

Single-dose periarticular steroid infiltration for pain management in total knee arthroplasty: a prospective, double-blind, randomised controlled trial

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ABSTRACT

Introduction: Post total knee replacement pain control using parenteral opioids results in significant side effects like nausea and vomiting. Periarticular injections are used to control pain without these side effects. This study aimed to evaluate the safety and efficacy of periarticular steroid injection in patients undergoing total knee arthroplasty, as well as assess the patient's functional outcomes over a period of two years.

Methods: A total of 100 patients who underwent total knee arthroplasty were randomised into two groups. The treatment group received periarticular infiltration with triamcinolone acetone, bupivacaine and epinephrine. The control group received only bupivacaine and epinephrine. The postoperative analgesic regime was standardised for all patients. The immediate postoperative outcomes evaluated included pain score, morphine consumption, time to ambulation, straight leg raise, range of motion and duration of hospital stay. Longer-term outcomes were assessed at 1, 3, 6 and 24 months using the SF-36 questionnaire and Oxford Knee Score.

Results: Patients in the treatment group had significantly lower pain scores, reduced morphine consumption and earlier discharge. They also had better range of knee motion and were able to regain muscular strength earlier. There was no increase in major complications such as infection or tendon rupture in the treatment group. There was no difference between the groups with regard to the medium-term outcomes of up to two years.

Conclusion: This modality of pain control is safe and efficacious for post total knee replacement pain control.

Table 1. Demographic data of the study groups.

	Non-steroid	Steroid	p-value
Mean age (yrs)	65.4	67.9	0.104
BMI (kg/m ²)	27.3	26.7	0.499
Weight (kg)	66.1	62.9	0.171
Right side	32	30	0.837
Left side	18	20	0.839
Pre-Hb (g/dl)	13.3	13.1	0.498
Post-Hb (g/dl)	10.9	11.0	0.742

BMI: body mass index; Hb: haemoglobin

Keywords: knee arthroplasty, rehabilitation, steroid

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INTRODUCTION

Total knee arthroplasty (TKA) is associated with significant postoperative pain, which may adversely affect the rehabilitation of the patient.⁽¹⁾ The use of parenteral opioids may be effective but causes dose-related complications of nausea, vomiting, constipation, urinary retention, drowsiness and respiratory depression.^(2,3)

Multi-modal analgesic regimes are used to relieve pain in patients who have undergone TKA. Various papers have described the use of periarticular injections of anaesthetic concoctions to relieve pain.⁽⁴⁻⁶⁾ These drug cocktails commonly include combinations of nonsteroidal anti-inflammatory drugs (NSAIDs), local anaesthetics and opioids such as morphine. Studies conducted by Fu et al⁽⁷⁾ and Pang et al⁽⁸⁾ on unicompartmental knee arthroplasty have shown the efficacy of periarticular steroid injection in postoperative pain control following TKA. Concerns with the use of periarticular steroids in this group of patients include the risk of postoperative infection and patellar tendon rupture. The study aimed to evaluate the safety and efficacy of periarticular steroid injection in patients undergoing TKA and to further assess the patient's functional outcomes over a period of two years.

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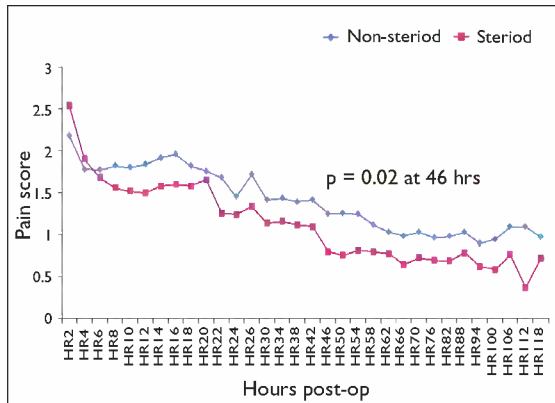


Fig. 1 Line graph shows the comparison of postoperative pain scores between the two groups.

