Analgesic requirement in first 24 hours following Total Knee Arthroplasty with or without Peri-articular Levobupivacaine Infiltration

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Received: 28 February, 2019
Accepted: 11 March, 2019
Published: 12 March, 2019

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Keywords: Knee arthroplasty; Local anesthesia; Morphine; Postoperative analgesia

Introduction

Total knee arthroplasty is a painful procedure [1,2], which requires significant postoperative analgesia. Good postoperative pain relief is essential for patient comfort as well as early rehabilitation. The pain management varies from patient to patient and some analgesics that would have adequate effect in one patient may not be suitable for the others.

Various different techniques have evolved over the years to provide adequate pain relief following the operation and to keep the side effects to minimum possible level. Some common methods in practice today are epidural infusion, systemic opioids including PCA pumps, NSAID administration, Peripheral nerve blocks and local anesthetic infiltration around the operation site at the time of surgery.

The efficacy of epidural analgesia has been proven but its use is not without problems. Its use is associated with side effects like spinal headache, respiratory depression, neurogenic bladder, hypotension [3] and rarely spinal hemorrhage and epidural abscess. Systemic administration of opioids in the various forms like PCA pumps, systemic injection or oral intake also provides good pain relief but in the elderly population its risks are significant like cardiorespiratory depression, constipation, confusion and allergic reaction etc. [4]. NSAIDs when used in postoperative period are usually required in significantly high doses and can potentially cause serious side effects including GI hemorrhage and renal dysfunction.

Significant interest has developed recently to infiltrate the operative site with local anesthetic agent to provide pain relief. Kohan and Ker in Sydney Australia developed an injection technique with a mixture of local anesthetic, NSAID and epinephrine, which they infiltrated intraoperatively, as well as postoperatively via a catheter [5]. Lombardi et al 2004, Reilly et al 2005, Anderson et al 2007 Parvataneni et al 2007 and Essving et al 2009 reported less requirement of breakthrough narcotics.
reduced risk of narcotic overdose, and reduced hospital bed occupancy with soft tissue local anaesthetic infiltration [6-10]. Busch et al 2006, Anderson et al 2008, and Venditelli et al 2006 reported in their randomized trials that LA infiltration provided effective pain relief comparable with peripheral nerve block despite variation in the LA infiltration technique [11-13]. However these trials did not show any evidence of shortening in the length of stay post operatively.

The primary outcome of our study was to observe the effect of intraoperative LA infiltration without postoperative infusion on analgesic requirement during the first 24 hours in patients undergoing primary total knee arthroplasty (TKA). We would also report on the length of stay of our patients who received LA infiltration vs no infiltration.

**Patients and Methods**

The study was carried out at a tertiary care elective orthopaedic unit. It involved retrospective analysis of case notes from 28 patients undergoing primary TKA. Age of the patients ranged from 47 to 84 years (mean 67.7). Patients were selected from two different consultant practices. Group A included 14 patients who had their TKA performed by surgeon A who did not use LA infiltration and Group B included 14 patients who underwent TKA with surgeon B who routinely injected LA intra operatively. Both surgeons used same medial parapatellar approach for TKA under tourniquet. There was no major variations in the surgical technique between the two surgeons. The local anesthetic agent used in all the cases was Levobupivacaine diluted with saline without epinephrine. The sites injected were posterior capsule, periarticular soft tissue and subcutaneous tissues. All patients had their procedure done under spinal anesthesia and all had received spinal morphine 150-200 micrograms (average: 187.49) as well (Table 1). Postoperatively the amount of morphine, paracetamol, diclofenac, tramadol and oxynorm used in first 24 hours was recorded. It also included the amount used intraoperatively in the operating room. The data was recorded at 6, 12 and 24 hours from the case progress notes. Visual analogue pain scale (VAS) was also recorded at 6, 12 and 24 hours. Length of stay was recorded from the progress notes.

Exclusions included patients undergoing revision knee arthroplasty or dependence upon any chronic pain medication.

