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Single intra-articular analgesic cocktail for immediate postoperative pain management following total knee replacement in a teaching hospital.

RP Olonisakin[1], PT Sotunmbi[1] and SS Adeoye[2]
Departments of Anaesthesia[1] and Orthopaedics[2], College of Medicine, University of Ibadan, Ibadan, Nigeria

Abstract

Background: Inadequate pain relief after Total Knee Replacement (TKR) could hinder early ambulation with increased morbidity and mortality. Several analgesic models had been deployed with varying outcomes with recent evidence in favor of addition of peri or intra-articular infiltration of analgesic cocktail as part of the multimodal analgesia.

Objective: We prospectively compared the effectiveness of a single intra-articular analgesic cocktail with epidural analgesia on the immediate postoperative pain management in TKR patients.

Method: Following institutional ethical clearance and consent from patients, 20mls of 0.5% plain bupivacaine, 10mg of morphine, and 1mg of Adrenaline constituted into 50ml was given intra-articularly (l_A) to first 7 of the 22 patients, ASA II, aged 47-82 years, who had TKR. 15 patients had Epidural (E_p) top ups of 6ml of 0.1% plain bupivacaine. Pain was assessed. Opioid use, complications and length of hospital stay were documented. Data was analyzed. Non parametric test was used to test for significance with p value < 0.05.

Results: The mean Numerical Rating Scale (NRS) values I_A vs Ep. were 3.1 ± 0.37, 3.2 ± 0.69, 3.4 ± 0.53, 3.4 ± 0.53 at 4hrs, 12hrs, 24hrs and 48hrs vs 4.2 ± 0.47, 4.8 ± 0.58, 3.7 ± 0.49 and 3.5 ± 0.51 with $p < .05$ at 4hrs and at 12hrs. There was no significant difference in the opioid use with the percentage having opioid related complications comparable in both groups; the length of hospital stay was, however, not significant.

Conclusion: Single intra-articular analgesia, as part of the multimodal analgesia, was effective in the immediate postoperative pain management in TKR patients, where early ambulation and rehabilitations were key to successful outcome.

Keywords: *Intra-articular cocktail analgesia, immediate postoperative pain management, Total Knee Replacement.*

Correspondence: Dr. R.P. Olonisakin, Department of Anaesthesia, College of Medicine, University of Ibadan, Ibadan, Nigeria. E-mail: polonisakin@gmail.com

Résume

Contexte : Un soulagement inadéquat de la douleur après une arthroplastie totale du genou (TKR) pourrait entraver la marche précoce avec une morbidité et une mortalité accrues. Plusieurs modèles analgésiques avaient été déployés avec des résultats variables avec des preuves récentes en faveur de l'ajout d'une infiltration péri ou intra-articulaire de cocktail analgésique dans le cadre de l'analgésie multimodale.

Objectif : Nous avons comparé prospectivement l'efficacité d'un cocktail analgésique intra-articulaire unique avec l'analgésie péridurale sur la gestion de la douleur postopératoire immédiate chez les patients PTK.

Méthode : Après autorisation éthique institutionnelle et consentement des patients, 20 ml de bupivacaïne simple à 0,5 %, 10 mg de morphine et 1 mg d'adrénaline constitués dans 50 ml ont été administrés par voie intra-articulaire (lA) aux 7 premiers des 22 patients, ASA II, âgés de 47 ans. -82 ans, qui avait TKR. 15 patients ont eu une recharge épidurale (Ep) de 6 ml de bupivacaïne simple à 0,1 %. La douleur a été évaluée. L'utilisation d'opioïdes, les complications et la durée d'hospitalisation ont été documentées. Les données ont été analysées. Un test non paramétrique a été utilisé pour tester la significativité avec une valeur $p < 0,05$.

Résultats : les valeurs moyennes de l'échelle d'évaluation numérique (ENR) IA vs Ep. étaient de $3,1 \pm 0,37$, $3,2 \pm 0,69$, $3,4 \pm 0,53$, $3,4 \pm 0,53$ à 4h, 12h, 24h et 48h vs $4,2 \pm 0,47$, $4,8 \pm 0,58$, $3,7 \pm 0,49$ et $3,5 \pm 0,51$ avec $p < 0,05$ à 4h et à 12h . Il n'y avait pas de différence significative dans l'utilisation d'opioïdes avec le pourcentage de complications liées aux opioïdes comparables dans les deux groupes ; la durée d'hospitalisation n'était cependant pas significative.

