Intra-articular Morphine and Ropivacaine Injection Provides Efficacious Analgesia As Compared With Femoral Nerve Block in the First 24 Hours After ACL Reconstruction

Results From a Bone–Patellar Tendon–Bone Graft in an Adolescent Population

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Background: Opioid consumption and patient satisfaction are influenced by a surgeon's pain-management protocol as well as the use of adjunctive pain mediators. Two commonly utilized adjunctive pain modifiers for anterior cruciate ligament (ACL) reconstruction are femoral nerve blockade and intra-articular injection; however, debate remains regarding the more efficacious methodology.

Hypothesis: We hypothesized that intra-articular injection with ropivacaine and morphine would be found to be as efficacious as a femoral nerve block for postoperative pain management in the first 24 hours after bone–patellar tendon–bone (BTB) ACL reconstruction.

Study Design: Cohort study; Level of evidence, 3.

Methods: Charts were retrospectively reviewed for BTB ACL reconstructions performed by a single pediatric orthopaedic surgeon from 2013 to 2019. Overall, 116 patients were identified: 58 received intra-articular injection, and 58 received single-shot femoral nerve block. All patients were admitted for 24 hours. Pain scores were assessed every 4 hours. Morphine milligram equivalents (MMEs) consumed were tabulated for each patient.

Results: Opioid use was 24.3 MMEs in patients treated with intra-articular injection versus 28.5 MMEs in those with peripheral block ($P = .108$). Consumption of MMEs was greater in the intra-articular group in the 0- to 4-hour period (7.1 vs 4.6 MMEs; $P = .008$). There was significantly less MME consumption in patients receiving intra-articular injection versus peripheral block at 16 to 20 hours (3.2 vs 5.6 MMEs; $P = .01$) and 20 to 24 hours (3.8 vs 6.5 MMEs; $P < .001$). Mean pain scores were not significantly different over the 24-hour period (peripheral block, 2.7; intra-articular injection, 3.0; $P = .19$).

Conclusion: Within the limitations of this study, we could identify no significant difference in MME consumption between the single-shot femoral nerve block group and intra-articular injection group in the first 24 hours postoperatively. While peripheral block is associated with lower opioid consumption in the first 4 hours after surgery, patients receiving intra-articular block require fewer opioids 16 to 24 hours postoperatively. Given these findings, we propose that intra-articular injection is a viable alternative for analgesia in adolescent patients undergoing BTB ACL reconstruction.

Keywords: anterior cruciate ligament; ACL reconstruction; human; intra-articular injection; morphine milligram equivalents; peripheral nerve block; pain

The intra-articular use of the analgesic opioid morphine in the setting of knee arthroscopy first rose to prominence in 1991 after Stein et al[26] demonstrated an improved reduction in postoperative pain. This seminal study established that local administration of morphine confers advantages as regards length of effect and safety. In a follow-up study, Brandsson et al[1] showed that intra-articular injection of morphine has relatively minimal systemic absorption, reinforcing the idea that morphine can act locally at the level of the peripheral nerves. Additionally, intra-articular morphine has been shown clinically to improve pain scores and decrease the need for supplemental postoperative

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narcotics, with enhanced efficacy when used in combination with local anesthetics for patients undergoing anterior cruciate ligament (ACL) reconstruction.[13,16,24,27,30,32]

Despite these benefits, the intra-articular injection of morphine fell out of favor with the rise of peripheral nerve blocks. Early literature indicated that peripheral nerve block was more efficacious; however, these studies were limited by the use of continuous peripheral nerve blocks and the absence of morphine in their intra-articular injection cocktail.[7,10,15] Furthermore, these studies did not take into account the increased cost of peripheral nerve block relative to intra-articular injection or the associated risks thereof, including muscle weakness and local anesthetic-induced myotoxicity.[5,8,11] More recent data have highlighted the potential strengths of intra-articular injection over single-shot peripheral nerve block, regardless of the choice of femoral or adductor nerve blockade.[9,18,23,25]

Despite this changing tide, there is a paucity of literature comparing intra-articular injection with peripheral nerve block in the pediatric population in the first 24 postoperative hours. Furthermore, few studies have monitored pain scores and morphine milligram equivalent (MME) consumption in an inpatient setting for a 24-hour period. We sought to compare the outcomes of pediatric patients who underwent bone–patellar tendon–bone (BTB) ACL reconstruction and were treated with either a single-shot femoral nerve block injection of ropivacaine, dexamethasone, and dexmedetomidine or an intra-articular injection of ropivacaine and morphine for the management of postoperative pain in the first 24 hours postsurgically. To our knowledge, this is the first study to compare these cocktails and their utility in the pediatric population. Our hypothesis was that the intra-articular injection would be as efficacious as a femoral nerve regional block injection for postoperative pain management in the first 24 hours.

