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Optimal volume of local anaesthetic for adductor canal block: using the continual reassessment method to estimate ED_{95}

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Abstract

Background: Theoretically, the ideal volume of local anaesthetic for adductor canal block (ACB) would ensure sufficient filling of the canal and avoid proximal spread to the femoral triangle. In this dose-finding study, we aimed to investigate the minimal effective volume for an ACB needed to fill the adductor canal distally in at least 95% of patients (ED_{95}).

Methods: We performed a blinded trial, enrolling 40 healthy men. All subjects received an ACB with lidocaine 1%. Volumes were assigned sequentially to the subjects using the continual reassessment method followed by Bayesian analysis to determine the ED_{95}. Distal filling of the adductor canal was assessed by magnetic resonance imaging (primary outcome). Secondary outcomes were the effect of volume on proximal spread to the femoral triangle (also assessed by magnetic resonance imaging), quadriceps muscle weakness (decrease by ≥25% from baseline) and sensory block.

Results: The ED_{95} was 20 ml, with an estimated probability of sufficiently filling the canal of 95.1% (95% credibility interval: 0.91–0.98). Proximal spread to the femoral triangle was seen in 0/4 (0%), 7/12 (58%), 4/8 (50%), and 8/16 (50%) subjects with the 5, 10, 15, and 20 ml doses, respectively (P=0.25). Seven subjects had a reduction in muscle strength, but there was no difference between groups (P=0.85).

Conclusions: For an ACB, the dose closest to the ED_{95} needed to fill the adductor canal distally was 20 ml. There was no significant correlation between volume and proximal spread or muscle strength.

Clinical trial registration: NCT02033356.

Key words: anaesthetics, local; knee; muscle strength; nerve block

The adductor canal block (ACB) is a novel technique used for treatment of pain after knee surgery. There is nascent evidence that the ACB reduces pain and morphine consumption compared with placebo[1–4] and provides analgesia to a similar degree as the femoral nerve block.[5 6] In contrast to the femoral nerve block, the ACB is predominately a sensory nerve block. It has been shown to preserve muscle strength compared with a femoral nerve block, both in patients and in healthy volunteers,[5–8] with the potential for enhancing early rehabilitation and thereby functional outcome.

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Editor's key points

- Adductor canal block (ACB) may provide good analgesia without reduced power after knee surgery.
- Twenty millilitres of local anaesthetic filled the adductor canal in the majority of healthy volunteers.
- The volume of local anaesthetic was not correlated with muscle strength or proximal spread.
- Further studies are needed to determine the optimal technique for ACB after knee surgery.

As the ACB is in its infancy, the ideal volume of local anaesthetic for an ACB has not yet been investigated. In terms of anatomy, four nerves pass through the adductor canal: the saphenous nerve, the nerve to the vastus medialis, the medial femoral cutaneous nerve, and the terminal end of the posterior division of the obturator nerve.[9–11] Injection of a large volume of local anaesthetic will, in theory, anaesthetize these four nerves, but injection of excess volume may spread to other nerves and muscles outside the adductor canal. Specifically, because the adductor canal runs in a continuation of the femoral triangle, excess volume may spread to the common femoral nerve. In theory, the ideal volume for an ACB will ensure sufficient spread to all nerves within the adductor canal, including the obturator nerve in the distal part of the canal, and at the same time avoid proximal overfilling to the common femoral nerve in the femoral triangle.

The continual reassessment method (CRM) combines a Bayesian estimation approach with a trial design in which doses are assigned sequentially to cohorts in the study population based on the updated results of previously completed cohorts.[12] Compared with traditional up-and-down trial designs, the CRM is considered to be more efficient and has the advantage that any percentile of the dose–response relationship can be estimated.[13–15]

In this dose-finding study, we used the CRM to determine the minimal effective volume (dose) of lidocaine 1% needed for an ACB to fill the adductor canal distally, as assessed by magnetic resonance imaging (MRI), in at least 95% of subjects (ED_{95}). Secondary outcomes were the impact of local anaesthetic volume on proximal spread to the femoral triangle, muscle strength, and sensory block.

Methods

Recruitment

After approval of the study protocol by the Regional Research Ethics Committee (H-1-2013-117), the Danish Medicine Agency (2013-004462-33), and the Danish Data Protection Agency, we conducted this prospective, blinded, dose-finding study using the CRM. The study was conducted at Aleris-Hamlet Hospitals in Copenhagen, Denmark, monitored by the Copenhagen GCP (Good Clinical Practice) Unit, Copenhagen University and prospectively registered at clinicaltrials.gov (NCT02033356). The enrolment period ran from January 31 to February 15, 2014, and we obtained written informed consent from each subject before enrolment.