METHODS

This study was a two-year, double-blind, prospective, randomised controlled trial. Approval for the study protocol was obtained from the hospital ethics committee, and written consent was given by all the patients enrolled in the trial. Using an alpha error of 0.05, a power of 80% and a standard deviation of 25 mg of morphine consumption per 24 hours, 32 patients (16 in each group) were required for the study in order to detect a difference of 25 mg of morphine consumption between the two groups.^(9,10)

A total of 100 patients who underwent TKA performed by the three senior authors in 2004–2005 were recruited into the study. These patients were randomised into the two arms of the study using randomisation tables. Patients with diabetes mellitus, previous surgery to the knee, immunodeficiency, hypothyroidism, renal failure, or allergies to either the components of the periarticular injection or to oral NSAIDs were excluded. In the study group, 50 patients received an intraoperative periarticular injection of a local anaesthetic agent with adrenaline (0.5% bupivacaine with epinephrine 1:200,000) (Marcaine, AstraZeneca, Sodertalje, Sweden) and the corticosteroid, triamcinolone acetonide (Kenacort, Bristol-Myers, New York, NY, USA). In the control group, the other 50 patients received a similar concoction but without the corticosteroid.

Surgery was performed by either of the three senior surgeons in this study. General or spinal anaesthesia was used, as determined by the anaesthetist, who was unaware of the cocktail used. The surgeon was only notified of the injection cocktail that the patient received through sealed envelopes during the surgery. The distribution of patients receiving either general or spinal anaesthesia was comparable. A total of 21 patients in the study arm and 20 patients in the control arm underwent general anaesthesia,

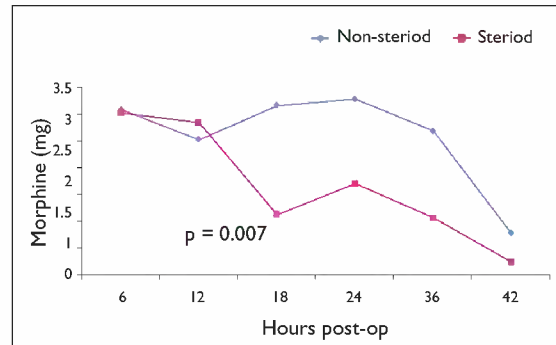


Fig. 2 Line graph shows the six-hourly parenteral morphine consumption of the two groups.

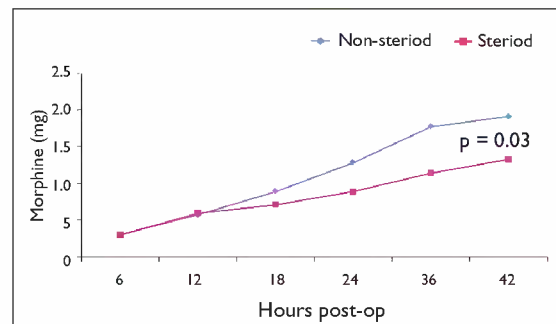


Fig. 3 Line graph shows the cumulative morphine consumption of the two groups.

while 29 patients in the study group and 30 patients in the control group received spinal anaesthesia. No long-acting analgesics were used, and spinal anaesthesia was accomplished with 0.5% bupivacaine. Tourniquet was used in all the patients, and the standard medial parapatellar, quadriceps splitting approach was used in all the cases. All the implants were cemented and the injection cocktail delivered into the periarticular tissues of the knee joint after the cement had set.

The study group received an infiltrative mixture of 0.5 ml/kg⁽¹¹⁾ of 1:200,000 epinephrine and 0.5% bupivacaine diluted with 30 ml of normal saline. 40 mg of corticosteroid (triamcinolone acetonide)⁽¹²⁾ was added to half of the above mixture. The solution with the corticosteroid was then injected into the deep tissues, including the quadriceps muscle, medial collateral ligament, posterior capsule and synovium. The other half of the solution, which did not contain the corticosteroid, was injected into the skin incision before closure. This was to prevent steroid-induced skin atrophy along the incision.⁽¹³⁾ The control group received a similar concoction of identical volume without the corticosteroid, with the volume also divided in two halves. All the patients received postoperative oral naproxen and patient-controlled analgesics (with morphine bolus of 1 mg, lock-out time of five minutes, and a maximum dose of 8 mg/hr) for 48 hours.

Immediate postoperative pain control was assessed

Table II. Comparison of results between the study groups.

