

Intra-articular Injection of Local Anaesthetic and Corticosteroid: A Potentiation Effect of Pain Relief in Grade IV Gonarthrosis and an Alternative to Arthroplasty Operations

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ABSTRACT

Background and Aim: There are few nonsurgical options for treatment of grade IV knee osteoarthritis. This randomised controlled clinical trial was performed to evaluate the efficacy and safety of intra-articular injection of local anaesthetic and corticosteroid for pain management in patients with grade IV osteoarthritic knee joints. **Methods:** A total of 240 patients with grade IV osteoarthritic knee joints were enrolled and separated into four groups. They were administered different intra-articular injections: Group A received local anaesthetic (prilocaine); Group B received methylprednisolone; Group C received methylprednisolone+ saline; and Group D received methylprednisolone+prilocaine. The number of pain-free days following injection was recorded. **Results:** The mean number of pain-free days was 3.7 ± 0.2 days in Group A vs. 62.1 ± 0.3 days in Group B vs. 75.5 ± 0.8 days in Group C vs. 157 ± 0.5 days in Group D ($P < 0.05$). Patients were asked to report to the clinic if pain recurred and the same injection was repeated. After the second injection, once again, the number of pain-free days was significantly higher in Group D (161 days) than in the other groups. Adverse events encountered included syncope ($n=14$) and cellulitis at injection site ($n=2$). **Conclusion:** Intra-articular combination of methylprednisolone and prilocaine appears to be a safe and effective method for potentiating pain relief in grade IV knee osteoarthritis. The injection can be repeated at intervals to provide a permanent pain-free knee for patients. **Key words:** Osteoarthritis, Intra-articular, Local anesthetic, Steroid, Arthroplasty.

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INTRODUCTION

Osteoarthritis (OA) is a common cause of morbidity in the elderly and patients often suffer years of pain and disability. Knee pain secondary to OA accounts for up to 30% of visits to primary care physicians. OA is characterized by an imbalance between the synthesis and degradation of articular cartilage and subchondral bone and is accompanied by capsular fibrosis, osteophyte formation and variable grades of inflammation of the synovial membrane.^[1] The incidence of symptomatic OA increases with age and, at all ages, women are more commonly affected than men.^[2]

The most effective treatment for grade 4 osteoarthritis is arthroplasty. When the patient is unwilling or unsuitable for surgery, oral paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) may provide temporary relief; however, these drugs cannot fully control the pain of advanced knee OA and their prolonged use can lead to gastrointestinal and cardiovascular side effects. Intra-articular injection is a useful alternative; it can provide pain relief, improve quality of life and help postpone surgical intervention. In our orthopaedic practice, we routinely use this treatment for grade 4 gonarthrosis patients

who refuse or are unsuitable for surgery. The pain relief is surprisingly good and patients often ask for a repeat injection after several months. However, there are few well-designed, controlled studies that have evaluated the use of intra-articular corticosteroids and local anaesthetics in the treatment of knee OA.^[3] The aim of this randomised controlled study was to determine the efficacy and safety of intra-articular injection local anaesthetic+corticosteroid in patients with grade IV OA of the knee.

MATERIALS AND METHODS

Study participants were selected from among knee OA patients attending our orthopaedic clinic during 2014-2016. Patients were eligible for enrolment if they 1) had grade 4 osteoarthritis of the knee, 2) were unwilling to undergo arthroplasty or had contraindication for surgery and 3) were willing to accept intra-articular injection. Patients with rheumatoid arthritis, diabetes mellitus, thyroid abnormalities, abnormal pain responses and major psychiatric disorders were excluded. A total of 240 patients were consecutively enrolled. They were randomized into

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four groups according to their order of recruitment into the study. Thus, patient number 1 was allocated into group A, patient number 2 into group B, patient number 3 into group C and patient number 4 into group 4. This cycle was repeated until there were 60 patients in each group.