Conclusion : L'analgésie intra-articulaire unique, dans le cadre de l'analgésie multimodale, s'est avérée efficace dans la prise en charge immédiate de la douleur postopératoire chez les patients atteints de PTG, où la déambulation et les rééducations précoces étaient la clé du succès.

Mots clés *: Analgésie cocktail intra-articulaire, prise en charge immédiate de la douleur postopératoire, arthroplastie totale du genou.*

Introduction

Postoperative pain management following Total Knee Replacement has been a challenge to both the care givers and the patients. Patients suffer from severe pain, edema, and spasms in the early postoperative period after total knee arthroplasty operations with increased morbidity and mortality. Adequate pain relief has a considerable role in patients' recovery, early start of physiotherapy, which is key to successful outcome, and reducing hospital length of stay [1,2].

Balancing this need for early mobilization with the use of strong opioids and its consequent side effects has made the management of the postoperative pain for these patients a serious challenge. Several analgesic models had been deployed with varying outcomes. Modalities such as oral NSAID, Opioids administrations, Epidural and Femoral Nerve blocks, with more recent use of peri and intra-articular injections of analgesic cocktail had been popularized [3].

These modalities, either used singly or in combination, they all have their advantages and drawbacks with the current evidence in favour of peri and intra-articular analgesics injection as part of the multimodal approach. Agents such as local anaesthetics, vasoconstrictors, steroids, opioids and NSAID have been used in various cocktails for the intraarticular injections, giving either in continuous infusion through catheter over 24 to 48 hours or as a single large volume bolus dose [4,5]. With the resuscitation of the procedure (TKA) in our centre in collaboration with the experts both locally and abroad. We compared the effectiveness of a single small volume of analgesic cocktail given intra-articularly with epidural top ups in controlling pain in the immediate post-operative period following Total Knee Replacement in Ibadan.

Material and method

It was a prospective, non-randomized experimental study. After institutional ethical clearance and consent obtained from the patients. The study took place in UCH, main theatre between June 2015 –June 2018. All the patients that met the orthopaedic criteria were further evaluated for anaesthetic fitness. Twenty-two patients, who had unilateral severe osteoarthritis belonging to ASA II, aged 47 - 82years were recruited. Patient with allergic history to opioid, local anaesthetic agents, or with bleeding disorder were excluded. Those with severe spine deformities and obesity > 35kg/m² were also excluded. They were placed into intra articular and epidural groups based on the lead surgeon2 s preferred technique for post-operative pain management.

All patients were premedicated with oral lorazepam 3mg a night before the surgery. They all had 2 wide bore cannula, each on the dorsum of the hand. They were all pre – loaded with 500ml – 1000ml of 0.9% Normal Saline. They all had i.v cefuroxime 1.5g and i.v tranexamic acid 10mg/kg. All patient had multiparameter monitors for monitoring: NIBP, Oxygen Saturation, ECG and Temperature.

Combined Spinal Epidural were instituted for all the patients at L3 –L4 interspace at sitting position by Consultant Anaesthetist on the list. The epidural space was accessed with 18 touhy needle using loss of resistance to air, and after a negative test dose of 4mls lidocaine with adrenaline, a 26G pencil point spinal needle was introduced through the touhy needle and pierced the dura with free flow of CSF. Spinal Anaesthesia was effected with a dose of 3ml (5mg/ml) hyperbaric bupivacaine and 25mcg of fentanyl. Patients lied supine immediately and sensory level assessed with pin prick. Surgery were allowed to commence at sensory level T6/T8. Hypotension were corrected with fluids with or without vasoconstrictors. Blood was also transfused intraoperatively if need be.

The first 7 consecutive patients were operated with a leading expert from Germany who preferred intra-articular injections for post-operative pain control (Intra-articular group I_A), while the remaining 15 patients were operated with a leading expert from UK who preferred epidural injections (Epidural group E_p). However, the same surgical method was followed using the standard medial parapatellar approach. A tourniquet above the knee was used in all the patients. The I_A group received intra- articular cocktail of 20ml of 0.5% plain bupivacaine, 1mg of Adrenaline and 10mg of morphine with 28ml of water for injection added to make a total of 50ml. This was injected intra-articularlly before the closing of the capsule. At the end of the surgery, following the last suture all the patients were given 6ml of 0.1% plain bupivacaine through the epidural catheter. The catheter was removed for the group I_A.