We enrolled men, aged 18–30 yr with an ASA physical status of I, and a body mass index of 18–25 kg m^{-2}. Subjects who presented with intake of opioids or steroids within the last 4 weeks (except oral inhalation), intake of any drug within the last 48 h, any pathology, former trauma or surgery to the leg, diabetes mellitus, alcohol or drug abuse, history of allergy to local anaesthetics, inability to cooperate, contraindications to MRI, or who were non-Danish speakers, were excluded.

Performance of the block

All subjects received an ultrasound-guided (GE Logiq e; GE, Waukesha, WI, USA) ACB with lidocaine 1%. For performance of the block, the subject was placed in the supine position, with the leg slightly rotated externally. To standardize the needle insertion point, we measured the distance between the base of the patella and the superior anterior iliac spine, and performed the ACB at the exact midpoint. After skin preparation with chlorhexidine gluconate and isopropyl alcohol, the femoral artery was identified in the ultrasound image. An 18-gauge Tuohy needle (B. Braun Medical, Melsungen, Germany) was inserted lateral to the transducer, using an in-plane technique. The study medication was injected in incremental doses after negative aspiration to minimize the risk of intravascular injection, and after ensuring expansion of the injectate around the femoral artery.

Outcomes and assessments

The primary outcome was the minimal ED_{95} of lidocaine 1% needed for an ACB to ensure distal filling in the adductor canal as assessed by MRI and estimated using the CRM. Secondary outcomes were proximal spread to the femoral triangle, quadriceps muscle weakening (reduction by more or less than 25% from baseline), and presence of sensory block of the saphenous nerve (pinprick and cold sensation).

All subjects were positioned supine in a GE Signa 1.5 T MRI scanner (GE Healthcare, Milwaukee, WI, USA) 15 min after induction of the block. A fish-oil pill (visible on the MRI) was placed directly on the skin to mark the needle insertion point for the block. The MRI protocol consisted of three different sequences: T1 weighted, T2 weighted, and a short tau inversion recovery (STIR) sequence. All MRI data were reviewed in real time by one of the investigators (V.B., with 18 yr experience in body MRI), and conveyed to another of the investigators (P.J.), who used the CRM program to calculate the dose to be used for the next subject. Axial MRI was used to determine distal and proximal spread of the injectate in the adductor canal, each of which was evaluated as a binary outcome (success or failure). We considered there to be distal filling (success) if the lidocaine injectate could be identified inside the adductor canal in the distal slice adjacent to the most distal point of the adductor longus muscle's insertion on the femur. Concurrently, proximal spread to the femoral triangle was considered if the injectate could be traced into the femoral triangle, defined as identification of local anaesthetic in the proximal slice adjacent to where the sartorius muscle and the adductor longus muscle were seen to separate from each other.

Quadriceps muscle strength was assessed as maximal voluntary isometric contraction with a hand-held dynamometer (Lafayette Instrument, Lafayette, IN, USA), as described previously.[7] In brief, the subject was placed seated on an examination couch with their feet hanging free of the floor. The dynamometer was placed on the anterior tibia ~5 cm proximal to the transmalleolar axis and fixed to the examination couch with a non-elastic band with Velcro closure. The subject was familiarized with the procedure before performing baseline measurements. We assessed muscle strength before the block (baseline) and 1 h after the block. At each time point, the subject performed three consecutive contractions, and the mean value for each time point was calculated. We considered a mean reduction from baseline by ≥25% to be substantially weakened.

Block success rate was assessed in the saphenous innervation area (medial aspect of the lower leg), both by pinprick and by using alcohol swabs to test cold sensation.

A single investigator (K.L.H.) performed all assessments of muscle strength and sensory block.

Blinding

All subjects, the outcome assessor (K.L.H.), the radiologist (V.B.), and the radiology assistant were blinded to treatment (dose). The investigators responsible for updating the data obtained from each subject and determining doses for the next subjects (P.J. and V.S.), the two investigators performing the blocks (M.T.J. and J.L.), and their assistant (M.L.) were not blinded to volume. However, none of these investigators was involved in outcome assessments or MRI evaluation, and the subjects' view of the injection site was carefully blocked by blankets during block performance.

A computer-generated randomization list assigning the side on which to perform the ACB (right or left) was generated by one of the investigators (P.J.) before study commencement, in a 1:1 ratio and in blocks of 10. This was done strictly to ensure generalization of the result regardless of right or left limb, and was therefore not blinded.

Statistical analysis

We used CRM to estimate the minimal effective dose needed for an ACB to fill the adductor canal distally in at least 95% of patients (ED_{95}).

