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Effect of Methylprednisolone in Peri-articular Infiltration for Primary Total Knee Arthroplasty on Pain and Rehabilitation

A PROSPECTIVE COMPARATIVE STUDY

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Abstract:

Background: Optimal pain management post-total knee arthroplasty is important to ensure timely rehabilitation and patient satisfaction. This study examines the efficacy of adding corticosteroid in peri-articular infiltration cocktail with relation to post-operative pain management and rehabilitation in patients undergoing simultaneous bilateral total knee arthroplasty.

Methods: 50 patients with symptomatic end-stage bilateral knee osteoarthritis undergoing bilateral TKA under the same anaesthetic were recruited. More painful knee was operated first and the study solution containing ropivacaine, clonidine, epinephrine, and ketorolac with methylprednisolone was infiltrated in one knee and an identical mixture but without methylprednisolone was infiltrated in the second knee. Outcome measures included comparison of VAS on movement of each knee and range of motion achieved during the first three days post-surgery.

Results: Difference of VAS score and ROM at day one and three between the two groups of knees were significant ($p<0.05$). Post-operative inflammation as well as ability to straight leg raise showed better trends in the knees receiving prednisolone although this did not reach statistical significance.

Conclusion: Addition of Methylprednisolone to periarticular infiltration cocktail for patients undergoing TKA has significant influence on reduction of pain in early post-operative period and patients are able to regain knee flexion more quickly.

Key Words: Periarticular infiltration, Methylprednisolone, Post-operative Pain, Range of motion, Total Knee Arthroplasty.

Introduction:

Total knee arthroplasty (TKA) is established as treatment of choice for end-stage symptomatic knee osteoarthritis (OA). It provides reliable function and implant survival is reported at around 95% at 10 years[1,2]. One key unresolved issue is post-operative pain in the peri-operative period. Effective post-operative pain relief helps early rehabilitation, prevention of deconditioning, and timely discharge to ensure optimal outcomes and make resources more available. Pain has been shown to be one of the main clinical reasons for hospital stay after knee arthroplasty and finding the best post-operative pain control regimen is at the top of priority setting partnerships[3].

Intra-operative peri-articular infiltration is routinely used to reduce the intensity and severity of post-operative pain[4,5,6,7] . This infiltration typically contains a mixture of various agents including a local anaesthetic, an anti-inflammatory agent and epinephrine. In addition, use of intermediate acting corticosteroid such as Methylprednisolone is recommended by some experts due to its anti-inflammatory properties[8, 9, 10]. However, use of corticosteroids can increase the risk of infection and therefore not routinely used in the peri-articular filtration.

At present, there is no consensus about the use of corticosteroids in the peri-operative period following knee arthroplasty. In addition, the intensity of post-operative pain after surgery varies among different patients. It not only depends upon patient factors but also upon surgeon factors. It is difficult to control for various confounders to establish whether indeed addition of a corticosteroid to local infiltration is safe and effective. One way to overcome this is to assess the impact in a cohort of patients who undergo bilateral TKA performed by the same

surgeon using the same surgical technique under the same anaesthetic. This study aims to compare the safety and efficacy of adding a corticosteroid to the peri-articular infiltration in patients undergoing single-stage bilateral TKA.

Materials and Methods:

This prospective non-randomized study was conducted over a nine month period (September 2017 to June 2018). Institutional scientific advisory committee and ethical committee approval was duly obtained and all patients consented to taking part in the study. 50 patients with bilateral symptomatic end-stage knee OA listed for single staged bilateral TKA were approached. Eligible patients were aged between 50 and 80 years. Patients with any of the following were excluded from the study: poorly controlled Diabetes (HbA1C > 7.0), history of inflammatory arthritis, renal insufficiency (eGFR<90 mL/min per 1.73m^2), hypersensitivity to the study drug, prolonged QT interval in ECG and/or patients with history of knee infection were excluded from the study.

Pre-operative knee range of motion was documented. Patients were asked about the more painful knee pre-operatively. All patients received similar pre-operative medications which included 650 mg of oral Paracetamol and 100 mg of oral Gabapentin on the previous night of surgery and at 2 hours before surgery. All the patients received spinal anaesthesia with plain 0.5% Bupivacaine and 500 mg of systemic Tranexamic acid was given pre-operatively, and in addition three hours and six hours from the time of first dose.

Ropivacaine was the long acting local anaesthetic used in the cocktail along with Epinephrine to prolong its action. Clonidine being an alpha-2 receptor agonist acts

on C and Aδ fibers, and decreases the conduction to prolong the action of local anesthetic and also through vasoconstrictor effect which reduces the drug wash-out from perineural tissues. Ketorolac is the adjuvant NSAID in the cocktail.

