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REPORTS OF ORIGINAL INVESTIGATIONS

Adductor canal block with or without added magnesium sulfate following total knee arthroplasty: a multi-arm randomized controlled trial

Bloc du canal des adducteurs avec ou sans ajout de sulfate de magnésium à la suite d'une arthroplastie totale du genou : une étude randomisée contrôlée de plusieurs modalités

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Abstract

Purpose *Postoperative analgesia following total knee arthroplasty (TKA) often includes intrathecal opioids, periarticular injection (PAI) of local anesthetic, systemic multimodal analgesia, and/or peripheral nerve blockade. The adductor canal block (ACB) provides analgesia without muscle weakness and magnesium sulphate ($MgSO_4$) may extend its duration. The purpose of this trial was to compare the duration and quality of early post-TKA analgesia in patients receiving postoperative ACB (± $MgSO_4$) in addition to standard care.*

Methods *Elective TKA patients were randomized to: 1) sham ACB, 2) ropivacaine ACB, or 3) ropivacaine ACB with added $MgSO_4$. All received spinal anesthesia with intrathecal morphine, intraoperative PAI, and multimodal systemic analgesia. Patients and assessors remained blinded to allocation. Anesthesiologists knew whether patients had received sham or ACB but were blinded to $MgSO_4$. The primary outcome was time to first analgesic (via patient-controlled analgesia [PCA] with iv morphine) following ACB. Secondary outcomes were morphine consumption, side effects, visual analogue scale pain scores, satisfaction until 24 hr postoperatively, and length of stay.*

Results *Of 130 patients, 121 were included. Nine were excluded post randomization: four were protocol violations, three did not meet inclusion criteria, and two had severe pain requiring open label blockade. There were no differences in the median [interquartile range] time to first PCA request: sham, 310 min [165–550]; ropivacaine ACB, 298 min [120–776]; and ropivacaine ACB with $MgSO_4$, 270 min [113–780] ($P = 0.96$). Similarly, we detected no differences in resting pain, opioid*

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consumption, length of stay, or associated side effects until 24 hr postoperatively.

Conclusion *We found no analgesic benefit of a postoperative ACB, with or without added $MgSO_4$, in TKA patients undergoing spinal anesthesia and receiving intrathecal morphine, an intraoperative PAI, and multimodal systemic analgesia.*

Trial registration *www.clinicaltrials.gov (NCT02581683); registered 21 October 2015.*

Résumé

Objectif *L'analgésie postopératoire suivant une arthroplastie totale du genou (ATG) inclut souvent des opioïdes intrathécaux, une injection périarticulaire (IPA) d'anesthésique local, une analgésie multimodale systémique, et/ou des blocs des nerfs périphériques. Le bloc du canal des adducteurs (BCA) permet une analgésie sans faiblesse musculaire et le sulfate de magnésium ($MgSO_4$) pourrait prolonger sa durée. L'objectif de cette étude était de comparer la durée et la qualité de l'analgésie post-ATG précoce chez les patients recevant un BCA postopératoire (± $MgSO_4$) en plus des soins standard.*

Méthode *Des patients devant subir une ATG non urgente ont été randomisés à recevoir : 1) un BCA placebo (groupe témoin), 2) un BCA avec ropivacaïne, ou 3) un BCA avec ropivacaïne et $MgSO_4$. Tous ont reçu une rachianesthésie avec morphine intrathécale, une IPA peropératoire, et une analgésie multimodale systémique. L'allocation a été faite à l'insu des patients et des évaluateurs. Les anesthésiologistes savaient si les patients avaient reçu un placebo ou un BCA, mais n'étaient pas informés de l'ajout ou non de $MgSO_4$. Le critère d'évaluation principal était le temps jusqu'à la première prise d'analgésique (via une analgésie contrôlée par le patient [ACP] avec de la morphine iv) après le BCA. Les critères secondaires comprenaient la consommation de morphine, les effets secondaires, les scores de douleur sur l'échelle visuelle analogue, la satisfaction jusqu'à 24 heures postopératoires, et la durée de séjour.*

Résultats *Sur 130 patients, 121 ont été inclus. Neuf ont été exclus après la randomisation : quatre l'ont été en raison de violations du protocole, trois ne répondaient pas aux critères d'inclusion, et deux ont ressenti des douleurs graves nécessitant un bloc sans insu. Aucune différence n'a été observée dans le temps médian [écart interquartile] jusqu'à la première demande d'ACP : placebo, 310 min [165-550]; BCA ropivacaïne, 298 min [120-776]; et BCA ropivacaïne avec $MgSO_4$, 270 min [113-780] ($P = 0,96$). De la même manière, nous n'avons détecté aucune différence dans la douleur au repos, la consommation d'opioïdes, la durée de séjour, ou les effets secondaires associés jusqu'à 24 heures postopératoires.*