As there have been no previous dose-finding studies regarding ACB, the selection of six doses (from 5 to 30 ml) used in the present study was based on our previous experiences with and previous reports of the ACB.[1 5 7 8 16 17] The previous estimates for the probabilities of a successful block (distal filling) were 0.5, 0.75, 0.90, 0.95, 0.98, and 0.99 for the doses of lidocaine 1% of 5, 10, 15, 20, 25, and 30 ml, respectively. We set up the CRM to assign new doses after each cohort of two subjects (because of the time lag in performing the block and assessment of the outcome) and used exact methods to calculate the quantiles of the posterior distribution. The first cohort was administered the dose of 20 ml, corresponding to the best guess of the ED_{95} based on previous estimates. Then, for each further cohort of two, the success probabilities were re-estimated based on the data from all previous cohorts and allocated the dose with an updated probability of response closest to the target rate of 95%. We used a one-parameter power function for the dose–response model to assign success probabilities to the various volumes of local anaesthetic. The CRM continued until the planned total sample size of 40 subjects was reached or when the estimated probability of response was either too low or too high for all doses, as proposed by Zohar and Chevret.[18] We performed the dose-finding allocation using the bcrm package (http://www.jstatsoft.org/v54/i13/) of the R software version 3.0.1 (R CRAN, Vienna, Austria).

For our secondary outcomes, data were analysed using SPSS version 19.0 (SPSS, Chicago, IL, USA). Continuously valued data are presented as mean (sd) or median (10th–90th percentile) and categorical data as frequency (percentage). Categorical data (proximal spread to the femoral triangle and quadriceps muscle weakening ≥25%) were analysed using a χ^2 test with Monte Carlo estimation of the *P*-value. Furthermore, we performed a *post hoc* analysis comparing muscle strength in subjects with or without proximal spread using Student's unpaired *t*-test. A *P*-value of <0.05 was considered statistically significant.

Results

We screened 43 subjects for inclusion in the study. Forty subjects were included, and no subjects were excluded after dose allocation. A schematic presentation of the CRM design and the flow of subjects through the study are shown in Figure 1. There were no breaches of the protocol, but one subject had baseline testing of quadriceps strength performed on the wrong leg, resulting in missing data for muscle strength. The clinical characteristics of the subjects are shown in Table 1.

Outcomes

In total, 34 out of 40 blocks were successful in ensuring distal filling of the adductor canal (Fig. 2). Figure 2 shows the series of successful and non-successful blocks. The dose closest to the ED_{95} after 40 blocks had been performed was 20 ml, with an estimated success probability of 95.1% (95% credibility interval: 91–98%; Fig. 3). As a result of the high success rate encountered with the 20 ml dose, the CRM never recommended higher doses. Thus, the 25 and 30 ml doses were never tested.

Proximal spread to the femoral triangle was not seen with the 5 ml dose (0/4 subjects), but was seen for all other tested volumes, with no difference in the fraction of subjects with proximal spread: 7/12 (58%), 4/8 (50%), and 8/16 (50%) with doses of 10, 15, and 20 ml, respectively (*P*=0.25). The dose having the highest number of subjects with distal spread without proximal spread was the 10 ml dose (7/12 subjects, 58%).

Quadriceps strength across volumes is presented in Figure 4. Muscle strength decreased by >25% in seven subjects, but there was no difference between doses: zero, two, one, and four subjects at the 5, 10, 15, and 20 ml doses, respectively (*P*=0.65).

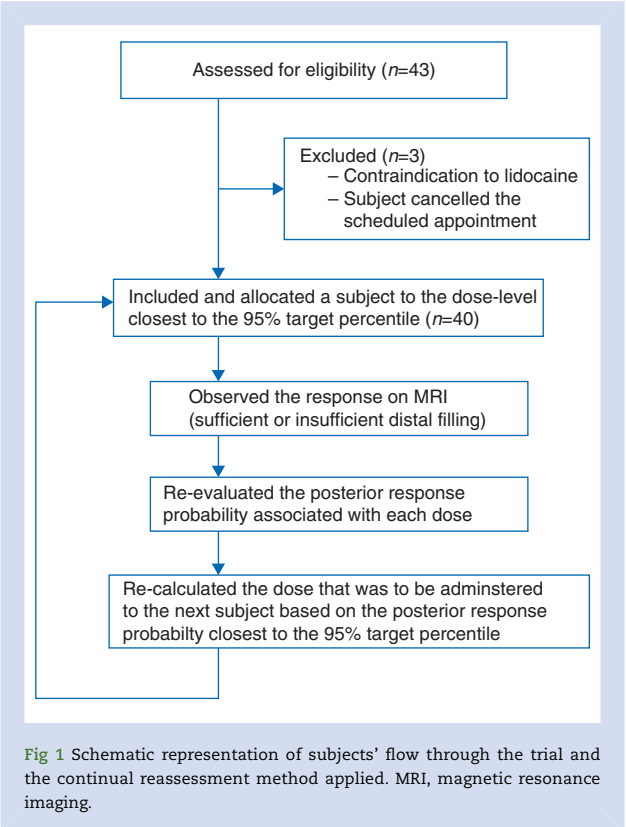

Fig 1 Schematic representation of subjects' flow through the trial and the continual reassessment method applied. MRI, magnetic resonance imaging.