	Non-steroid	Steroid	p-value
Average LOS (days)	6.8	5.2	0.022
Mean drop in Hb (g/dl)	2.4	2.1	0.084
Drainage (ml)	246	281	0.340
SLR on postoperative day (days)	2.8	2.3	0.042
Infection	1	1	-
Tendon rupture	0	0	-

LOS: length of stay; Hb: haemoglobin; SLR: straight leg raise

via patient-reported pain scores using a visual analogue scale, and performed by an independent assessor who was blinded to the injection regime. All patients were asked to score their pain on a scale of 0 to 10, with 0 being no pain and 10 being maximum pain. The pain score was collected every six hours for the first five postoperative days. Parenteral morphine consumption was measured using the patient-controlled pump at six-hourly intervals for the first 48 hours.

The range of motion (ROM) was recorded daily by a physiotherapist who was blinded to the injection regime, for the duration of admission and during subsequent follow-ups. The other parameters used as a measure of recovery of muscular strength included length of time required to perform a straight leg raise and time to independent walking, in addition to duration of hospitalisation, mean drop in haemoglobin and total drainage. Upon discharge, patients were further evaluated using the SF-36 questionnaire⁽¹⁴⁾ and the Oxford Knee Score⁽¹⁵⁾ at three-month, six-month and two-year intervals. Complications such as infection and tendon ruptures were recorded. All measurements and recordings were made by the same physiotherapist who was blinded to the study group.

Statistical analysis was performed using the Statistical Package for the Social Sciences version 11.0 (SPSS Inc, Chicago, IL, USA). Univariate analysis was performed with the chi-square test or the Fisher's exact test for comparison of proportions between two categorical data. The Mann-Whitney U test was used to compare the non-parametric data between two independent samples. A p-value < 0.05 was considered statistically significant.

RESULTS

The demographic data was similar between the two groups (Table I). For patients in the group receiving steroid injection, significantly lower pain scores from the second postoperative day were noted (Fig. 1). Patients in the steroid arm also had statistically significant reduced demands for parenteral morphine at 18 hours,

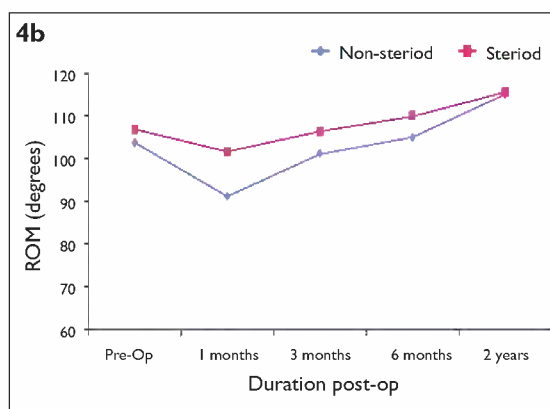
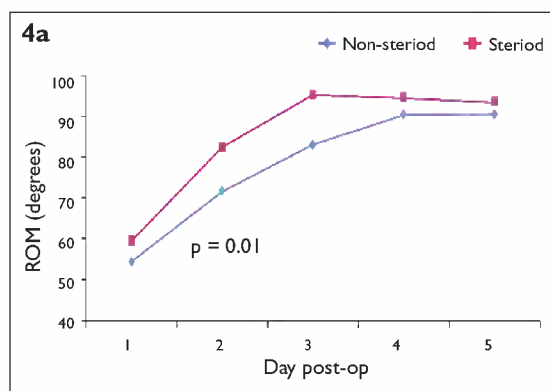


Fig. 4 Line graphs show the range of motion of the two groups (a) postoperatively and (b) at follow-up.

24 hours and 36 hours postoperatively (Fig. 2). Patients receiving steroid injection also consumed significantly less morphine overall compared to non-steroid patients (Fig. 3).

Patients who received periarticular steroid had better ROM, and this was statistically significant from the second day onward. Even at one, three and six months, the patients in the steroid group continued to have better ROM compared to the control group (Fig. 4). The steroid group was also able to achieve straight leg raise at a mean of 2.3 days compared to 2.8 days for the control group (Table II). The length of hospital stay was also shorter in the steroid group. The mean length of stay was 5.2 days in the steroid group compared to 6.8 days in the control group ($p = 0.02$). The mean drop in haemoglobin was lower in the steroid group by 0.3 mg/dl, although it was not statistically significant. There was no significant difference in the postoperative drainage between the two groups (Table II). At follow-up of up to two years, there was no statistically significant difference in the SF-36 questionnaire and the Oxford Knee Score for the two groups of patients.

