difference seen throughout the study but still methyl prednisolone corrected more number of patients than triamcinolone when the mean values were calculated.

Safety end-points

No serious adverse events were reported by the subjects during the study period.

Workers performing repetitive tasks as part of their occupations for many years are at high risk of developing OA in the joints they use repeatedly (Brandt, 2005). first 4 weeks, and their effects gradually reduced over a period of 12 weeks. There are studies suggesting that intraarticular corticosteroid agents provide symptomatic

Intra-articular corticosteroid agents have been used by the doctors for about five decades. However, since their effects are relative and they may have local harmful effects, the use of intra-articular corticosteroid agents is still controversial. Dieppe *et al.*, (1980) reported that the intra-articular corticosteroid agents provided a clinical improvement as compared to placebo in the patients with knee osteoarthritis, but this is a short-time effect. In 6 months randomized study, Valtonen *et al.*, (1981) showed that multiple triamcinolone injections provided long term beneficial effects in the patients with symptomatic osteoarthritis. In a double blind study, Raynauld *et al.*, (2003) administered triamcinolone or placebo to the patients with 3 months interval for 24 months. At the end of the study, corticosteroid injection provided symptomatically effective and safe outcomes; however, radiologically, these agents did not improve the pathological processes in the anatomical structures. In a study, Ravaud *et al.*, (1999) showed that intraarticular corticosteroids provided symptomatic improvement in the and functional improvement in a short time in patients with knee and hip osteoarthritis. (Kruse, 2008; Lambert *et al.*, 2007; Qvistgaard *et al.*, (2006)

The primary efficacy criterion in our study was the change in 100mm VAS scale after the patient was asked to take a 20m walk. In a comparative, double blind, randomized study conducted by Pyne *et al.*, (2005) comparing effects of Triamcinolone hexacetonide and Methylprednisolone it was shown that there was no significant difference between the two drugs in functional endpoints at either 3 or 8 weeks. Triamcinolone was more effective than methyl prednisolone at week 3, but its effect is lost by week 8. MPA still has an effect at week 8. In few other studies conducted by Gaffney *et al.* in 1995 and Bellamy *et al.*, (2005) it was stated that on comparing the VAS scoring card there was significant difference in the pain reduction of OA knee by the use of IA corticosteroids during the first 6 weeks but the effects are short termed and get reduced by the 12th week with negligible side effects. However, the present study gave contradictory results proving that methylprednisolone and triamcinolone has similar efficacy by the end of 8th and 12th week. But methylprednisolone gave early symptomatic pain relief and had longer duration of action in comparison to triamcinolone as statistically significant difference is seen at the end of 4th week ($p= 0.016$)

WOMAC has 3 sub scores which add up to make the overall score. Raynauld *et al.*, (2003) performed a trial in 2003 to evaluate the safety and efficacy of triamcinolone acetone in OA knee using WOMAC as the efficacy criteria. He found that there was significant improvement in the knee pain and stiffness. Also long-term treatment of knee OA with repeated steroid injections appears to be clinically effective for the relief of symptoms of the disease. In

another study by Smith *et al.*, (2003) it was proved that methyl prednisolone showed improvement in the pain, function and stiffness from the starting of 4th week till end of the 12th week using WOMAC score. The present study of ours also used the WOMAC score card as the secondary criteria for assessing the efficacy of drugs in which overall comparison of all the scores revealed that both the drugs were effective in giving symptomatic pain relief which diminishes at the end of the 12th week. But Methyl prednisolone was proven better than Triamcinolone by giving early onset of pain relief starting from the 4th week and having longer duration of action. Methylprednisolone also improves the normal functioning as well as stiffness in the osteoarthritic knee.

Studies conducted by Valtonen *et al.*, (1981) and Blyth *et al.*, (1994) proved that triamcinolone hexacetonide (TH) is much better in giving symptomatic pain and relieving stiffness as compared to triamcinolone acetone (TA). We support this conclusion with our results and extensive literature search done during the period of the study that TH gives pronounced effect and long duration of relief in pain when compared with TA.

Most of the studies done in the past compared only a single agent with placebo. We evaluated daily use of the most preferred two intra-articular steroid agents and compared their efficacies with each other. Therefore, in this context, our study is the first prospective study on knee osteoarthritis comprising all the main pain and function score cards as well as comparing the change in the quality of life among patients taking different drugs for OA. Also our study demonstrated that single dose administration provided symptomatic and functional relief till the end of 12th week.

SF-36 Quality of Life Questionnaire is a general form to measure the quality of life. There was a significant difference in the two groups with regard to quality of life. This might have happened because of the early onset of pain relieving action of methylprednisolone which made the patients more satisfied and helped them in their day to day work with increased functionality and decreased stiffness in the OA of knee joint. But the overall mean score of SF-36 decreased at the end of the 12th week in both the groups which suggests that patients do go through some sort of mental and physical disturbances during the course of treatment.

Patient compliance

While recruiting patients for the study investigators realized that most patients have little, if any, idea of what the disease is. They had been coming to the hospital for regular checkup to get relief from pain. The importance of exercise and physiotherapy was explained to them in detail by the doctor but most of them were unable to follow the regimen because of their busy schedule or incapability of coming to the hospital on regular basis. As the investigator provided adequate counseling to the patients while conducting the study, it helped us in a way as none of the subjects withdrew from the study.

To decrease the incidence of withdrawal from the study subjects were recruited following strict inclusion and exclusion criteria. It was also made sure that patients lived within 15 kilometers of the hospital premises to diminish their difficulty in reaching the hospital and thereby decreasing drop-out. The compliance in both the groups was high (methylprednisolone – 95% and triamcinolone – 93%). A visit after 2

weeks and regular counseling helped patients in adhering to their scheduled treatment regimen.

So use of intraarticular corticosteroids (Methylprednisolone and Triamcinolone) is quite safe and can be beneficial in providing short term as well as long term pain relief from OA of knee as well as improves the functionality and stiffness of the knee joint with repeated steroid injections at regular controlled intervals.

Patients suffering from OA at an early age must be counseled regarding the disease along with all the treatment modalities available. They must also be counseled regarding the value of exercise and physiotherapy. Women are more in number suffering from OA of knee because of the continuous squatting, bending and climbing stairs which make them use specific joints repeatedly. Pain during walking is decreased both by methylprednisolone and triamcinolone. But if overall activity of subject is taken into account, methylprednisolone is better than triamcinolone.

No adverse effects are seen with these drugs except some localized irritation and infections because of unhygienic conditions so these are comparatively safer and effective in providing early and short term symptomatic pain relief. Long-term treatment of knee OA with repeated steroid injections at reasonable intervals appears to be clinically effective for the relief of symptoms of the disease. The results of the study can be extrapolated on patients who are co-operative and suffer from moderate to severe diseases

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