All doses ensured effective sensory block of the saphenous nerve, defined as loss of either cold sensation or sensation to pinprick at 1 h after the block; however, one subject had loss of only cold sensation, with retained sensation to pinprick (15 ml dose). We identified the local anaesthetic inside the adductor canal at the level of the insertion point (marked by a fish-oil pill on the MRI) in all 40 subjects (Fig. 5).

Table 1 Characteristics of subjects. Values are reported as number of subjects, mean (sd) or median (range)

Characteristic	Value
Number of subjects	40
Age (yr)	24 (18–30)
Height (cm)	185 (5)
Weight (kg)	78 (6)

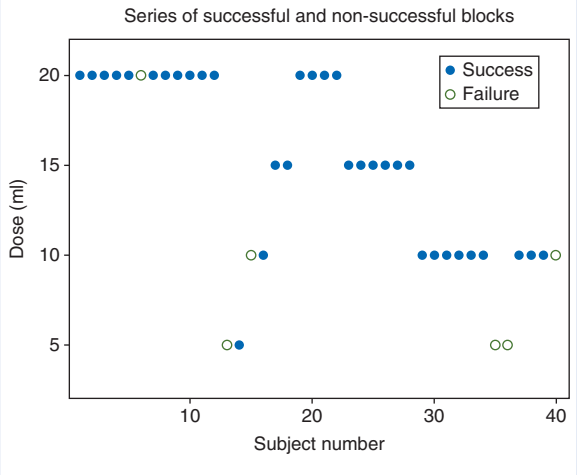

Fig 2 Schematic representation of the series of successful and non-successful blocks. In total, 34 out of 40 blocks were successful in ensuring distal filling of the adductor canal.

Exploratory analyses

The injectate spread 0–1.2 cm from the apex and into the femoral triangle [median (range): 5 ml, 0 cm (–1.6 to 0); 10 ml, 0.8 cm (–0.8 to 5); 15 ml, 1.2 cm (0–4); and 20 ml, 1.2 cm (–1.8 to 6.4)]. There was no correlation between quadriceps strength and the extent of spread of local anaesthetic (in centimetres) into the femoral triangle (Spearman's correlation coefficient –0.24, P=0.14), between proximal spread (in centimetres) and volume (Spearman's correlation coefficient 0.14, P=0.40), or between proximal spread (in centimetres) and height of the subject (Spearman's correlation coefficient 0.26, P=0.10). Mean (sd) values for quadriceps strength were lower in subjects with proximal spread to the femoral triangle, compared with those without [85 (26) *vs* 99 (14)%, respectively; P=0.04].

Adverse events

During the first half of the trial, 11 (out of 21) subjects developed superficial infections in the skin surrounding the needle insertion point, as a result of contamination of the glass containing the fish-oil pills that we had used to mark the insertion point on the MRI. After changing the procedure (replacing the glass and placing a sterile dressing over the injection site underneath the fish-oil pill), there were no more infections in the remaining study population. All infections were superficial and resolved without treatment or responded to treatment with antibiotics. No other adverse or serious adverse events occurred during the study.

Discussion

This study found that injection of lidocaine 1% (20 ml) ensures distal filling of the adductor canal with a response probability