METHODS

This was a cohort study utilizing the electronic medical record to retrospectively review charts of patients treated with ACL reconstruction by a single surgeon (H.G.C.) at a single institution between January 2013 and December 2019. Patients remained hospitalized postoperatively for 24 hours, while opiate administration and subjective pain scores were recorded at 4-hour intervals. Patients were provided 650 mg of acetaminophen every 6 hours in the postoperative setting. Oxycodone (5 mg) was prescribed as needed with the indication of a subjective pain score >3 of 10. If pain persisted to ≥7 of 10 at 1 hour after oxycodone administration, a 1-mg intravenous dose of morphine was provided.

Before August 2016, all patients undergoing ACL reconstruction received regional anesthesia in the form of a single-shot femoral nerve block before surgery. In August 2016, the attending surgeon elected to change his clinical practice and transition from femoral nerve block to intra-articular injection. In this fashion, a sequential protocol was attained for the comparison of these 2 analgesic modalities.

Patients aged <21 years with a complete ACL tear who were treated by a single surgeon with BTB reconstruction were included in this study. Patients were treated with a femoral peripheral nerve block (January 2013 to August 2016) or an intra-articular injection (August 2016 to December 2019). Patients were excluded for the following reasons: revision ACL reconstruction (n = 10) or receipt of both an intra-articular injection and a peripheral nerve block (n = 2). A total of 116 adolescents met the study criteria. Patients were selected consecutively.

In patients receiving the peripheral nerve block, a single-shot injection into the area of the femoral nerve was performed by a board-certified pediatric anesthesiologist using ultrasound guidance before case start. The injection consisted of bupivacaine or ropivacaine with or without clonidine, as determined by anesthesia physician preference and patient weight. In patients receiving intra-articular injection, a single-injection cocktail of 5 mg of morphine and 10 mg of 0.2% ropivacaine diluted into 40 mL of lactated Ringers solution was administered at the closure of all incisions.

Patients were admitted for 24 hours postoperatively, during which subjective pain scores were assessed every 4 hours on a scale of 0 to 10, with 10 representing the worst pain, as part of the standard hospital nursing protocol for postsurgery inpatients. MMEs consumed were tabulated for each patient during the course of their postoperative stay beginning at the immediate postoperative period.

Statistical analysis was performed using SPSS software (IBM). A Mann-Whitney *U* test was performed to account for the nonparametric continuous nature of our outcomes measures. A repeated measures analysis of variance (ANOVA) test was performed to assess for between-group differences across the multiple periods. Alpha was set at $P < .05$ to declare significance. There was 19% power to detect a small effect size (0.1), 75% power to detect a medium effect size (0.25), and 99% power to detect a large effect size

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Ethical approval for this study was obtained from the University of California, San Diego (project 161895XL).

TABLE 1
Patient Demographics [a]

	PB Group	IA Group	*P* Value
Age, y, mean (range)	16.4 (14.2-19.9)	16.9 (14.1-20.2)	.063
Sex, No. (%)			.853
Male	27 (46.5)	28 (48.3)	
Female	31 (53.5)	30 (51.7)	
Mean body mass index	27.6	27.7	.919

[a] IA, intra-articular; PB, peripheral block.

(0.4). The study had 80% power to detect a difference somewhere between a medium and large effect size.

RESULTS

Patient Demographics

Of the 116 adolescents who were included in our study, 58 received intra-articular injection, and 58 received single-shot femoral nerve block. Of the intra-articular group, 28 were male and 30 were female. Of the peripheral block group, 27 were male and 31 were female. There were no significant differences between the groups in age, sex distribution, or body mass index. Demographic data are summarized in Table 1.