All intra-articular injections were administered under sterile conditions by the author. For the procedure, the patient was seated on the examination table, with the knee in 90°C flexion. The injection site was cleaned with povidone-iodine. Approach was through the anterolateral portal of the knee. Group A patients received 10 cc of 2% prilocaine; group B patients received a flacon of 40 mg methylprednisolone; group C received a flacon of methylprednisolone+ 10 cc of saline; and group D received a flacon of methylprednisolone+ 10 cc of prilocaine. After injection, no additional medications, including anti-inflammatory drugs, were prescribed. The patients were requested not to take any oral medication and to attend follow-up without fail. Cell phone numbers and addresses were recorded so that they could be contacted if necessary.

Written informed consent was obtained from all patients before the procedure.

Primary outcome was the number of pain-free days following intra-articular injection. This was recorded for each patient. The patients were told to report to the clinic if they experienced pain again. If the patient did not report to the clinic even 5 months after the first injection, they were contacted to determine if they had experienced pain. A total of 53/60 (88.3%) in group A, 57/60 (95%) in group B, 59/60 (98.3%) in group C and 57/60 (95%) in Group D completed the study, reporting back to the polyclinic when pain recurred. A total of 11 patients were lost to follow-up. Three patients (1 patient each from group A, group B and group D) opted for arthroplasty. When patients experiencing recurrence of pain came for their second clinic visits, they were administered the same injection that they had received earlier and, again, advised to report back if pain recurred. The pain-free duration following the second injection was recorded. The duration of pain-free intervals was compared between the groups.

Statistical Analysis of Data

Data were summarized as means \pm standard deviation. The Mann-Whitney *U* test and Kruskal-Wallis test were used for comparisons between groups. Statistical significance was at $P \leq 0.05$.

RESULTS

A total of 240 patients were enrolled in the study, with 60 patients per group. Mean age, mean weight and gender composition were comparable between the groups (Table 1).

The mean pain-free duration after the first injection was 3.7 ± 0.2 days when only local anaesthetic was used (Group A) and 62.1 ± 0.3 days when only corticosteroid was used (Group B). When the two drugs were combined (Group D), pain relief lasted for 157 ± 0.8 days, indicating potentiation of effect. The pain-free intervals after the second injections were similar to that after the first injections in all groups and, once again, group D had the longest pain-free interval. With two intra-articular

Table 2: Mean number of pain-free days in the four groups.

	Group A	Group B	Group C	Group D	P
Pain-free days after first injection	3.7 \pm 0.2	62.1 \pm 0.3	75.5 \pm 0.8	157 \pm 1.2	<0.05
Pain-free days after second injection	5.3 \pm 1.3	75.3 \pm 0.7	83.1 \pm 1.2	161.8 \pm 2.3	<0.05
Total pain-free days	9 \pm 1.5	137.4 \pm 1	158.6 \pm 2	318.8 \pm 3.5	<0.05

injections, 13 patients in group D achieved complete pain relief for 1 year (Table 2).

The combination of corticosteroid and saline (group C) also produced a slight increase of the pain-free duration to 75.5 days. However, the improvement over that achieved with corticosteroid alone (75.5 days vs. 62.1 days) was not statistically significant ($P > 0.05$). The slightly enhanced effect was likely due to a simple dilution effect of saline on intra-articular enzymes and debris.

DISCUSSION

Despite the immense impact that OA has on the lives of many people there are very few effective, nonsurgical treatments available.^[4] One commonly used treatment is intra-articular injection of corticosteroid and local anaesthetic. This study is the first long-term, prospective, randomized controlled trial to examine the safety and efficacy of intra-articular injection of different combinations of drugs in grade IV knee OA.

Thorn, in 1940, was the first to report the use of intra-articular corticosteroid for treatment of knee OA. In 1951, Hollander confirmed the effectiveness of the practice.^[5] Since then it has been widely used and many international guidelines now advocate the use of intra-articular corticosteroids for painful knee OA. Corticosteroids can provide substantial short-term pain relief for up to 8 weeks and some authors suggest that the benefits may last as long as 6 months.^[6]

Corticosteroids have both anti-inflammatory and immunosuppressive effects. They act on nuclear steroid receptors and interrupt the inflammatory immune cascade at several levels. They reduce vascular permeability; decrease erythema, swelling and tenderness; and inhibit accumulation of inflammatory cells and inflammatory mediators. Corticosteroids are reported to reduce prostaglandins production and increase vasodilatation when injected into the knee joint.^[7]

Dieppe *et al.* found that although pain relief was significantly better with intra-articular corticosteroid than with placebo, the benefit was short lived.^[8] However, depot formulations such as methylprednisolone persist at the injection site for long periods. According to Valtonen *et al.*^[9] Matzkin *et al.*^[10] and Juni *et al.*^[11] long-acting corticosteroids might provide pain relief for up to 6 months. In our study, however, the mean pain-free duration in patients receiving corticosteroid injection alone was only for 2 months.