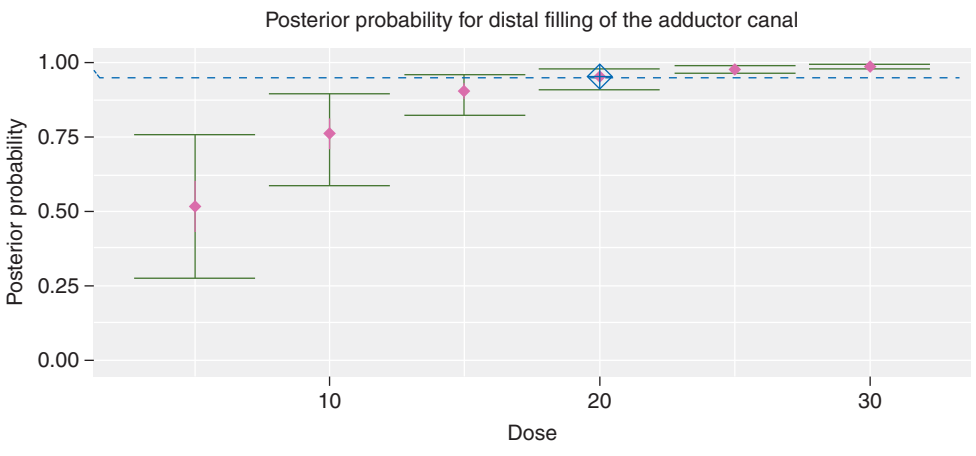

Fig 3 Posterior probability for distal filling of the adductor canal as assessed by magnetic resonance imaging. After 40 blocks had been performed, the dose closest to the targeted 95% response probability (ED_{95}) was the 20 ml dose, with an estimated success probability of 95.1% (95% credibility interval: 91–98%). Posterior probability quantiles: 2.5, 25, 50, 75, and 97.5%. Diamond shows estimated ED_{95}. Of note, because of the high success rate encountered with the 20 ml dose, the CRM never recommended higher doses. Hence, the 25 and 30 ml doses were never tested, and the posterior probabilities estimated for these doses are therefore based on the prior probabilities and an extrapolation of the results from the lower doses using the dose–response model.

of 95.1%, closely followed by the 15 ml dose with a response probability of 90.2% (Fig. 3). Distal filling of the adductor canal will, in theory, ensure optimal analgesic effect of the ACB by blocking the four nerves traversing the canal. However, proximal spread to the femoral triangle was avoided only with the 5 ml dose, which in turn failed to ensure an adequate probability of distal filling. Unfortunately, there was no correlation between volume and the extent of proximal spread, and the 10, 15, and 20 ml doses all resulted in overfilling in ~50% of subjects. Thus, anatomical differences may have more influence on extent of spread rather than volume, and in particular, the many fascia associated with the adductor canal may affect spread of the injectate.[19 20]

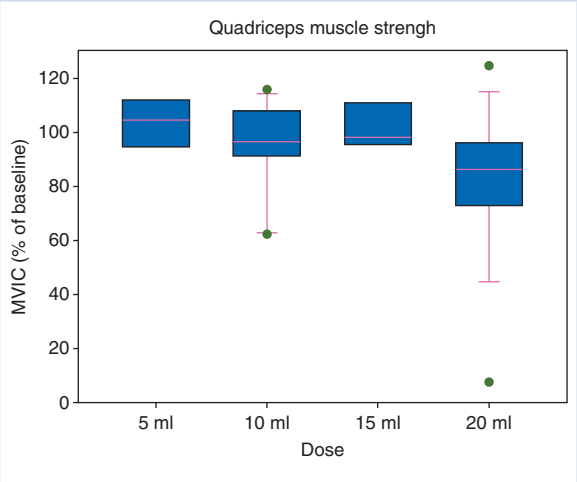

Fig 4 Quadriceps muscle strength at different doses. Muscle strength was assessed as maximal voluntary isometric contraction (MVIC) and is presented as a percentage of the baseline value. Data are expressed as median (horizontal bar) with 25th–75th (box) and 10th–90th percentiles (error bars).

Figure 4 indicates that a reduction in muscle strength may be more pronounced for an ACB with 20 ml than for lower doses, but there was no statistically significant difference between volumes and number of subjects with quadriceps weakening. Neither was there a clear relationship between proximal spread and muscle strength. Quadriceps strength was lower in subjects with proximal spread (85 *vs* 99%), and six out of the seven subjects with a quadriceps weakening of >25% had proximal spread on the MRI. However, 12 subjects with observed local anaesthetic in the femoral triangle showed no clinically relevant reduction in quadriceps strength (median value 96%, range 86–114%), and we found no correlation between muscle strength and the extent of proximal spread (in centimetres).

Although spread of local anaesthetic to the femoral triangle via the adductor canal seems difficult to avoid, the concurrent effect on quadriceps strength is modest (Fig. 4). This may be explained by branching of the motor fibres immediately distal to the inguinal ligament.[17] In the present study, quadriceps strength after an ACB with 20 ml was reduced by 16% from baseline, whereas in a previous study we found that ACB with 30 ml reduced strength by only 8%.[7] The reason for this small discrepancy is unknown, but the set-up of the present trial may have affected the result, because muscle strength was assessed immediately after a period of ~1 h of immobility. Furthermore, one subject developed what seemed to be a full femoral block (20 ml dose) with a 92% reduction in quadriceps strength. After removal of this outlier, the mean reduction was only 11%. Maximal voluntary isometric contraction assessed with a handheld dynamometer is a validated and reliable measurement tool for assessing knee extensor strength.[21] However, the absolute strength value or percentage change that corresponds to safety in ambulation is unknown. A side-to-side difference of