Conclusion *Nous n'avons trouvé aucun avantage analgésique à un BCA postopératoire, avec ou sans ajout de $MgSO_4$, chez les patients subissant une ATG sous rachianesthésie et recevant de la morphine intrathécale, une IPA peropératoire, et une analgésie multimodale systémique.*

Enregistrement de l'étude *www.clinicaltrials.gov (NCT02581683); enregistrée le 21 octobre 2015.*

Keywords adductor canal block · analgesia / methods · arthroplasty, replacement, knee · saphenous nerve · nerve block / methods

More than 75,000 total knee arthroplasties (TKAs) were performed in Canada in 2018–2019,[1] and more than one million knee replacements were performed in the United States in 2017.[2] Following surgery, functional outcomes are improved and patients are discharged earlier if they ambulate within several hours of surgery.[3] To facilitate ambulation, postoperative pain must be minimized without concomitant muscle weakness and/or excessive opioid-related side effects.[3]

In many centres, postoperative analgesia following TKA includes a multimodal approach with the co-administration of several different systemic medications in addition to a periarticular injection (PAI) of local anesthetic (LA) and/or a peripheral nerve block such as the femoral nerve block (FNB) or a saphenous nerve block (adductor canal block [ACB]).[4] Although the FNB provides additional analgesia, it is associated with weakening of the quadriceps muscle, which may increase the risk of falls during early ambulation.[4] The ACB provides analgesia comparable with the FNB but without the associated muscle weakness.[4]

Recent attention has been given to adding magnesium sulphate ($MgSO_4$) to LA to improve and/or prolong analgesia following a number of different nerve blocks (i.e., interscalene, thoracic paravertebral, femoral, axillary brachial plexus, supraclavicular brachial plexus).[5,6] Magnesium is an N-methyl-D-aspartate (NMDA) receptor antagonist,[6] and the fact that peripherally administered $MgSO_4$ does not increase cerebrospinal fluid concentrations of magnesium[7] suggests that the mechanism of action is through peripheral rather than central NMDA receptors. In arthroscopic knee surgery, intra-articular $MgSO_4$ in combination with bupivacaine provides superior analgesia compared with $MgSO_4$ or bupivacaine alone.[8] To our knowledge, there are currently no published investigations that have examined the analgesic efficacy of $MgSO_4$ administered via an ACB in TKA patients. The purpose of this randomized controlled trial (RCT) was to assess the duration of analgesia in TKA

patients receiving ACBs with or without $MgSO_4$ in addition to our institutional standard care consisting of spinal anesthesia with intrathecal morphine, intraoperative PAI, and multimodal systemic analgesia. We hypothesized that patients receiving an ACB with added $MgSO_4$ will have prolonged analgesia and improved pain scores, which will contribute to a shorter hospital length of stay (LOS).

Methods

This prospective RCT was approved by the Queen's University Health Sciences and Affiliated Teaching Hospital's Research Ethics Board (ANAE -273-15, 7 May 2015). Written informed consent was obtained preoperatively from all participating patients. The trial was registered at clinicaltrials.gov (NCT02581683). Approval was obtained from Health Canada for the off-label use of $MgSO_4$ prior to the initiation of patient recruitment (NOL185053, 26 June 2015). Given the low dose of $MgSO_4$ and the route of administration, the likelihood of adverse effects associated with the addition of $MgSO_4$ to the ACB was considered low.[9] The current report is in compliance with the applicable CONSORT guidelines.[10]

Participants were eligible for inclusion if they were 18–85 yr of age, had been assigned an American Society of Anesthesiologists Physical Status class of I–III, and were presenting electively for unilateral primary TKA at either of our two affiliated hospitals. Participants were excluded if they were pregnant or breastfeeding, had cardiovascular disease (i.e., congestive heart failure, severe valvulopathies, symptomatic coronary artery disease, and/or congenital/anatomical cardiac abnormalities), had any conditions that precluded the use of regional analgesia or any of the study medications, had a chronic pain condition for which they had routinely taken opioids during the preceding three months, were unable to operate PCA, could not comprehend English, or could not provide informed consent. Data were collected from the patient, the bedside chart, the electronic medical record, and the acute pain service database by research personnel blinded to treatment allocation.