All patients underwent single stage bilateral TKA. More painful knee was operated first and received methylprednisolone which was added to the peri-articular infiltration (study group: Group S). The second knee received peri-articular infiltration identical to the first except the methylprednisolone (Group C). The surgeries were performed by either of the two senior surgeons (MK or HW). All surgeries were performed under tourniquet control with a standard midline incision and a medial parapatellar arthrotomy. Posterior stabilized prosthesis was used in all patients and in none of the cases patella was resurfaced. Patellar osteophyte excision with circumferential denervation was done with diathermy. After preparation of the bony surfaces and just prior to cementation of the definitive TKA components the solution containing ropivacaine, clonidine , epinephrine, and ketorolac (details of dosage provided in table 1) with one ml of methylprednisolone(40 mg) was infiltrated in the peri-articular tissues using a standardized protocol in the first knee and similar procedure was repeated for the second knee with the infiltration used being identical to the first solution except methylprednisolone. Infiltrated sites in order being posterior capsule, medial and lateral meniscal bed, synovium, iliotibial band, collateral ligaments before cementing and quadriceps, retinaculum, patellar tendon after implanting the components. Tourniquet was released and haemostasis achieved before closing the joint. No drain was used.

DVT chemoprophylaxis included 40mcg of sub cutaneous low molecular weight heparin for five days post operatively followed by oral Rivaroxaban 10mg for fourteen days. Patients were also provided with below knee anti-embolism compression stockings to be used in the post-operative period for six weeks.

Patients were encouraged to stand with support on the same day of surgery and used ice packs to both the knees four times a day during their hospital stay. Patients received six hourly intravenous (IV) Paracetamol 1g along with twelve hourly IV Tramadol 50 mg and Diclofenac 75 mg post-operatively for the first 48 hours post-surgery. Later, PRN oral analgesics were prescribed (Paracetamol and tramadol). All patients received standard DVT chemoprophylaxis for first two week post-surgery.

Pain on movement was recorded separately for each knee as VAS (Score 0 -10; 0 - No pain; 10 - worst pain) at 24 hours and 72 hours post-surgery. Active range of motion (ROM) was measured with a goniometer on post-operative day one and day three. Time for straight leg raise in both lower limbs and appearance of any ecchymosis/inflammation were documented. Patients were assessed for any local (hypersensitivity reaction, infection, bleeding or tendon rupture) or systemic (cardiovascular issues, renal impairment, stroke) adverse events. All assessments were conducted by an independent blinded observer who was not a part of operating team. The assessor did not know the order in which surgeries were performed (or which knee received which peri-articular injection). The assessor asked questions about either knee in a random sequence. All patients were assessed at 2 weeks post-surgery, at one month and contacted a 6 months post-

surgery to check if they needed any further intervention or treatment for their bilateral TKAs. Methylprednisolone knee was identified with data in operative records showing the first operated knee.

Statistical analysis:

Baseline data, range of motion and VAS scores at first day and third day post-surgery were compared using paired T test. Categorical data was compared using chi-squared test. All analysis was performed using SPSS (IBM SPSS statistics version 20) with $p < 0.05$ deemed statistically significant.

Results:

Mean age of patients was 67 years (range: 53 - 82, SD 7.5) of which 13 were males and 37 were females. The two groups were well matched for pre-operative flexion deformity, further flexion and surgical time (table 2).

No patient died in the first six months post-surgery. No patient was lost to follow up and none of the patients needed any further intervention related to their replaced knees. At six months follow up none of the patients included in study had suffered from superficial or deep infection in either of the knees.

The mean VAS at 24 hours post-surgery was 2.9 (range: 1 - 6, SD 1.2) and 4.6 (range: 2 - 6, SD 1.0) for group S and group C respectively. The difference between the two groups was statistically significant ($p < 0.05$). The mean VAS at 72 hours post-surgery was 2.0 (range: 1 - 4, SD 0.9) and 3.5 (range: 1 - 6, SD 1.0) for group S and group C respectively. The difference between the two groups was statistically significant ($p < 0.05$).

The mean ROM at 24 hours post-surgery was 67^0 (range: 30^0 - 90^0, SD 13.7) and 55^0 (range: 30^0 - 80^0, SD 12.1) for group S and group C respectively. The difference between the two groups was statistically significant ($p < 0.05$). The mean ROM at 72 hours was 80^0 (range 50^0 - 100^0, SD 12.0) and 72^0 (range: 50^0 - 90^0, SD 12.0) for group S and group C respectively. The difference between the two groups was statistically significant ($p < 0.05$). Inflammatory signs (redness, edema and tenderness) were present in 9 knees with steroid infiltration compared with 17 knees without steroid. The difference was non-significant ($p > 0.05$). The mean time to achieve straight leg raise was 3.3 days (range: 1 - 4, SD 0.8) for group S as compared to 3.6 days (range: 2 - 4, SD 0.6) for group C. The difference between the two was non-significant ($p > 0.05$).

Discussion:

This study has shown that addition of 40 mg of methylprednisolone in the peri-articular infiltration for patients undergoing TKA is effective in terms of reducing pain at least for the first 72 hours post-surgery and also helps to regain knee flexion more quickly. It is the first study in patients undergoing simultaneous

bilateral TKA under the same anaesthetic using same surgical technique by the same surgeon comparing the use of steroid in the local infiltration.