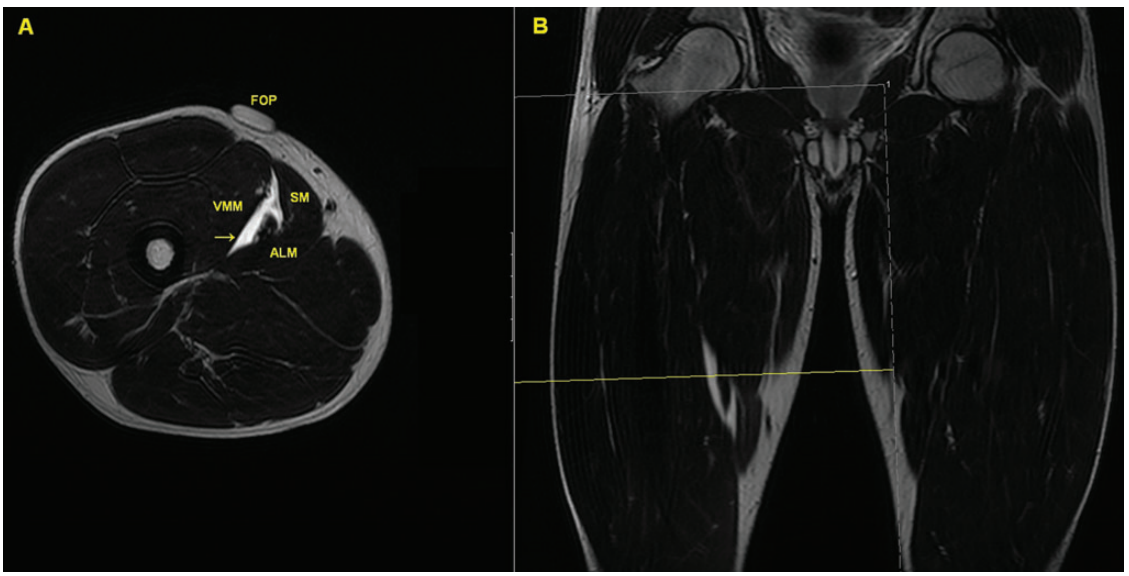

Fig 5 Magnetic resonance image showing the spread of local anaesthetic in the adductor canal. (A) Cross-sectional image of the adductor canal corresponding to the insertion point at the midthigh level. A fish-oil pill (FOP) was used to mark the insertion point. Spread of local anaesthetic can be seen as a triangular shape in the adductor canal (arrow). ALM, adductor longus muscle; SM, sartorius muscle; VMM, vastus medialis muscle. (B) Coronary image of the thigh showing longitudinal spread of local anaesthetic in the adductor canal. The yellow line marks the level of the corresponding cross-sectional image in a.

10% is normal and unnoticeable in healthy individuals,[22 23] and the smallest real change in strength is 22% for knee extension.[21] Thus, the mean reduction in quadriceps strength seen with the ACB is less than what is considered a real difference in knee-extension strength. The only person with affected ambulation after the block in the present study was the subject with the 92% strength reduction. Although a rare event, there have been two recent case reports on similar extensive quadriceps weaknesses after an ACB,[24 25] and brief assessment of muscle strength before mobilization of patients is advocated (i.e. straight-leg lift).

Our primary aim was to estimate the ED_{95} dose for filling the adductor canal distally, in order to potentiate a block of the terminal end of the obturator nerve. Although a direct evaluation of sensory block would have been the preferred end point, block of the obturator nerve in the adductor canal cannot be verified with current methods. Whether we genuinely increase the analgesic effect of the ACB by injecting a sufficient volume to ensure distal filling in the adductor canal, therefore, needs to be investigated in a surgical setting.

According to the present study, volumes >20 ml are not required for an ACB. However, the estimated success probability for the 15 ml dose was 90.2%, compared with 95.1% for the 20 ml dose. Considering that quadriceps strength was slightly higher with the 15 ml dose (Fig. 4), it may be an alluring alternative. Of note, our study was not powered to investigate a difference in muscle strength between the 15 and 20 ml volumes. In a previous cadaver study,[19] it was shown that 15 ml filled the adductor canal, but there are two important limitations in the interpretation of that study. First, cadavers have reduced tissue elasticity compared with living subjects, and second, the cadavers may have had altered pressure conditions because the femur was cut from the cadaver close to the apex of the femoral triangle. Both factors may have substantially affected the extent of injectate spread, making it difficult to extrapolate the volume from the cadaver study to living subjects. Future studies should investigate whether a reduction in volume may lead to better preservation of muscle strength, but the analgesic effect, block duration, and effect on other nerves (i.e. medial femoral cutaneous nerve) should also be considered. As it has been suggested that total dose may be the primary determinant of local anaesthetic pharmacodynamics,[26 27] the effect of dose on the effectiveness of an ACB should also be studied.