Sample size

There were no studies to our knowledge that had investigated the analgesic effects of $MgSO_4$ administered via an ACB. Hence, we used the data on the time to first analgesic request from Lee *et al.* (2012)[5] in which shoulder arthroscopy patients received an interscalene block (bupivacaine) with *vs* without $MgSO_4$ and experienced a significant increase in the mean (SD) duration of analgesia (i.e., 553 [155] min *vs* 664 [188] min for saline *vs* $MgSO_4$, respectively), and calculated that we would require a minimum of 38 patients per group with an α of 0.05 and power of 80% (https://www.stat.ubc.ca/~rollin/stats/ssize/n2.html, using two sample Z test comparison of means with common variance). Our primary hypothesis was that there would be a difference between ACB and standard care, so we extrapolated this value to the comparison of ACB *vs* standard care, and ACB with added $MgSO_4$ *vs* standard care. We aimed to include a minimum of 40 participants per group (120 patients total). To account for potential losses and to ensure that a minimum of 120 patients would complete the trial, we randomized an additional ten patients.

Recruitment took place between 27 July 2015 and 13 February 2017. In total, 130 elective TKA patients were randomized without blocking to one of three groups using a computer-generated table prepared by the institutional biostatistician (http://www.randomization.com/). Group 1 was sham ACB ($n = 45$), group 2 was ropivacaine ACB ($n = 42$), and group 3 was ropivacaine ACB with added $MgSO_4$ ($n = 43$). The randomization table was then sent directly to the departmental research secretary who had no involvement in this study other than preparing the study packages according to the randomization table. All study drugs were prepared in identical syringes. Blinded research personnel obtained informed consent and randomized patients with their assignments concealed in envelopes. Patients, attending anesthesiologists (both providing intraoperative care and supervising acute pain management), surgeons, clinical nursing staff, and research personnel remained blinded to the treatment allocation for the duration of the study. The anesthesiologist performing the ACB knew which patients were assigned to the sham ACB but did not know whether the block solution contained $MgSO_4$ in those randomized to receive an ACB.

For surgery, patients received a spinal anesthetic in the sitting position with hyperbaric bupivacaine 0.75% 10.5 to 12 mg (dosage at the discretion of the attending anesthesiologist), fentanyl 10 μg, and morphine 100 μg. Intraoperatively, all patients received a PAI with ropivacaine 0.2% 100 mL (to a maximum of 2 $mg \cdot kg^{-1}$), epinephrine 0.3 mg, and ketorolac 30 mg. The PAI was performed by one of four participating surgeons, or a fellow (M.A.) under direct supervision. The same technique (injection into the posterior capsule of the knee medial and lateral to the neurovascular bundle, posterior to tibia and femur, and into the pes aeserinus and deep fascia including quadriceps towards the area of the adductor canal, and into the wound edges) was used. Postoperatively, all patients received patient-controlled intravenous morphine analgesia (PCA), acetaminophen

(650 mg every six hours), and celecoxib (100 mg every 12 hr).

Treatment/intervention

In the postanesthetic care unit (PACU), when spinal anesthesia had receded to a sensory T12 block, as assessed by the blinded PACU nurse every 15–30 min, a drape was positioned so participants could not observe the anesthesiologist performing the intervention. Participants were assigned to one of three groups. In group 1 (sham ACB), they received a sham ACB whereby an ultrasound (US) probe and blunt needle were applied to the skin without puncture. In group 2 (ropivacaine ACB), they received a single-shot US-guided ACB consisting of 10 mL of ropivacaine 0.5% + 10 mL of normal saline. In group 3 (ropvacaine ACB with added $MgSO_4$), they received an US-guided ACB consisting of 10 mL of ropivacaine 0.5% with an addition of 2 g of 10% $MgSO_4$. The ACBs were either performed by the attending anesthesiologist or a senior resident using a standardized approach as described by Manickam *et al.*[11]

Ambulation and physical therapy were initiated on the same day of surgery or the morning of postoperative day (POD) 1. Patients were discharged 24 hr after surgery if their visual analog scale (VAS) pain score was $\leq$ 4/10 (0 = no pain; 10 = the worst pain imaginable), they were stable, and they could ambulate with a cane/walker.

Outcome measures

The primary outcome was time to first analgesic request following the ACB intervention as recorded by the *iv* morphine PCA pump. Secondary outcomes were cumulative PCA morphine consumption over the first 24 hr following surgery; VAS pain scores at two, four, eight, 12, 18, 24 and 48 hr following the ACB intervention; patient satisfaction with analgesia 24 hr postoperatively; and LOS based upon admission time and the time of hospital discharge as determined by a physiotherapy assessment of functionality. The incidence of nausea, pruritus, and sedation within the first 24 hr postoperatively was also compared between groups.