At High Dependency Unit (HDU), dedicated for pooling the patients and also to minimize the risk of cross infection from the recovery room patients, the analgesic protocol was: i.v Paracetamol 600mg 8hrly, i.m Diclofenac 75mg 12hrly, i.m pentazocine

30mg prn and also for breakthrough pain. The second group (E_p) with epidural catheter retained received 6ml of 0.1% plain bupivacaine if pain score is > 4 by the anaesthetist on call who assessed the pain with Numerical Rating Scale (NRS) 2 hourly and documented any complication, and also available during the scheduled physiotherapist visit.

The Pain score done with NRS at the following "points in time" were recorded

- 1 TO - Arrival at HDU
- 2 T1 - At straight leg raise @ 4hrs postoperative
- 3 T2 - At Walking Assisted (Walker) @ 12hrs postoperative
- 4 T3 - At 24hrs postoperative
- 5 T4 - At 48hrs post-operative.

All patients were discharged from the HDU after 24 hours postoperatively and then placed on syrup morphine 5ml (5mg) 4-6hrly. (Pentazocine was discontinued and epidural catheter was removed) They continued rehabilitation in the wards. All the patients were followed up until 48hours postoperative. The level of satisfaction was assessed by simple yes or no scale. Length of hospital stay was also noted.

Statistical analysis of data obtained was carried out with the SPSS version 20 Windows software program. Mean ± SD, range, percentage and tables were used to present the data. Non-parametric test was used to compare the two groups, Chi-Square or Fisher's Exact test for categorical variable and Mann- Whitney U test and unpaired t-test for continuous variable. P value < 0.05 was considered significant.

Results

Both groups were comparable in demographics. The age range was 47 - 82 yrs, with female preponderance in both groups. The mean age for I_A group was 66 yrs and 65.5yrs for E_p. group.

Table1: Demographics: Values are in numbers, mean and (range)

	Intra-articular Grp (n = 7)	Epidural Grp (n=15)
Gender: M/F	2/5	3/12
Age (yr.) (mean)	66	65.5
(range)	(57 -82)	(47 – 75)
ASA Physical status I / II	1 / 6	5 /10
Length of stay (mean)	5.8	6.0
(range)	(5-7)	(5 -7)

There was no significant difference in the operative condition for both groups in terms of the estimated blood loss (EBL) and the duration of the surgery (DOS)

Table 2: Operative condition

	Intra articular (7)	Epidural (15)	U - test value	p-value
Age	14.57/102.00	12.39/223.00	52.00	0.504
EBL	13.07/91.50	12.97/233.50	62.50	0.975
DOS	13.64/95.50	12.75/299.50	58.5	0.784

The pain scores in the High Dependency Unit (HDU) were lower in the Intra-articular group with significant difference in the first 12 hours postoperatively.

Table 3: Pain assessment using NRS

	Intra articular (7)	Epidural (15)	P-Value
Mean Pain score ± SD @ 4HRs	3.1 ± 0.37	4.2 ± 0.47	0.00
Mean Pain Score ± SD @12HRs	3.2 ± 0.69	4.8 ± 0.58	0.003
Mean Pain Score ± SD @24HRs	3.4 ± 0.53	3.7 ± 0.49	0.078
Mean Pain Score ± SD @48Hrs	3.4 ± 0 .53	3.5 ± 0.51	0.50

There was no significant difference in opioid consumption and the length of hospital stay in both groups

Table 4: Opioid consumption, Length of Hospital stay

	Intra-articular (7)	Epidural (15)	U test value	p - value
Pentazocine Mean Rank/sum of ranks	12.50/87.50	13.19/237.50	59.50	0.818
Morphine Mean Rank/sum of ranks	16.21/113.50	11.75/211.50	40.50	0.150
LOSMean Rank/ sum of ranks	12.79/83.00	13.08/242.00	61.50	0.900

Discussion

This study compared the effectiveness of two modalities for postoperative pain management for patients who had TKA: Intraoperative intra-articular analgesia and epidural analgesia (I_A & E_p)

The I_A group had lower pain scores with significant difference at 4hrs, 12hrs postoperatively, and were able to mobilize at these points in time, this

Table 5: Complications/level of satisfaction values in number, frequency (%)