A common method for potentiating the effect of intra-articular injection is to combine a depot form of corticosteroid (for its anti-inflammatory effect) with a local anaesthetic (for providing immediate analgesia). Intra-articular local anaesthetic provides immediate pain relief that lasts 4-5 h. In addition, local anaesthetic can decrease sensitization, which is a feature of chronic or persistent pain and thereby prolong the treatment effect beyond the normal pharmacological duration of action.^[12]

In this study each injection of the combination of local anaesthetic and corticosteroid provided pain relief for about 5 months. Repeated intra-articular injection of this combination could be an effective long-term management option in patients unwilling or unable to undergo surgical

Table 1: Demographic features of patients in the four groups.

	Group A	Group B	Group C	Group D	P
Mean age (years)	65.6 \pm 1.2	63.7 \pm 1.8	64.68 \pm 0.9	63.42 \pm 0.4	>0.05
Mean weight (kg)	82.1 \pm 0.8	92.3 \pm 2.1	87.8 \pm 1.6	97.1 \pm 0.5	>0.05
Gender (male/female)	7/53	6/54	10/50	4/56	>0.05

treatment. Although there is no conclusive evidence on the ideal treatment frequency, it is generally recommended to keep the injections limited to once every 3 months.^[13]

Sahin *et al.* reported that significant pain reduction was achieved for 2 years after injection of corticosteroid + local anaesthetic into the sacroiliac joint.^[14] In another study, 82% of patients with De Quervain tendinitis treated with corticosteroid injections remained symptom free for 12 months.^[15] These results were better than that in our study, but this may be because the target was soft tissue and not a joint.

The prolonged effect of intra-articular injection may be due to osteoarthritic cartilage morphology. Healthy adult cartilage is devoid of blood vessels and nerve endings. Osteoarthritic cartilage, in contrast, may be invaded by blood vessels and nerves from the subchondral bone. Hypertrophic chondrocyte differentiation may underlie cartilage angiogenesis in osteoarthritis.^[16] In osteochondral angiogenesis, subchondral bone marrow is replaced by fibrovascular tissue expressing vascular endothelial growth factor and there is increased expression of nerve growth factor within vascular channels.^[17] These factors, especially the nerve growth into osteoarthritic cartilage, may explain the potentiation of pain relief seen with the use of a combination of local anaesthetic and corticosteroid.

Hollander injected corticosteroids on 1034 osteoarthritic knees and reported that 80% of patients achieved pain relief for 1-4 weeks.^[5] A systematic review of intra-articular corticosteroid injections for treatment of knee OA concluded that the beneficial effect of treatment commenced 1 week after injection and lasted for 3-4 weeks.^[18] In our study, however, we observed 2 months of pain relief with each injection of depot corticosteroid.

Adverse effects following intra-articular corticosteroid injections have included septic arthritis, post injection flare, local tissue atrophy, tendon rupture, cartilage damage, flushing and increased serum glucose level. Only a few mild adverse events were encountered in our series; these included syncope ($n=14$) and cellulitis at the injection side ($n=2$). These patients were withdrawn from the study and replaced by other patients.

CONCLUSION

Intra-articular corticosteroid and local anaesthetic injection appears to be a safe and effective surgery-sparing procedure. An intra-articular injection of a combination of corticosteroid and local anaesthetic performed twice a year may be sufficient to provide a painless knee for patients unwilling or unsuitable for knee surgery. Potentiation of pain relief with the use of the combination, the low cost of treatment and the few risks make this an attractive alternative to arthroplasty in selected patients.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

OA: Osteoarthritis; NSAID: Non-steroidal Anti-inflammatory Drugs.

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