The inclusion of young men only may be considered a limitation to this dose-finding study. As men are taller than women, this may have influenced our results. While the mean difference in femur length between sexes is ~3 cm,[28] the length of the adductor canal is considered to be one-third of the length of the femur. Consequently, the mean difference between sexes in the length of the adductor canal can be only ~1 cm. The finding in the present study that height was not correlated with proximal spread into the femoral triangle (in centimetres) suggests that this 1 cm difference between sexes is probably without importance.

The CRM methodology has become popular in dose-finding studies, partly because of superior efficiency with less experimentation than more traditional methods.[12–15] In the present study, however, the superiority of the CRM approach was challenged by a seemingly unfortunate dose allocation; the CRM recommended a dose of 20 ml for the first six cohorts (12 volunteers). This lack of exploration led us to challenge the methodology by testing the lower dose intervals (5, 10 and 15 ml) for cohorts 7–9. Regardless of the successful filling of the canal with doses 10 and 15, the CRM still recommended a dose of 20 ml for cohort number 10. This led us to incorporate the following rules: (i) when one dose was successful in three subsequent cohorts, we performed a one-step reduction in dose for the next cohort; and (ii) when one failure was encountered, we increased the dose by one step. This *ad hoc* allocation of different volumes instead of an orthodox adherence to the CRM methodology ensured exploration, but may have resulted in lower efficiency. The apparent lack of exploration of the conventional CRM may be the result of a combination of a 'greedy allocation method' (always choosing the best estimate of the ED_{95}), the high success threshold (when the success probability is somewhere around 95% it takes considerable experimentation to obtain one failure), an unfortunate choice of dose–response function (insensitive to additional data for the very high probabilities), and a good initial guess of the ED_{95} (which we did not know at the start of the study). While our alternative dose allocation did not affect our results, future researchers using the CRM should be aware of these challenges, and we recommend altering the allocation method if the sequence generated by CRM does not appear to be explorative.

Regarding the unfortunate episode with the superficial infections, it is important to realize that the incident was not related to block performance or the ACB itself. The infections were solely related to the postblock, study-specific procedure (fish-oil pill placed directly on the wound from the injection site) and could have been avoided if we had used sterile dressings to cover the injection site from the beginning.

Conclusion

The dose closest to the ED_{95} of lidocaine 1% needed to fill the adductor canal distally with an ACB is 20 ml, closely followed by the 15 ml dose. Thus, larger volumes are not required to ensure distal spread in the canal. Notably, we found no significant difference in quadriceps weakening or proximal spread of local anaesthetic to the femoral triangle between volumes.

Authors' contributions

Study conception: P.J., J.B.D.
Study design: P.J., M.T.J., J.L., V.S., V.B., K.L.H., J.B.D.
Participant recruitment: P.J., K.L.H.
Data collection: P.J., M.T.J., J.L., K.L.H.
Data analysis: P.J., V.S., V.B., J.B.D.
Writing up the first draft and the final paper: P.J.
Revision of drafts: M.T.J., J.L., V.S., V.B., K.L.H., J.B.D.
Final approval: M.T.J., J.L., V.S., V.B., K.L.H., J.B.D.

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Declaration of interest

P.J. has received speaker's honoraria from Smiths Medical, St. Paul, MN, USA. No other author has any conflict of interest.