Time	Complications	Intra articular n=7	Epidural n=15	P value
0-24hrs	•Nausea	0	0	-
	•Vomiting	0	0	-
	•Sedation	0	0	-
	•Itching	0	0	-
	•Hypotension	1 (14.28%)	1 (6.6%)	0.49
	•Muscle weakness	0	12 (805)	0.0052
	•Urinary Retention	0	6 (40%)	0.037
Level of satisfaction		6 (85.71)	2 (13.3%)	0.001
24-48hrs	•Nausea	1 (14.28%)	2 (13.3%)	1.000
	•Vomiting	1 (14.28%)	2 (13.3%)	1.000
	•Sedation	2 (28.57%)	6 (40.0%)	1.000
	•Itching	0	1 (6.6%)	1.000
	•Hypotension	-	-	
	•Muscle weakness	-	5 (33.3%)	
	•Urinary Retention	-	-	
Level of satisfaction		2 (28.57%)	6 (40.0%)	0.659

enabled early rehabilitation which study has shown to be an independent factor in influencing positively the outcome of TKA [2]. Early joint movements post-operative has been identified to be key in improving outcome and reducing morbidity and mortality [2,3]. The pain relief experienced by the intra articular group allowed this to be possible during the commencement of physiotherapy. It was noted that the patients that had epidural analgesia recorded significantly higher pain scores, they attempted to mobilize, but could not commence rehabilitation in the HDU, with many complaining of weakness of the lower limbs at these "point in time".

Following the study of Kerr and Kohan [6] who first observed reduced pain scores, opioid use and early mobilization postoperatively by the patients who had intraoperative intra-articular injection during knees and hip surgery and similar outcome reproduced in another study by Andersen et al [7] in TKA patients, various adjuvants with different components and volumes had been made into a cocktail. Additives such as epinephrine, ketorolac, clonidine, opioid, steroids have been added. The combinations in this study was 100mg bupivacaine, 1mg epinephrine and 10 mg morphine with outcome comparable with other studies [6,7].

The impact of the cocktail in this study extended to 12 hours. Studies [5,8,9] that used higher volume or repeated boluses through indwelling intra articular catheter, had significant impact extended to 48 -72 hrs. However, the issues of infection/delayed wound healing with the use of indwelling catheter is shifting the pendulum in favour of single injection which was deployed in this study.

To our knowledge, this is the first study that used a low volume (50ml) cocktail with outcomes comparable to other studies [8,9] where high volume: 100ml (250mg ropivacaine, 0.5mg epinepherine, 30mg ketorolac 80mcg clonidine) and 150ml {300mg Ropivacaine, 30mg Ketorolac, 5mg Morphine, 0.5mg Epinepherine} cocktails were used. The concern of the possible toxic effect on the chondrocytes with high volume is also making the use of single low volume gain popularity.

The mode of actions of these drugs are local with addition of epinephrine helping to keep the drugs at the site and also prevent possible systemic toxicity of LAs. It is also now well established that opioid receptors are not only centrally present but are also present peripherally particularly following inflammation, and that employing it locally could be more effective than systemic administration as side effects are much reduced [10]. The future of postoperative pain management is procedure/site specific analgesic modalities [10].

Although there was no significant difference in the opioid use and length of hospital stay over the study period, The I_A group recorded less side effect in HDU and level of satisfaction was significant in the first 24hrs. This study also corroborated the drawbacks with the use of epidural analgesia for postoperative in TKA patients [11], the group had more of patients who experienced weakness of the lower limbs, the non-operated limb inclusive and

urinary retention in the early postoperative period and could not ambulate early.

Although, we were lacking in the ideals for postoperative pain management such as availability and use of Patient Controlled Analgesia (PCA) our patients still benefited from multimodal approach to managing their immediate postoperative pain following TKA with the use of intra-articular injection of analgesic cocktail, epidural analgesia, systemic analgesics and oral morphine and the length of stay in the hospital was comparable to other established centers with high technologic analgesia [10,11].

Conclusion

The analgesic cocktail of local anaesthetic agent, vasoconstrictor and morphine given as a single bolus intra-articularly at the end of surgery impacted significantly on the pain scores and other favourable outcomes essential for the success of TKA in the immediate postoperative period.

It is an effective and safe anagesic modality for our environment. Simple and promotes collaboration with the surgeons who actually injected the intra-articular space. It was also observed that it was less intensive in terms of personnel involvement in the immediate postoperative period.

Recommendations

As we still grapple with facilities and personnel for high technology analgesic modalities in our environment, the use of this modality of analgesia is recommended for TKA patients for the immediate postoperative pain management.

Limitations

- Bias because of single blinded nature of the study
- The need to have a randomized controlled study as lead surgeons' preference for a particular modality of analgesia affected our randomization.

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