One patient each in both the steroid and control group developed early postoperative wound infection with persistent sinus discharge. In both cases, the infection

resolved and the sinus healed after a single-stage arthrotomy, washout and change of the polyethylene insert. Cultures taken from the patient in the steroid group were negative, whereas the patient in the control group had a positive culture of methicillin-resistant *staphylococcus aureus* (MRSA). Both patients recovered well subsequently and at the last follow-up, had good ROM of 0°–120°.

DISCUSSION

TKA is associated with significant postoperative pain,⁽¹⁾ and good pain relief allows effective rehabilitation.⁽¹⁶⁾ Effective pain relief should be delivered pre-, peri- and postoperatively to prevent the establishment of pain hypersensitivity.⁽¹⁷⁾ Postoperative pain hypersensitivity is caused by the sensitisation of both the central and peripheral nervous system. Surgical trauma decreases the threshold for afferent nociceptors in the peripheral nerves, as well as increases the excitability of the central spinal neurons. Together, these changes result in an increase in the response to noxious stimuli and decrease the pain threshold at the site of the injured and surrounding uninjured tissues.⁽⁴⁾ The administration of preemptive analgesics directly into the operative site has been shown to prevent central sensitisation and improve postoperative pain control.⁽¹⁸⁻²⁰⁾

The safety of bupivacaine in periarticular injections is well documented. Previous studies have shown that the mean serum concentrations in patients who received up to 30 ml of 0.5% bupivacaine were well below the toxic level.⁽¹⁷⁾ Lombardi et al have found no perioperative complications related to the injection.⁽⁶⁾ The addition of epinephrine helps to reduce the toxicity of the local anaesthetic by keeping it localised to the area of injection. It has also been demonstrated that periarticular epinephrine injection reduces blood loss from the operative site.⁽⁶⁾ Few studies have investigated the efficacy of periarticular injection of local anaesthetics, and while some authors have found it effective,^(5,6,17) others have not found a reduction in narcotic consumption after surgery.⁽²¹⁻²⁴⁾ Our study was a double-blind randomised controlled trial that has demonstrated the efficacy and safety of corticosteroid (triamcinolone) periarticular injection for pain relief following TKA.

The anti-inflammatory effect of corticosteroid stems from its inhibition of phospholipase A2, resulting in a reduction of the pro-inflammatory derivatives of arachidonic acid.⁽²⁵⁾ Injection of corticosteroid into the surrounding tissues can thus provide effective pain relief by reducing the inflammatory response at the sites of the surgical trauma.^(26,27) In addition, it can decrease blood

loss by reducing the production of prostaglandins with vasodilatory effects.⁽²⁸⁾

In conclusion, our study has demonstrated the efficacy and safety of periarticular injection of corticosteroid, bupivacaine and epinephrine following TKA. Patients who received the steroid cocktail have reported better visual analogue pain scores and required less parenteral morphine postoperatively. They also had better ROM from the second day onward, and continued to have better ROM up to six months postoperatively compared to the control group. Postoperatively, the steroid group was also able to perform straight leg raises earlier, had a shorter hospital stay and a smaller drop in haemoglobin. There was no increased risk of infection at two years follow-up and no incidence of patellar tendon rupture among our patients.