Our initial study design defined the time to first analgesic request as the time from the end of surgery to the first analgesic request (as recorded on the PCA pump). Nevertheless, upon trial initiation, we decided it was more informative to define time as from ACB completion to first analgesic request. In addition, we also initially intended to record the steps taken per day via a pedometer. However, we observed that very little ambulation occurred in this population postoperatively, so we decided not to collect postoperative ambulation data.

All outcome data including pain scores (VAS) and satisfaction scores (five-point Likert scale) were collected by research personnel and/or clinical nursing staff blinded to the randomization assignment. Side effects were assessed by asking the patient whether they were experiencing nausea, pruritus, or sedation, to which a "yes" or "no" response was recorded.

Statistical analyses

Data analyses were as per protocol, as all participants included in the analysis remained in their originally allocated group. For those patients excluded post randomization, no further data were collected. No imputations or adjustments were made for missing data points. Data were entered into IBM® SPSS® Statistics (version 26.0 for Windows; IBM, Armonk, NY, USA) for statistical analysis. All continuous data were tested for normality using the Shapiro–Wilk test. All continuous variables (time to first analgesic request, opioid consumption, VAS scores, and hospital LOS) were analyzed using one-way analysis of variance (ANOVA) or Kruskal–Wallis tests depending upon the underlying distribution of the data, with the Tukey's or Dunn's (as appropriate) test used for more specific inter-arm comparisons. Patient satisfaction scores were compared using the Kruskal–Wallis test. The incidence of side effects was compared using the Pearson Chi squared test or Fisher's Exact test (as appropriate). Repeated measures ANOVA was used to compare the pain levels over time, using arm as a factor. Statistical significance was defined as $P < 0.05$ and no adjustments were made for multiple comparisons other than those inherent in the post-hoc tests.

Results

Of 130 patients enrolled, data were collected and analyzed for 121 participants (Fig. 1). Table 1 shows their baseline characteristics. In total, nine patients were lost post randomization, two of whom had pain and required an open label block (Fig. 1). No additional data were collected and analyzed for the nine patients excluded post randomization (Fig. 1). Outcomes are summarized in Table 2. No differences were detected in median [interquartile range (IQR)] time to first PCA analgesic request between the groups: sham ACB, 310 min [165–550]; ropivacaine ACB, 298 min [120–776]; and ropivacaine ACB with added $MgSO_4$, 270 min [113–780] (difference across groups, $P = 0.96$). Since the global test was not significant, the Dunn's post-hoc tests for the significance of inter-arm differences were not relevant so were not produced by the software. Figure 2 provides the

