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Intraoperative Cocktail Injection for Pain Management after Total Knee Replacement

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Abstract: ***Background: Postoperative pain control following total knee replacement is still a big task for early postoperative rehabilitation. Our study was performed to evaluate the outcome of periatricular cocktail injection in patients undergoing TKR with respect to pain and knee motion recovery postoperatively. Method: 80 patients who underwent simultaneous bilateral TKR were included in this study and received intraoperative periarticular cocktail injection in right knee (intervention) while left knee serves as control. Postoperative pain was recorded using VAS for knee. Result: Right knee had significantly less pain as compared to left knee and has shorter period for postoperative 90 degree of knee flexion. Conclusion: Periarticular cocktail injection significantly reduces pain and early knee motion is possible.***

Keywords: Total Knee Replacement, cocktail injection, Visual Analog Scale, periarticular, cruciate substituting

1. Introduction

Total knee replacement (TKR) is gold standard surgical treatment for advanced or end stage osteoarthritis of knee, but the promising postoperative pain management is still controversial[1, 2, 3]. Approximately 60% of the patients experience severe pain following TKR and approximately 30% patient's experience moderate pain[4]. This is due to severe soft tissue dissection and trauma involved; TKR is one of the most painful surgical procedures known. Failure in postoperative pain management inhibits early rehabilitation of the knee joint. This can cause quadriceps muscle spasm, capsular contractures and muscular atrophy, which cause further pain[1].

Pain control can be achieved by multiple ways, but they all have some undesirable side effect, risks and benefits. Epidural anesthesia is one of the most commonly demanding techniques for pain control following TKR, but it requires patients monitoring for hypotension, nausea, vomiting and it hinders the early mobilization of patients which increases the chances of Deep Vein Thrombosis (DVT) and pneumonia[5]. Administration of opioids intravenously (IV) postoperatively increases the chances for hypotension, cardiac arrest, nausea, vomiting, drowsiness, respiratory depression, urinary retention and constipation[3, 6, 7]. Nerve block has the chances of injuring neurovascular structures, infection, hematoma formation and failure of block effect[7].

Various studies about cocktail intraoperative injection reported good results in pain management by controlling local pain pathway and knee receptors. It has the advantage of minimizing the pain, minimum side effect and not causing motor blockade[8, 9]. Various drug combinations are being used in various centers such as bupivacaine, ropivacaine, ketorolac, morphine sulfate, epimorphine, methylprednisolone, epinephrine, cefuroxime and normal saline[10 - 15].

Our study aims to compare the pain management scores between both the knees of patient who underwent bilateral TKR in one sitting. Intraoperative periarticular cocktail injection was given in right knee (intervention) and normal saline in left knee (control). In our cocktail we used bupivacaine, methylprednisolone, cefuroxime and normal saline. Postoperatively pain scores of both the knee were compared.

2. Material and Methods

We included 80 patients who went simultaneous bilateral TKR from 2019 to 2021 in our institute. All included patients were operated under spinal anesthesia. Exclusion criteria: rheumatoid arthritis, allergy to drugs we are using, impaired liver or renal function test, diabetes and unable to administrate spinal anesthesia. Full understanding for 10 point Visual Analog Scale (VAS) was given to all the patients.

Antibiotic prophylaxis of injection cefuroxime 1.5gm was given 20 – 30 minutes before incision. After the induction of spinal anesthesia 1gm of injection tranexamic acid was given, patient was catheterized, bilateral lower limb was scrubbed and shifted to operation theater. Lower limb was then prepared and draped. Anterior midline incision, medial Para patellar arthrotomy approach was used for surgery.

For all patients cocktail injection was given in right knee and left knee was used as control. Cocktail consists of: injection bupivacaine 0.5% 20ml, methylprednisolone 2ml, cefuroxime 1.5 gm, normal saline 10ml. It's then infiltrated at the following sites: medial retinaculum, lateral retinaculum, medial collateral ligament and capsular attachment, lateral collateral ligament and capsular attachment, patellar tendon, posterior capsule and quadriceps muscle.

In postoperative period systemic analgesic was used injection diclofenac 75mg and injection tramadol 100mg. for DVT prophylaxis injection clexane 0.6 subcutaneous once daily was used. Patient was mobilized same day once the effect of spinal anesthesia completely goes away and routine isometric exercises were started.

Postoperatively pain in both the knee was recorded using VAS at 6, 12, 24 and 48 hours and then once daily till 4th day. Data obtained is then tabulated and analyzed using SPSS - 17 of Microsoft. Statics was reported as mean and standard deviation. Unpaired t test was used to test the statistical association between the intervention and control.

We used repeated measures analysis of variance for analyzing the change in pain scores in the same knee during the follow - up. Post hoc test was conducted to assess the presence of any statistical significance between the 2 time points.

3. Result

It was found that intraoperative cocktail injection reduces the pain after TKR, as local anesthesia may have attenuated or blocked nociception. The cocktail also helped in increasing early range of motion in right knee as compared to left knee. A total of 80 patients were included in our study. The demographic data of patients were tabulated in **Table - 1**.

Table 1: Demographic data

Demographic Data	*Mean*
Mean age (in years)	64.7
Mean weight (in kg)	81.5
Gender (male, female)	47, 33
Type of deformity	
Varus	76
Valgus	1
Neutral	3
Type of implant	Cruciate substituting

The VAS score at 6, 12, 24 and 48 hours and on 3rd and 4th day in both the knees were tabulated in **table - 2**. When right knee (intervention) is compared to left knee (control), there is statistically significant reduction in VAS score in right knee at 6, 12, 24 and 48 hours (P<.001). However the difference in the mean VAS score in between both the knees at 3rd (P =.685) and 4th (P =.252) day were not significant.