REFERENCES

1. Bonica JJ. Postoperative pain. In Bonica JJ, ed. *The Management of Pain*. 2nd ed. Philadelphia: Lea and Febiger, 1990: 461-80.
2. DeWeese FT, Akbari Z, Carlone E. Pain control after knee arthroplasty: intraarticular versus epidural anesthesia. *Clin Orthop Relat Res* 2001; (392):226-31.
3. Singelyn FJ, Deyaert M, Joris D, Pendeville E, Gouverneur JM. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. *Anesth Anal* 1998; 87:88-92.
4. Busch CA, Shore BJ, Bhandari R, et al. Efficacy of periarticular multimodal drug injection in total knee arthroplasty. A randomized trial. *J Bone Joint Surg Am* 2006; 88:959-63.
5. Venditelli PA, Makinen P, Drolet P, et al. A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. *J Bone Joint Surg Am* 2006; 88:282-9.
6. Lombardi AV Jr, Berend KR, Mallory TH, Dodds KL, Adams JB. Soft tissue and intra-articular injection of bupivacaine, epinephrine, and morphine has a beneficial effect after total knee arthroplasty. *Clin Orthop Relat Res* 2004; 428:125-30.
7. Fu P, Wu Y, Wu H, et al. Efficacy of intra-articular cocktail analgesic injection in total knee arthroplasty – a randomized controlled trial. *Knee* 2009; 16:280-4.
8. Pang HN, Lo NN, Yang KY, Chong HC, Yeo SJ. Peri-articular steroid injection improves the outcome after unicompartmental knee replacements: a prospective, randomised controlled trial with a two-year follow-up. *J Bone Joint Surg Br* 2008; 90:738-44.
9. Hirst GC, Lang SA, Dust WN, Cassidy JD, Yip RW. Femoral nerve block. Single injection versus continuous infusion for total knee arthroplasty. *Reg Anesth* 1996; 21:292-7.
10. Ng HP, Cheong KF, Lim A, Lim J, Puhaindran ME. Intraoperative single-shot “3-in-1” femoral nerve block with ropivacaine 0.25%, ropivacaine 0.5% or bupivacaine 0.25% provides comparable 48-hr analgesia after unilateral total knee replacement. *Can J Anaesth* 2001; 48:1102-8.
11. DRUGDEX® from Thomson Micromedex. 2007 information. Available at: www.micromedex.com. Accessed August 26, 2007.
12. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000; 43:1905-15.

13. Reddy PD, Zelicof SB, Ruotolo C, Holder J. Interdigital neuroma. Local cutaneous changes after corticosteroid injection. Clin Orthop Relat Res 1995; (317):185-7.
14. Ware JJ, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30:473-83.
15. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. J Bone Joint Surg Br 1998; 80:63-9.
16. Shoji H, Solomonow M, Yoshino S, D'Ambrosia R, Dabezies E. Factors affecting postoperative flexion in total knee arthroplasty. Orthopedics 1990; 13:643-9.
17. Badner NH, Bourne RB, Rorabeck CH, MacDonald SJ, Doyle JA. Intra-articular injection of bupivacaine in knee replacement operations. Results of use for analgesia and for preemptive blockade. J Bone Joint Surg Am 1996; 78:734-8.
18. Ringrose NH, Cross MJ. Femoral nerve block in knee joint surgery. Am J Sports Med 1984; 12:398-402.
19. Heard SO, Edwards WT, Ferrari D, et al. Analgesic effect of intraarticular bupivacaine or morphine after arthroscopic knee surgery: a randomized, prospective, double-blind study. Anesth Analg 1992; 74:822-6.
20. Woolf CJ, Chong MS. Preemptive analgesia--treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 1993; 77:362-79.
21. Klasen JA, Opitz SA, Melzer C, Thiel A, Hempelmann G. Intraarticular, epidural, and intravenous analgesia after total knee arthroplasty. Acta Anaesthesiol Scand 1999; 43:1021-6.
22. Klasen JA, Opitz SA, Melzer C, Thiel A, Hempelmann G. Intraarticular, epidural, and intravenous analgesia after total knee arthroplasty. Acta Anaesthesiol Scand 1999; 43:1021-6.
23. Browne C, Copp S, Reden L, Pulido P, Colwell C Jr. Bupivacaine bolus injection versus placebo for pain management following total knee arthroplasty. J Arthroplasty 2004; 19:377-80.
24. Mauerhan DR, Campbell M, Miller JS, et al. Intra-articular morphine and/or bupivacaine in the management of pain after total knee arthroplasty. J Arthroplasty 1997; 12:546-52.
25. Creamer P. Intra-articular corticosteroid injections in osteoarthritis: do they work and if so, how? Ann Rheum Dis 1997; 56:634-6.
26. Mirzai H, Tekin I, Alincak H. Perioperative use of corticosteroid and bupivacaine combination in lumbar disc surgery: a randomized controlled trial. Spine (Phila Pa 1976) 2002; 27:343-6.
27. Glasser RS, Knego RS, Delashaw JB, Fessler RG. The perioperative use of corticosteroids and bupivacaine in the management of lumbar disc disease. J Neurosurg 1993; 78:383-7.
28. Thébault J, Blatrix C, Blanchard J, Panak E. A possible method to control prolongations of bleeding time under antiplatelet therapy with ticlopidine. Thromb Haemost 1982; 48:6-8.

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