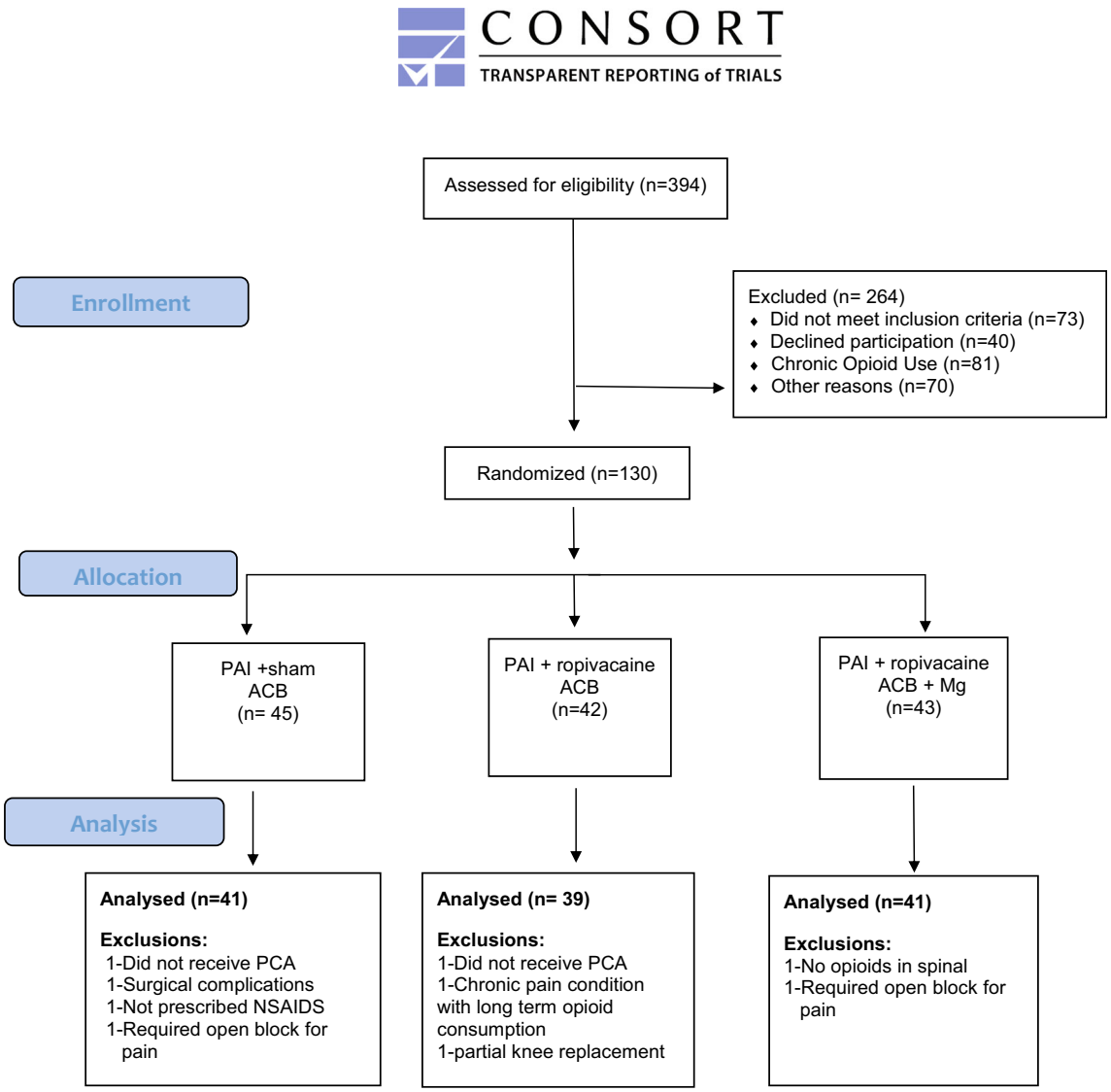

Fig. 1 CONSORT flow diagram

Table 1 Patient baseline characteristics

	Group 1 (Sham ACB) $N = 41$	Group 2 (Ropivacaine ACB) $N = 39$	Group 3 (Ropivacaine ACB with added $MgSO_4$) $N = 41$
Age (yr), mean (SD)	67.5 (6.4)	66.7 (7.8)	67.5 (10.6)
BMI ($kg \cdot m^{-2}$), mean (SD)	33.2 (6.9)	32.4 (5.8)	32.8 (6.1)
Surgical time (min), mean (SD)	58 (11)	63 (16)	58 (16)
Female, *n*/total *N* (%)	19/41 (46)	18/39 (46)	19/41 (46)
ASA Physical Status, *n*/total *N* (%)			
I	1/40 (2.5)*	0/39 (0)	0/41 (0)
II	18/40 (45)*	18/39 (46)	17/41 (41)
III	21/40 (52.5)*	21 (54)	24/41 (59)

*One patient in Group 1 did not have the ASA Physical Status documented

ACB = adductor canal block; ASA = American Society of Anesthesiologists; BMI = body mass index; SD = standard deviation

Table 2 Primary and secondary outcomes

	Group 1 (Sham ACB) $N = 41$	Group 2 (Ropivacaine ACB) $N = 39$	Group 3 (Ropivacaine ACB with added $MgSO_4$) $N = 41$	*P* value
Time to first analgesia post ACB (min), median [IQR]	310 [165–550]	298 [120–776]	270 [113–780]	0.96
	$n = 41$	$n = 38$	$n = 41$	
VAS pain scores, mean (95% CI)				
Baseline	1.6 (0.9 to 2.3)	2.1 (1.3 to 2.8)	2.2 (1.3 to 3.0)	0.57
	$n = 39$	$n = 38$	$n = 39$	
2 hr post ACB	0.24 (-0.07 to 0.56)	0.81 (0.03 to 1.58)	1.2 (0.31 to 2.2)	0.23
	$n = 29$	$n = 31$	$n = 30$	
4 hr post ACB	1.8 (0.9 to 2.6)	1.4 (0.6 to 2.2)	0.58 (0.05 to 1.1)	0.13
	$n = 28$	$n = 31$	$n = 26$	
8 hr post ACB	2.0 (1.2 to 2.8)	1.8 (1.0 to 2.7)	2.9 (1.6 to 4.2)	0.45
	$n = 36$	$n = 35$	$n = 27$	
12 hr post ACB	1.8 (1.0 to 2.6)	3.0 (2.2 to 3.9)	2.7 (1.8 to 3.6)	0.06
	$n = 32$	$n = 30$	$n = 33$	
18 hr post ACB	3.3 (2.5 to 4.1)	3.9 (3.2 to 4.7)	3.3 (2.4 to 4.3)	0.39
	$n = 41$	$n = 36$	$n = 37$	
24 hr post ACB	3.7 (2.8 to 4.7)	4.0 (3.3 to 4.7)	4.6 (3.7 to 5.4)	0.40
	$n = 35$	$n = 35$	$n = 33$	
48 hr post ACB	3.2 (2.4 to 4.0)	2.9 (2.0 to 3.8)	3.1 (2.4 to 3.9)	0.86
	$n = 36$	$n = 32$	$n = 32$	
24-hr postoperative opioid consumption (MME), median [IQR]	27.2 [20.5–33.9]	40.3 [22.9–57.8]	33.8 [20.5–47.1]	0.94
	$n = 41$	$n = 39$	$n = 41$	
Patient satisfaction with analgesia 24 hr postoperatively, *n* (%)	$n = 37$	$n = 32$	$n = 34$	0.32[a]
Poor	2 (5)	3 (9)	0 (0)	
Satisfactory	6 (16)	5 (16)	2 (6)	
Good	13 (35)	12 (27)	19 (56)	
Excellent	16 (43)	12 (38)	13 (38)	
Postoperative length of stay (days), median [IQR]	2.1 [1.9–2.9]	2.1 [1.9–3.9]	2.2 [2.0–3.1]	0.55
	$n = 41$	$n = 39$	$n = 40$	