Corticosteroid is an established post-operative pain control drug via systemic routes[11]. Intra articular use of corticosteroids in knee osteoarthritis management has been studied extensively both for benefits and complications[12, 13]. Studies related to periarticular use of the drug are limited. The aim of our study was to compare the effect of using a corticosteroid in periarticular infiltration solution with reference to its effect in post-operative pain control. This study compared the effect with periarticular infiltrations between the knees of same patient. This greatly reduced bias of the subjective difference in pain perception as it occurs of different patients. Many previous studies have shown the beneficial effects[14, 15, 16] of corticosteroid in the infiltration cocktail with some reporting complications[17] related to its use. Our study showed statistically significant improvement in VAS score and knee flexion on day one and three between two groups. The use of steroid in the infiltration helped patients achieve straight leg raise more quickly and the incidence of post-operative inflammation was less although the differences were not statistically significant.

The study[17] conducted by Christian P. Christensen et al. with two different groups for steroid and without steroid infiltration (steroid: 37 patients, no steroid: 39 patients) suggested that the addition of a corticosteroid to intraoperative periarticular injections does not provide benefit when compared with injections that do not contain a corticosteroid. They also reported complications like deep knee joint sepsis and requirement of manipulation under anaesthesia at nine

weeks post knee replacement surgery in steroid patients group. However our study did not encounter any such complications during the study period.

Sae Kwang et al. conducted a study[18] with 76 patients who underwent sequential bilateral TKA with an interval of three months between the two surgeries. In this study, one knee was randomly assigned to the steroid (40 mg triamcinolone acetonide) or non-steroid peri-articular infiltration group. After 3 months, the contralateral knee was assigned to the opposite group. Patients were assessed for nighttime pain, functional recovery [straight leg raising (SLR) ability and maximal flexion], patient satisfaction, and complications during the post-operative period. Authors reported significantly lower pain level in the steroid than the non-steroid group on the night of the operation (VAS, 1.2 vs. 2.3; p=0.021). No significant differences were reported in maximum flexion between the two groups although the authors did notice earlier ability to achieve straight leg raise in the steroid group. S. Tsukada et al. conducted a double blind randomized control study[10] with total of 77 patients. They noticed that the corticosteroid group had a significantly lower cumulative pain score than the no corticosteroid group during the first 24 hours after surgery (p = 0.024). The rate of complications, including surgical site infection, was not significantly different between the two groups up to one year postoperatively. In a study[19] conducted by Chia et al. they concluded that injecting steroid to the extensor mechanism has the risk of delayed tendon rupture. In our study also infiltration of steroid into extensor mechanism was avoided. Probably owing to that, post operatively no difference was noticed in number of days required by the patient to perform straight leg raising.

This study has certain limitations. Period of post-operative follow up is short and range of motion and pain scores beyond third day were not compared between two groups. As the effect of methylprednisolone is unlikely to last after 72 hours, we do not expect any difference in pain scores or ROM in the long-term although this needs to be proven. Although there were no complications in this specified period, long term follow up will be helpful for monitoring complications. In our practice, patients travel from far and wide and find it difficult to attend routine face to face follow up appointment. We did manage to communicate with all the patients to establish that none of them needed further intervention (either surgical or medical including use of oral antibiotics) for suspected infection in either of the replaced knees.

One key strength of this study is patients undergoing simultaneous bilateral TKAs for end-stage OA under the same anaesthetic by the same surgical team using identical technique and implants in both the knees. This has minimized the effect of potential confounders and allowed us to conduct a meaningful comparison.

Conclusion:

Addition of Methylprednisolone to periarticular infiltration cocktail in patients undergoing total knee arthroplasty has significant influence on reduction of pain in early postoperative period. It also helps patients to regain knee range of motion quickly and thus may help in reducing length of stay. Longer follow up is

required to assess if these advantages are maintained in the long-term and also if indeed any of the patients develop any possible complications.

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Tables:

Table 1: Periarticular infiltration cocktail

Details	Solution in ml used in each knee in patients with weight < 70 KGs	Solution in ml used in each knee in patients with weight ≥ 70 KGs
Ropivacaine (0.75%)	40	54
Clonidine(150mg/ml)	0.6	0.8
Adrenaline	0.3	0.3
Ketorolac(30 mg)	2	2
Normal Saline (0.9%)	57	63
TOTAL (Both Knees)	100 (50ml for each knee)*	120 (60 ml for each knee)*

* After preparation of the solution for peri-articular infiltration for each patient, the solution was divided into two equal parts. 40 mg of methylprednisolone was added to the first half of the solution which was used for the peri-articular infiltration in the first knee (Group S) and the second half of the solution was used for the peri-articular infiltration in the second knee (Group C).

Table 2: Preoperative FFD, flexion and operative tourniquet time comparison

Group	**Mean FFD in degrees (range, SD)**	**P value**	**Mean Flexion in degrees (range, SD)**	**P**	**Mean tourniquet time (Minutes)**	**P value**
Group S	7.8 (range: -5 to 30, SD 7.18)	0.44	107.2 (range:60 to 140, SD 16.66)	0.47	51.54 (range: 36 to 80, SD 10.24)	0.97
Group C	7.2 (range: -10 to 20, SD 5.72)		108 (range:70 to 140, SD 16.28)		51.48 (range: 38 to 70, SD 7.75)	

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