**Statistical analysis**

All the data between the two groups was statistically analyzed using SPSS software. Initially the demographic details of the two groups were compared. Length of stay and age were measured on a continuous scale, and the unpaired t-test was used to compare the results. Gender was measured on a categorical scale, so Fisher’s exact test was used for the comparison of this variable.

The amount of analgesia used between groups was compared on a continuous scale. The statistical method used was dependent on the distribution of the outcome variables. If the outcomes were normally distributed, the unpaired t-test was used to compare between groups, whilst if the outcomes were not normally distributed, the Mann–Whitney test was preferred. T-test was used to compare the mean VAS between the two groups.

**Results**

Firstly, the demographics were compared between groups, and the results are summarized in the table 1. For length of stay and age the mean and standard deviation was presented for each group. The percentages of males and females were also presented.

The results suggested that the two groups did not vary significantly in terms of their age, gender or length of stay.

Table 1.2 contains the results for the variables, which were found to be approximately normally distributed (Paracetamol). The analysis of these variables was performed using the unpaired t-test and the figures presented are the mean, standard deviation and range in each group.

The results suggested that the two groups did not differ at 6 and 12 hours.

The two groups were also found to vary in terms of the amount of oxynorm used after 12 hours. Although the median value was 0 in both groups, reflecting the low usage of this drug, the data also suggested that 4 patients in the no anesthetic group used this drug after 12 hours, whilst no patients in the anesthetic group used this drug by this stage. The two groups

| Drug                  | No Anaesthetic Mean (SD) | Anaesthetic Mean (SD) | P-value |
|-----------------------|--------------------------|-----------------------|---------|
| Paracetamol – 6 hours | 1.3 (0.5) [1, 2]          | 1.5 (0.7) [0.2]       | 0.37    |
| Paracetamol – 12 hours| 2.3 (0.5) [2, 3]          | 2.2 (0.9) [0.3]       | 0.79    |
| Paracetamol – 24 hours| 3.4 (1.1) [2, 5]          | 3.2 (1.2) [1, 5]      | 0.63    |

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were not found to vary in the amount of oxynorm used at either 6 or 24 hours.

The mean VAS in the group without infiltration at 6, 12 and 24 hours was 4.57 (95% CI 3.56 to 5.57, SD 1.72), 6.07 (95% CI 4.97 to 7.16, SD 1.90) and 7.28 (95% CI 6.42 to 8.14, SD 1.49) respectively. The mean VAS in LA infiltrated group was 2.63 (95% CI 1.69 to 3.59, SD 1.64), 3.35 (95% CI 2.55 to 4.16, SD 1.39) and 5.85 (95% CI 4.87 to 6.84, SD 1.70) at 6, 12 and 24 hours respectively (Figure 1).

Discussion

Pain following total knee arthroplasty is significant. It varies in intensity from moderate to severe in 30-60% of patients. Good post-operative pain relief is essential for rehabilitation as well as for reduction for release of stress hormones. The pain may result from traumatized tissues around the operative site as well as from hyper-perfusion of tissues after the release of tourniquet. Ideal pain relief would be one that is applied intra as well as post operatively to ensure reduction of tissue hypersensitivity that often results due to surgical trauma at the operative site.

Pain management following knee arthroplasty can be divided in three phases. Phase 1 starts preoperatively with patient education and building confidence. Phase 2 is intraoperative and requires suitable anesthesia. Postoperative period is phase 3, which requires careful titration of analgesics to provide sufficient comfort as well as avoid adverse effects. During phase 3 the patients are most vulnerable to side effects of opiates like hypotension, respiratory dysfunction, over sedation, nausea, vomiting, urinary retention. These could be minimized by adequate infiltration of the local anesthetic agent intraoperatively at sites like posterior capsule, synovial membrane and subcutaneous tissue. Browne et al observed that the bolus injection of bupivacaine in subcutaneous tissue alone provided some pain relief and reduction in narcotic intake postoperatively but this finding did not achieve statistical significance [14]. Randomized trials conducted by Busch et al., 2006, Anderson et al 2008, Venditelli et al 2006 and Essving 2009 had shown good post-operative pain relief with LA infiltration [9, 11-13]. Its effect was comparable to other forms of analgesia like peripheral nerve block. Local anesthetics such as levobupivacaine block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve and by slowing the propagation of the nerve impulse, thus reducing the rate of rise of the action potential.