MME Consumption

On average, opioid consumption as measured in MMEs was lower in the patients treated with intra-articular injection; however, this did not reach significance (24.3 vs 28.5 MMEs; $P = .108$). Consumption of MMEs was greater in the intra-articular group at 0 to 4 hours (7.1 vs 4.6 MMEs; $P = .008$). There was significantly less MME consumption in patients receiving intra-articular injection as compared with peripheral block at 16 to 20 hours (3.2 vs 5.6 MMEs; $P = .01$) and 20 to 24 hours (3.8 vs 6.5 MMEs; $P < .001$). In the intervals of 4 to 8 hours (3.9 vs 3.7 MMEs; $P = .776$), 8 to 12 hours (3.4 vs 4.6 MMEs; $P = .217$), and 12 to 16 hours (3.0 vs 3.6 MMEs; $P = .513$), there was no significant difference in MME consumption between the intra-articular injection and peripheral block groups. Repeated measures ANOVA demonstrated a significant difference in MME consumption trends, with an increase by patients receiving blocks over the 24-hour period and a decrease for those receiving intra-articular injection ($P < .001$). MME data are summarized in Figure 1 and Table 2.

Subjective Pain Scores

Mean subjective pain scores were not significantly different over the 24-hour period (peripheral block, 2.7; intra-articular injection, 3.0; $P = .19$). The scores were significantly different at only the 8- to 12-hour interval (intra-articular, 3.2; block, 2.3; $P = .027$). Repeated measures ANOVA demonstrated a significant difference between the groups in subjective pain score trend over the course of 24 hours

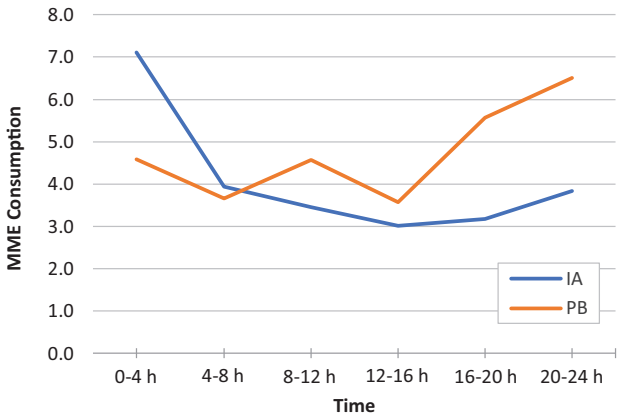

Figure 1. Trend in MME over the first 24 hours postoperatively. IA, intra-articular; MME, morphine milligram equivalent consumption; PB, peripheral block.

($P < .001$). Pain scores initially increased at a greater rate in the intra-articular cohort before downtrending over the next 8 hours and plateauing late. Alternatively, the femoral nerve block cohort saw an early rise and fall in pain score before incrementally increasing over the last 12 hours. Subjective pain scores are summarized in Figure 2 and Table 3.

DISCUSSION

Our study suggests that intra-articular injection provides equivalent pain control and similar consumption of MMEs as compared with single-shot peripheral nerve block in adolescents undergoing BTB ACL reconstruction. Previous literature comparing these 2 pain modalities has been inconsistent in technique, with a particular paucity of data focusing on the pediatric/adolescent patient population. In a 2016 review, Secrist et al[23] evaluated all randomized controlled trials examining pain control modalities for ACL reconstructions. Interestingly, of the 77 included studies, none compared single-injection femoral nerve block with ropivacaine-morphine intra-articular injection. The authors concluded that no consensus existed regarding the more efficacious analgesic modality, but they noted that peripheral nerve block and intra-articular injection both appeared effective. Woods et al[31] compared continuous femoral nerve block with intra-articular injection and found no difference in narcotic medication use or subjective pain scores. In the pediatric population, a continuous peripheral nerve catheter is of low utility for outpatient surgery due to concerns over lack of patient compliance.

In a 2005 study, Tran et al[28] compared single-injection femoral nerve block with intra-articular injection of bupivacaine-clonidine-morphine in 36 children. Limited by sample size, this study observed MME consumption in the form of patient-controlled analgesia with supplemental breakthrough morphine injections. The authors found that MME use was greater in the intra-articular group and therefore concluded that the femoral nerve block was more

TABLE 2
MME Consumption per 4-Hour Interval [a]