Table 2: Between group comparison

Postoperative duration	Group	Mean	Standard deviation	Standard error mean	P value
6 h	Control Intervention	3.74 1.97	1.928 1.407	.194 .142	<.001
12 h	Control Intervention	3.18 1.84	1.771 1.372	.177 .138	<.001
24 h	Control Intervention	2.63 1.59	1.362 .655	.137 .066	<.001
48 h	Control Intervention	2.35 1.14	1.057 .826	.107 .083	<.001
3 d	Control Intervention	1.23 1.17	1.051 1.033	.106 .104	.685
4 d	Control Intervention	1.11 .96	1.011 .822	.102 .083	.252

Time taken for 90 degree knee flexion in intervention and control knees was 1.71 and 2.83 days respectively. The difference was found to be statistically significant (P <.001). There was a significant difference in pain score within the intervention group over different time intervals **table - 3**. Post hoc analysis showed no significant difference at various time intervals in day 1st (6, 12, 24 hours). However there is significant difference in pain score at 48 h (P <.001), 3rd day (P<.001) and 4th day (P <.001), when compared to 24 hour score. Statistically significant improvement in VAS score was found only after 3rd day (P <.001) and 4th day (P <.001), compared with the 24 hour value.

Table 3: Within group repeated measure ANOVA

Group	Mean	Standard deviation	N	P value
Control				
6 h	3.74	1.928	80	<.001
12 h	3.18	1.771	80	
24 h	2.63	1.363	80	
48 h	2.35	1.057	80	
3 d	1.23	1.051	80	
4 d	1.11	1.011	80	
Intervention				
6 h	1.97	1.407	80	<.001
12 h	1.84	1.372	80	
24 h	1.59	.655	80	
48 h	1.14	.826	80	
3 d	1.17	1.033	80	
4 d	.96	.822	80	

ANOVA: Analysis of Variance

4. Discussion

Trauma to the tissue during TKR exaggerates neurological response to pain by reducing the threshold of nociceptive neurons and by central sensitization of excitatory neurons which leads to increased postoperative pain[15]. Our study revealed that after TKR there was significant pain relive in right knee as compared to left knee in first 48hours and also early rehabilitation.

The use of analgesic cocktail was to facilitate contraction of smooth muscle that lines the arterioles to potentially minimize intraarticular bleeding and prolong the time the agents would act locally. The component methylprednisolone in cocktail is especially conspicuous in this[7, 8, 15, 16].

In study of Badneret al[17], addition of an opioid like morphine in the periarticular cocktail mixture did not provide any significant advantage when compared to cocktail mixtures without opioids with respect to postoperative pain relief[18]. In accordance with their study, our study also excluded the use of opioids in the cocktail mixture.

In study of Christensen et al[19], addition of steroid to periarticular cocktail injection only reduced the length of hospital stay in patients undergoing TKR. It did not improve the pain relief or early postoperative ROM. They also posed an increased risk of postoperative infection[19, 20]. Although the existing randomized controlled trials have confirmed the safety of steroids, many surgeons still hesitate to use a drug which is thought to increase the risk of catastrophic complications such as infection and patellar tendon rupture[17, 21 - 23].

Immediate postoperative pain control by various authors is found to be promising. A study by Mullaji et al[24]used bupivacaine, fentanyl, methylprednisolone, and cefuroxime as their cocktail. Badneret al[17]used a combination of bupivacaine and epinephrine. Andersen et al[25]used subcutaneous ropivacaine, and Vaishya et al[26]used bupivacaine, adrenaline, morphine, ketorolac, and gentamycin. All of them show significant pain relief, increased early postoperative knee movements, and quadriceps function postoperatively.

As our study compared the results of both knees of the samepatient, the rehabilitation regime and systemic medications postoperatively (including antiinflammatories, analgesics, and antibiotics) will be same for both knees of a particular patient, thereby eliminatingthese confounding factors during the comparison. We injected the cocktail in already mentioned zones, which was similar to George et al[27].

The only difference was injecting cocktail in ACL and PCL as we used cruciate sacrificing implant.

In our study, cocktail injection was given in a periarticular manner. There was a significant reduction in pain postoperatively (by VAS) which was recorded overthe right knee where the cocktail injection was givenand compared withthe opposite side at 6, 12, 24, and 48 hours (P <.001). This was incomparison with the study by Fu et al[4]which showed VAS scoreat rest was significantly lower at 6, 10, 24, and 36 hours postoperatively in the trial group compared with the control group, although the difference was insignificant at 24 hours postoperatively, and at days 2, 7, and 15 between the 2 groups. VAS score during activity was also lower in the trial group at 24 and 36hours postoperatively than that in the control group, although the difference was insignificant at days 2, 7, and 15[4, 12]. Busch et al. noted that patients who received a periarticular intraoperative injection containing ropivacaine, ketorolac, epimorphine, and epinephrine used significantly less PCA during the first 24 hourspostoperatively[15]. Vaishya et al[26], in their study comparing 2groups of 40 knees each, reported that the cocktail injected patients reported significantly less PCA and postoperative pain recordings at 6, 24, 48, and 72 hours after TKR.

As with all other studies, our study also has few limitations in it. Patients included belongs to particular time frame, infiltration of normal saline to control site could initiate pain mechanically even though we presumed normal saline has no pharmological effects, optimal concentration of the individual components of cocktail could not be determined. This study was not attempt at evaluating long term clinical outcome of patients.

5. Funding

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6. Conflict of Interest

None declared.

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