The full dataset is available as Electronic Supplementary Material (eAPPENDIX)

ACB = adductor canal block; CI = confidence interval; IQR = interquartile range; MME = milligram morphine equivalents; VAS = visual analogue scale

P values are from the non-parametric Kruskal–Wallis test or [a]Fisher's Exact test

Samples sizes are provided for each consecutive column to indicate missing data

box plots for the three groups as a visual representation of the data. There were also no observed differences in total opioid consumption during the first 24 hr postoperatively ($P = 0.94$). Among the 103 participants who reported analgesia satisfaction scores at 24 hr post-intervention, there were no differences between the groups ($P = 0.32$).

Pain scores were reviewed at two, four, eight, 12, 18, 24, and 48 hr following the intervention. Pain scores remained low for the first eight hours and increased at 24 hr in all three groups. No statistically significant differences were detected at any of the time points examined (Table 2). Note that the data as presented are means and 95% confidence intervals (CI) for the pain scores, as the median [IQR] were often 0 [0–0]; as a result, the mean values were believed to be more informative. Repeated measures ANOVA indicated that pain scores changed significantly over time, but that there was no significant association for arm. Because of missing data, this analysis was run over all time points ($n = 30$) and then again for baseline, eight hours, 24 hr, and 48 hr ($n = 69$), to maximize the sample size. The results were equivalent, with $P < 0.001$ for the change in pain scores over time, but $P = 0.63$ and $P = 0.57$ for the effect of arm.

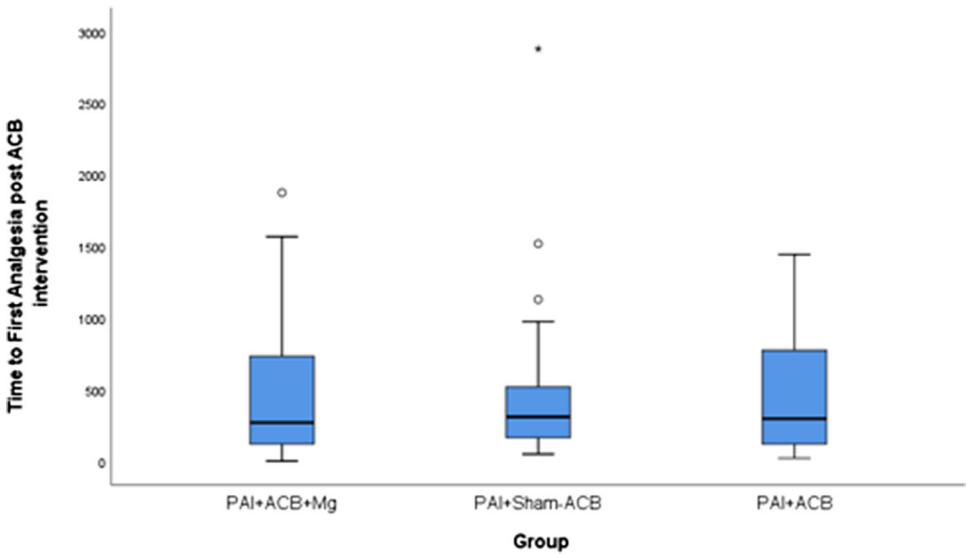

Fig. 2 Boxplot of time to first analgesic post ACB intervention, by treatment arm. These data are available in the supplemental data file as a variable with the heading "Time to Anal Recalc Min"