	MME Consumption					
Interval: Intervention	Mean	SD	SE	95% CI	Range	*P* Value[b]
0-4 h						**.008**
PB	4.6	4.7	0.6	3.3-5.8	0-18.6	
IA	7.1	5.0	0.7	5.8-8.4	0-23.86	
Total	5.8	5.0	0.5	4.9-6.8	0-23.86	
4-8 h						.776
PB	3.7	3.5	0.5	2.7-4.6	0-15	
IA	3.9	4.9	0.6	2.6-5.2	0-24.5	
Total	3.8	4.3	0.4	3.0-4.6	0-24.5	
8-12 h						.217
PB	4.6	4.3	0.6	3.4-5.7	0-17	
IA	3.4	3.6	0.5	2.5-4.4	0-11.5	
Total	4.0	4.0	0.4	3.3-4.7	0-17	
12-16 h						.513
PB	3.6	4.0	0.5	2.6-4.7	0-15	
IA	3.0	3.5	0.5	2.1-3.9	0-11.25	
Total	3.3	3.8	0.4	2.6-4.0	0-15	
16-20 h						**.010**
PB	5.6	5.1	0.7	4.2-6.9	0-25	
IA	3.0	3.5	0.5	2.3-4.1	0-11.25	
Total	4.4	4.5	0.4	3.5-5.2	0-25	
20-24 h						**<.001**
PB	6.5	4.3	0.6	5.4-7.6	0-15	
IA	3.8	4.4	0.6	2.7-5.0	0-23	
Total	5.2	4.5	0.4	4.3-6.0	0-23	
24 h total						.108
PB	28.6	15.2	2.0	24.5-32.6	0-77	
IA	24.4	13.8	1.8	20.7-28.0	5-67	
Total	26.5	14.6	1.4	23.7-29.1	0-77	

[a] IA, intra-articular; MME, morphine milligram equivalent; PB, peripheral block. No. of patients: n = 58 each for PB and IA; N = 116.
[b] Bold *P* values indicate statistically significant difference between the PB and IA groups ($P < .05$).
Patients, No. PB, 58; IA, 58; Total, 116.

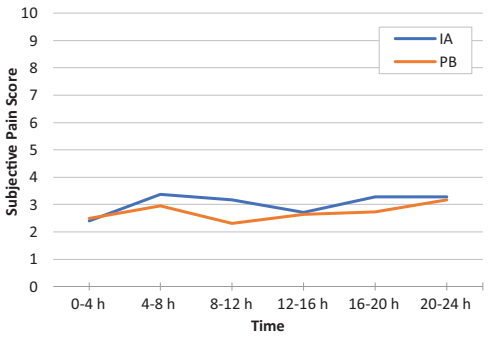

Figure 2. Trend in subjective pain scores over first 24 hours postoperatively. IA, intra-articular; PB, peripheral block.

efficacious. It should be noted that the grafts utilized for ACL construction were limited to hamstring autograft and Achilles allograft, which is different from the current study. Last, a more recent review by Vorobeichik et al[29] demonstrated a lack of superiority of femoral nerve block as compared with intra-articular injection.

Given that the majority of ACL reconstructions are performed on an outpatient basis, our data provide a unique understanding of a portion of the postoperative period that cannot typically be rigorously studied. Our results show that MME consumption was greater in the intra-articular group in the first 4 hours postoperatively. However, this switches as we progress out from 4 hours through the first 24 hours postsurgically. Given that the majority of patients will remain in the recovery unit when MME use is greatest, managing this early pain is already the standard of care. However, after the patient is discharged, fewer MMEs are required, and pain control should be easier to manage. This may even confer fewer patient calls for poorly controlled pain in the first 20 hours at home.

Intra-articular injection provides targeted analgesia with little risk or time commitment. Alternatively, peripheral nerve block is limited by its analgesic distribution, cost, and risk to the patient. As discussed earlier, femoral nerve block is associated with muscle weakness and local anesthetic-induced myotoxicity.[5,8,9,11] These complications can hinder recovery and early mobilization and have been shown to delay return to sport.[4,19] Additionally, a recent analysis showed that a single-shot peripheral nerve block takes a mean 505 seconds to complete when performed by an experienced regional anesthesia specialist.[2] This does

TABLE 3
Subjective Pain Scores by 4-Hour Interval [a]