In our study we found that the use of morphine was approximately half in patients who received LA infiltration compared to the other group. Whereas the use of tramadol was almost 1/4th in the LA infiltrated group. This however was not observed with the rest of analgesics. The dose of LA used was constant in our study as same surgeon operated all the patients and almost similar amount was injected each time. LA solution used by previous authors contained a mixture of LA, NSAID and epinephrine whereas we used plain levobupivacaine. Despite the use of levobupivacaine alone we still found less consumption of morphine in the postoperative period.

Table 1.3: Morphin, diclofenac, tramadol and oxynorm requirement.

| Drug       | No Anaesthetic Median (IQR) [range] | Anaesthetic Median (IQR) [range] | P-value |
|------------|-----------------------------------|-------------------------------|---------|
| Morphine – 6 hours | 0 (0, 0) [0, 10] | 0 (0, 0) [0, 10] | 1.00    |
| Morphine – 12 hours | 0 (0, 0) [0, 20] | 0 (0, 0) [0, 20] | 0.72    |
| Morphine – 24 hours | 10 (10, 10) [0, 30] | 0 (0, 0) [0, 30] | 0.009   |
| OT Diclofenac | 0 (0, 75) [0, 75] | 0 (0, 75) [0, 75] | 0.78    |
| Diclofenac – 6 hours | 0 (0, 75) [0, 75] | 0 (0, 75) [0, 75] | 0.78    |
| Diclofenac – 12 hours | 0 (0, 75) [0, 75] | 0 (0, 75) [0, 150] | 0.69    |
| Diclofenac – 24 hours | 75 (75, 75) [0, 150] | 25 (0, 150) [0, 250] | 1.00    |
| Oxynorm – 6 hours | 0 (0, 0) [0, 0] | 0 (0, 0) [0, 0] | (*)    |
| Oxynorm – 12 hours | 0 (0, 10) [0, 10] | 0 (0, 0) [0, 0] | 0.03    |
| Oxynorm – 24 hours | 10 (0, 10) [0, 10] | 0 (0, 10) [0, 10] | 0.46    |
| Tramadol – 6 hours | 0 (0, 0) [0, 100] | 0 (0, 0) [0, 100] | 0.15    |
| Tramadol – 12 hours | 0 (0, 0) [0, 200] | 0 (0, 0) [0, 100] | 0.49    |
| Tramadol – 24 hours | 0 (0, 0) [0, 200] | 0 (0, 0) [0, 100] | 0.49    |

(*) No formal analysis possible, as values were zero for all patients in both groups.

Citation: Memon AR, Gul R (2019) Analgesic requirement in first 24 hours following Total Knee Arthroplasty with or without Peri-articular Levobupivacaine Infiltration. Open J Orthop Rheumatol 4(1): 001-004. DOI: http://dx.doi.org/10.17352/ojor.000017
Some authors have described early discharge from hospital in patients with LA infiltration [5]. However, we did not observe this in our study. Further review of the study by Kohan revealed that mostly younger patients following resurfacing procedures did benefit from early discharge from the hospital. Most of the orthopaedic population requiring joint replacement is elderly with multiple medical co-morbidities and require longer inpatient stays for various medical reasons.

We found no adverse incidents in our studied patients. However, due to small sample size a definite conclusion could not be drawn. The plasma concentration of levobupivacaine following therapeutic administration depends on dose and also on route of administration, because absorption from the site of administration is affected by the vascularity of the tissue. The use of tourniquet during knee arthroplasty is also associated with reactive hyperemia of tissues and may lead to increased systemic absorption of the drug. Consideration should also be given to patients with impaired liver function as levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or faeces. Most of the analgesic effect was observed at 6 and 12 hours postoperatively. The VAS showed statistically significant differences in pain scores during these times. However, at 24 hours postoperatively no such difference was observed. This will correlate well with the longer duration of action of levobupivacaine.