Table 3 Incidence of opioid-related adverse events within the first 24 hr postoperatively

Adverse event	Group 1 (Sham ACB) $N = 41$	Group 2 (Ropivacaine ACB) $N = 39$	Group 3 (Ropivacaine ACB with added $MgSO_4$) $N = 41$	*P* value
Nausea, *n*/total *N* (%)	29/41 (71)	34/39 (87)	30/41 (73)	0.17
Pruritus, *n*/total *N* (%)	12/41 (29)	8/39 (21)	10/41 (24)	0.70
Sedation, *n*/total *N* (%)	1/41 (2)	2/39 (5)	2/41 (5)	0.87

The full dataset is available as Electronic Supplementary Material (eAPPENDIX)

P values are from Fisher's Exact test

ACB = adductor canal block

No differences were detected in the total doses of acetaminophen ($P = 0.94$) or celecoxib ($P = 0.10$) between groups when administered as per standing orders.

Similarly, no differences were observed in the incidence of nausea ($P = 0.17$), pruritus ($P = 0.70$), or sedation ($P = 0.87$) between groups within 24 hr following surgery (Table 3). Finally, no statistically significant differences were detected with respect to the LOS (see Table 2).

Discussion

Periarticular injection is an effective analgesic modality after TKA[12] but postoperative pain often remains a limiting factor in early postoperative ambulation and recovery even with the use of multiple adjuncts such as acetaminophen, celecoxib, gabapentinoids, and opioids.[12] There has been increasing interest in the potential of ACB as it provides sensory blockade to the anterior knee capsule without impairing motor function. Nevertheless, in the current study, no analgesic benefits were detected postoperatively with the administration of a postoperative ACB (ropivacaine either with or without $MgSO_4$) when patients had already received intraoperative PAI, intrathecal opioids, and had access to PCA with *iv* morphine and coanalgesics postoperatively.

Previous RCTs comparing a PAI with a PAI + ACB combination have shown conflicting results. Sawhney *et al.* found that PAI (ropivacaine 300 mg in 110 mL) plus ACB (150 mg in 30 mL) conferred less pain (mean change in numeric rating scale [NRS] score was 1.61 [95% CI, 0.37 to 2.86]) on walking on POD 1 than PAI alone in patients who had received spinal anesthesia with bupivacaine and morphine.[13] Of note, these authors also included a larger proportion of their LA into the ACB than we did in our study. On the other hand, Nader *et al.* portioned less LA to the ACB than we did but found that PAI ropivacaine 200 mg in 100 mL plus ACB ropivacaine 25 mg in 10 mL led to reduced opioid consumption ($P = 0.03$) and pain burden (area under the NRS curve for pain, $P = 0.009$) in the first

36 hr after surgery compared with PAI alone. Notably, these patients did not receive intrathecal morphine perioperatively, suggesting a prolonged analgesic effect of the PAI + ACB combination.[14] Two other studies also found PAI + ACB to be superior to PAI alone; however, these studies sited an ACB catheter for repeated bolus/continuous LA administration for the first two days postoperatively, thus making any comparison difficult.[15,16] In contrast, Lum *et al.* performed a single-shot ACB (12–15 mL ropivacaine 0.5%) and observed, as we did in our study, no difference in postoperative opioid consumption between the PAI (with either liposomal bupivacaine or plain ropivacaine) plus ACB group and those who received PAI (liposomal bupivacaine) alone.[17] Unlike our study, these patients did not receive intrathecal morphine. Similarly, Grosso *et al.* observed that PAI (ropivacaine 125 mg in 50 mL) plus ACB (75 mg in 15 mL) had no analgesic advantage over PAI alone in terms of VAS pain scores for up to three days postoperatively in patients who did not receive intrathecal morphine but did have access to postoperative *iv* morphine for breakthrough pain.[18] In a more recent study, Goytizolo *et al.* observed no difference in time to reach discharge criteria, NRS pain scores, opioid consumption, or associated side effects in TKA patients who received PAI alone compared with those who received PAI + ACB. Like the other studies mentioned above, which observed no analgesic benefit from the ACB, these patients did not receive any intrathecal opioids. In our study, there are two possible explanations for the lack of additional benefit from ACB in patients given PAI. As shown in Table 2, pain scores were quite low even at eight and 12 hr after the intervention in all groups, attesting to the effectiveness of the PAI performed by our surgeons and the benefit of neuraxial morphine. Notably, intrathecal morphine produces dose-dependent analgesia for up to 48 hr postoperatively[19] and its specific impact (as well as the specific impact of other agents included in our multimodal regimen) upon the results is difficult to determine; however, this was not within the objectives of the current investigation. Nevertheless, the ratio of ropivacaine used in the PAI to that used in the ACB was approximately 4:1, and might suggest that the PAI had simply outlasted the ACB (with or without $MgSO_4$). The other possibility is that our ACBs were not all on target. Because the blocks were done when the spinal anesthetic had regressed to the low thoracic region (T12), we could not test the effectiveness of the block. Nevertheless, this was necessary to standardize the starting point for comparing the duration of analgesia between groups and block completion and to maintain blinding of the patients randomized to the sham ACB without adversely impacting discharge from PACU.