Interval: Intervention	Subjective Pain Score					P Value[b]
	Mean	SD	SE	95% CI	Range	
0-4 h						.977
PB	2.5	2.6	0.3	1.8-3.2	0-8	
IA	2.4	2.3	0.3	1.8-3.0	0-8	
Total	2.5	2.4	0.2	2.0-2.9	0-8	
4-8 h						.206
PB	3.0	2.7	0.4	2.2-3.7	0-10	
IA	3.4	2.3	0.3	2.8-4.0	0-8	
Total	3.2	2.5	0.2	2.7-3.6	0-10	
8-12 h						**.027**
PB	2.3	2.6	0.3	1.6-3.0	0-10	
IA	3.2	2.2	0.3	2.6-3.8	0-8	
Total	3.7	2.4	0.2	2.3-3.2	0-10	
12-16 h						.646
PB	2.7	2.7	0.4	1.9-3.4	0-8	
IA	2.7	2.2	0.3	2.1-3.3	0-9	
Total	2.7	2.5	0.2	2.2-3.1	0-9	
16-20 h						.180
PB	2.7	2.9	0.4	2.0-3.5	0-10	
IA	3.3	2.6	0.3	2.6-4.0	0-9	
Total	3.0	2.8	0.3	2.5-3.5	0-10	
20-24 h						.780
PB	3.2	2.5	0.3	2.5-3.8	0-9	
IA	3.3	2.4	0.3	2.7-3.9	0-8	
Total	2.9	2.4	0.2	2.8-3.7	0-9	
24 h total						.190
PB	2.7	1.6	0.2	2.3-3.1	0.2-7	
IA	3.0	1.4	0.2	2.7-3.4	0.5-6.5	
Total	2.9	1.5	0.1	2.6-3.2	0.2-7	

[a] IA, intra-articular; PB, peripheral block. No. of patients: n = 58 each for PB and IA; N = 116.

[b] Bold *P* values indicate statistically significant difference between the PB and IA groups ($P < .05$).

Patients, No. PB, 58; IA, 58; Total, 116.

not account for the additional time required for patient preparation, supply preparation, and additional delays in the setting of less experienced practitioners. Additionally, a cost analysis of peripheral nerve block and intra-articular injection revealed patient savings of 2.63% in those receiving intra-articular injection; a separate study showed a cost savings of $400.[10,14]

However, we must also acknowledge that there are risks associated with intra-articular injection of local anesthetics, particularly the risk of chondrotoxicity. Studies have shown that local anesthetics have dose- and time-dependent deleterious effects on chondrocytes in vitro.[6,12,17] However, these risks are mitigated with proper dosing and selection of ropivacaine, which has the least chondrotoxic effect of the commonly used local anesthetics.[12] Still, one must consider this risk when selecting intra-articular injection for analgesia.

Our study is strengthened by a number of factors. Our data were collected from patients undergoing BTB ACL reconstruction by a single surgeon, limited to no variance in technique of surgery. Patients were selected consecutively, and the 2 comparison interventions were administered sequentially to limit selection bias. Additionally, the medications used for intra-articular injection and peripheral nerve block were consistent throughout the course of the study. A consistent postoperative protocol was utilized for the care of all patients. The 2 cohorts were demographically similar. Last, all patients remained inpatient for the entirety of the postoperative study period, thus protecting from the recall bias inherent in similar studies that include outpatient pain scores and MME consumption.

However, this study is not without drawbacks. There are inherent weaknesses associated with the retrospective nature of our study design. We are limited in sample size, although our cohorts are larger than those of most similar studies. We sought to mitigate this by performing a post hoc (observed) power analysis to assess our power to detect clinically relevant effect sizes. Data collection did not extend beyond the 24-hour postoperative period, and further studies would be needed to compare pain control beyond this window. We focused on single-shot femoral nerve blocks and did not include other types of regional anesthesia. Although the adductor canal nerve block has gained popularity, and one might argue that comparison of intra-articular injection would be better suited against it, 2 recent studies noted comparable pain control among the 3 analgesic modalities.[20,25] Furthermore, recent data suggest that patients with femoral nerve block and adductor canal block experience similar delays in quadriceps recovery up to 6 months from surgery.[3,22] In comparison, studies have shown that intra-articular injection results in a significantly smaller loss of quadriceps strength.[9] Last, we were unable to account for changes in public awareness and education campaigns regarding the nationwide opioid crisis, which may have affected patient and nursing perception and use of narcotic pain medication.

Moving away from the use of peripheral nerve block as an analgesic modality may be challenging given the multidisciplinary role of pain management in these patients. However, orthopaedic and anesthesia colleagues alike are beginning to recognize that it is a change that may benefit our patients.[21] Our study strengthens this argument and shows that there is no significant difference in MME consumption between the femoral nerve block group and intra-articular injection group in the first 24 hours postoperatively. While peripheral block is associated with lower opioid consumption in the first 4 hours after surgery, patients receiving intra-articular block require fewer opioids 16 to 24 hours postoperatively. This may be particularly relevant in the outpatient setting in which early postoperative pain (0-4 hours) can be managed before discharge, whereas pain after discharge can be more challenging to manage. Given these findings, we propose that intra-articular injection is a viable alternative for analgesia in pediatric patients undergoing BTB ACL reconstruction.

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