We are aware of the limitations of our study. As it was a retrospective study the information available was limited. Although same surgeon operated upon all the LA infiltrated patients, it is possible that some differences would have occurred at the site of infiltration of the LA agent. Although the total dose administered was constant but the amount infiltrated at any particular site would be different in different patients.

Despite above limitations it was obvious from our study that the administration of LA intraoperatively does decrease the postoperative morphine consumption. It thus reduces the side effects of narcotics like cardio-respiratory depression, urinary retention, pruritus, hypersensitivity reactions etc. It also has financial implications upon the unit. The use of PCA pumps incurs significant cost to the hospital and judicious use of LA infiltration intraoperatively could potentially replace the routine use of PCA pumps with a single shot of narcotic analgesic for break through pain.

References

1. Wang H, Boctor B, Verrier J (2002) The effect of single-injection femoral nerve block on rehabilitation and length of hospital stay after total knee replacement. Reg Anesth Pain Med 27: 139-144. Link: https://goo.gl/i3W34fV

2. Giuffre M, Asci J, Arnstein P, Wilkinson C (1991) Postoperative joint replacement pain: description and opioid requirement. J Post Anesth Nurs 6: 239-245. Link: https://goo.gl/Bd2weL

3. Shoji H, Solomonow M, Yoshino S, D’Ambrosia R, Dabezies E (1990) Factors affecting postoperative flexion in total knee arthroplasty. Orthopedics 13: 643-649. Link: https://goo.gl/CVKqfV

4. Pettinge KA, Wedel DJ, Cabanela ME, Weeks JL (1989) The use of epidural bupivacaine following total knee arthroplasty. Orthop Rev 18: 894-901. Link: https://goo.gl/nLjU7Jn

5. Kerr DR, Kohan L (2008) Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. Acta Orthop 79: 174-183. Link: https://link.springer.com/article/10.1177/000164700807900215

6. Lombardi AV Jr, Berend KR, Mallory TH, Dodds KL, Adams JB (2004) Soft tissue and intra-articular injection of bupivacaine, epinephrine, and morphine has a beneficial effect after total knee arthroplasty. Clin Orthop Relat Res 125-130. Link: https://goo.gl/Z3JmdA

7. Reilly KA, Beard DJ, Barker KL, Dodd CA, Price AJ, et al. (2005) Efficacy of an accelerated recovery protocol for Oxford unicompartmental knee arthroplasty—a randomised controlled trial 12: 351-357. Link: https://goo.gl/nM8sHi

8. Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Soballe K (2007) Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: a randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. Acta Orthop 78: 180-186. Link: https://goo.gl/W2PwuU

9. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, et al. (2009) Reduced hospital stay, morphine consumption, and pain intensity with local infiltration analgesia after unicompartamental knee arthroplasty. Acta Orthop 80: 213-219. Link: https://goo.gl/oYVQgb

10. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, et al. (2007) Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. J Arthroplasty 22: 33-38. Link: https://goo.gl/Ae8Edw

11. Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalder RW, et al. (2010) The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. Clin Orthop Relat Res 468: 2152-2159. Link: https://goo.gl/E4js9m

12. Vendittoli PA, Makenen P, Drolet P, Lavigne M, Fallaha M, et al. (2006) A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. J Bone Joint Surg Am 88: 282-289. Link: https://goo.gl/tTq5Sy

13. Andersen LO, Husted H, Otte KS, Kristensen BB, Kehlet H (2008) High-volume infiltration analgesia in total knee arthroplasty: a randomized, double-blind, placebo-controlled trial. Acta Anaesthesiol Scand 52: 1331-1335. Link: https://goo.gl/Rmuyr

14. Browne C, Copp S, Reden L, Pulido P, Colwell C Jr (2004) Bupivacaine bolus injection versus placebo for pain management following total knee arthroplasty 19: 377-380. Link: https://goo.gl/kjv79V