The analgesic properties of $MgSO_4$ have been shown in other regional blocks. For example, Gunduz *et al.* found that 150 mg of $MgSO_4$ added to prilocaine 5 mg/kg provided mean (standard error) sensory blockade of 304 (30) min compared with 196 (35) min with prilocaine alone (a gain of 1 hr 45 min) in axillary block.[20] Lee *et al.* showed that the addition of $MgSO_4$ to a long-acting LA mixture prolonged the duration of analgesia and reduced postoperative pain, but did not reduce postoperative opioid consumption in patients undergoing rotator cuff surgery with an interscalene block.[5] In another study, the addition of Mg 150 mg to ropivacaine prolonged the mean (SD) duration of sensory block from 290 (63) to 456 (98) min in supraclavicular block (a gain of 2 hr 30 min).[21] The relative durations of PAI and ACB with or without $MgSO_4$ suggest that the effect of ACB, even with the benefit of $MgSO_4$ supplementation, might not have significantly outlasted the duration of action of PAI in our patients. We can draw no conclusion from the current study on whether LA + $MgSO_4$ might have been superior to LA alone in ACB in the absence of PAI.

Limitations

Our study differed in that ACBs were given in the PACU. Most other studies report ACBs performed preoperatively. Although this is a significant difference in protocol design, it was necessary to standardize the starting point of our primary outcome (i.e., time to first analgesic) and maintain patient blinding. A drape was used to block patient visualization of the procedure, and with the residual effects of the spinal anesthetic they would have been unlikely to have felt whether their skin was punctured or not. The PAIs were performed by one of four orthopedic surgeons (including G.C.A.W.), with or without a fellow (M.A.), who had agreed on the PAI technique, but differences in techniques cannot be ruled out. Likewise, the ACBs were performed by the attending anesthesiologists, with or without a resident. We also did not control whether intraoperative *iv* dexamethasone was given; however, the intraoperative administration would not be temporally related to the block performance, so would be unlikely to have a significant impact on the duration of analgesia imparted by the ACB.[22] Time to discharge from hospital is a crude way to measure the effect of our intervention as many factors (patient expectation of LOS, home support, upper body strength, overall fitness, and other factors not captured by the demographics described) can influence such a parameter. Although we do report a number of patient-centred outcomes (i.e., pain scores and opioid-related side effects), the primary outcome of time to first analgesic request is not a patient-centred outcome which, given the

concurrent use of spinal anesthesia, may be of questionable clinical relevance. We acknowledge the lack of data on timing and quantity of ambulation that the patient was able to achieve (such as quantifying the steps taken) as a limitation in the design of this study. Another potential limitation is the exclusion of two patients (post randomization) because of severe pain requiring an open label block. These exclusions may have impacted outcomes if these patients had the highest pain scores. No additional data were collected from any of the nine patients excluded post randomization. Finally, given that this is a single-centre trial and in contrast to studies reported in the literature, examined postoperative, rather than a preoperative ACB, the results of the current study may not be readily generalizable to other centres. While we did not detect differences in analgesia, patient satisfaction, or LOS, we cannot rule out the possibility that small differences may exist.

Conclusion

In this prospective, double-blinded, single-centre, multi-arm RCT, we detected no analgesic benefit from administering a postoperative ACB (either with or without $MgSO_4$) in TKA patients undergoing spinal anesthesia and receiving an analgesic regimen of intrathecal opioids, intraoperative PAI, and multimodal systemic analgesia including PCA with intravenous morphine. No improvements were detected in analgesia, patient satisfaction, or LOS. The results of this study do not support the routine inclusion of a postoperative ACB (with or without $MgSO_4$) in a care pathway for TKA patients that already includes intrathecal opioids, a PAI, and systemic multimodal analgesia.

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