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References

1. Jenstrup MT, Jæger P, Lund J, *et al*. Effects of adductor-canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. *Acta Anaesthesiol Scand* 2012; **56**: 357–64
2. Grevstad U, Mathiesen O, Lind T, Dahl JB. Effect of adductor canal block on pain in patients with severe pain after total knee arthroplasty: a randomized study with individual patient analysis. *Br J Anaesth* 2014; **112**: 912–9
3. Andersen HL, Gyrn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. *Reg Anesth Pain Med* 2013; **38**: 106–11
4. Hanson NA, Allen CJ, Hostetter LS, *et al*. Continuous ultrasound-guided adductor canal block for total knee arthroplasty: a randomized, double-blind trial. *Anesth Analg* 2014; **118**: 1370–7
5. Jæger P, Zaric D, Fomsgaard JS, *et al*. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. *Reg Anesth Pain Med* 2013; **38**: 526–32
6. Kim DH, Lin Y, Goytizolo EA, *et al*. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. *Anesthesiology* 2014; **120**: 540–50
7. Jæger P, Nielsen ZJ, Henningsen MH, Hilsted KL, Mathiesen O, Dahl JB. Adductor canal block *versus* femoral nerve block and quadriceps strength: a randomized, double-blind, placebo-controlled, crossover study in healthy volunteers. *Anesthesiology* 2013; **118**: 409–15
8. Kwofie MK, Shastri UD, Gadsden JC, *et al*. The effects of ultrasound-guided adductor canal block versus femoral nerve block on quadriceps strength and fall risk: a blinded, randomized trial of volunteers. *Reg Anesth Pain Med* 2013; **38**: 321–5
9. Stavring S. *Gray's Anatomy, the Anatomical Basis of Clinical Practice*, 39th Edn. Edinburgh: Churchill Livingstone Elsevier, 2007; 1455
10. Horner G, Dellon AL. Innervation of the human knee joint and implications for surgery. *Clin Orthop Relat Res* 1994; **301**: 221–6
11. Gardner E. The innervation of the knee joint. *Anat Rec* 1948; **101**: 109–30
12. Houle TT, Turner DP. Bayesian statistical inference in anesthesiology. *Anesthesiology* 2013; **119**: 4–6
13. Kant A, Gupta PK, Zohar S, Chevret S, Hopkins PM. Application of the continual reassessment method to dose-finding studies in regional anesthesia: an estimate of the ED_{95} dose for 0.5% bupivacaine for ultrasound-guided supraclavicular block. *Anesthesiology* 2013; **119**: 29–35
14. Garrett-Mayer E. The continual reassessment method for dose-finding studies: a tutorial. *Clin Trials* 2006; **3**: 57–71
15. Zohar S, Resche-Rigon M, Chevret S. Using the continual reassessment method to estimate the minimum effective dose in phase II dose-finding studies: a case study. *Clin Trials* 2013; **10**: 414–21
16. Lund J, Jenstrup MT, Jæger P, Sørensen AM, Dahl JB. Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: preliminary results. *Acta Anaesthesiol Scand* 2011; **55**: 14–9
17. Davis JJ, Bond TS, Swenson JD. Adductor canal block: more than just the saphenous nerve? *Reg Anesth Pain Med* 2009; **34**: 618–9
18. Zohar S, Chevret S. The continual reassessment method: comparison of Bayesian stopping rules for dose-ranging studies. *Stat Med* 2001; **20**: 2827–43
19. Andersen HL, Andersen SL, Tranum-Jensen J. The spread of injectate during saphenous nerve block at the adductor canal: a cadaver study. *Acta Anaesthesiol Scand* 2015; **59**: 238–45
20. Tubbs RS, Loukas M, Shoja MM, Apaydin N, Oakes WJ, Salter EG. Anatomy and potential clinical significance of the vastoadductor membrane. *Surg Radiol Anat* 2007; **29**: 569–73
21. Lu YM, Lin JH, Hsiao SF, Liu MF, Chen SM, Lue YJ. The relative and absolute reliability of leg muscle strength testing by a handheld dynamometer. *J Strength Cond Res* 2011; **25**: 1065–71
22. Krishnan C, Williams GN. Evoked tetanic torque and activation level explain strength differences by side. *Eur J Appl Physiol* 2009; **106**: 769–74
23. Ostenberg A, Roos E, Ekdahl C, Roos H. Isokinetic knee extensor strength and functional performance in healthy female soccer players. *Scand J Med Sci Sports* 1998; **8**: 257–64
24. Veal C, Auyong DB, Hanson NA, Allen CJ, Strodtbeck W. Delayed quadriceps weakness after continuous adductor canal block for total knee arthroplasty: a case report. *Acta Anaesthesiol Scand* 2014; **58**: 362–4
25. Chen J, Lesser JB, Hadzic A, Reiss W, Resta-Flarer F. Adductor canal block can result in motor block of the quadriceps muscle. *Reg Anesth Pain Med* 2014; **39**: 170–1
26. Cappelleri G, Ambrosoli AL, Turconi S, Gemma M, Ricci EB, Cornaggia G. Effect of local anesthetic dilution on the onset time and duration of double-injection sciatic nerve block: a prospective, randomized, blinded evaluation. *Anesth Analg* 2014; **119**: 489–93
27. Madison SJ, Monahan AM, Agarwal RR, *et al*. A randomized, triple-masked, active-controlled investigation of the relative effects of dose, concentration, and infusion rate for continuous popliteal–sciatic nerve blocks in volunteers. *Br J Anaesth* 2015; **114**: 121–9
28. Gillespie RJ, Levine A, Fitzgerald SJ, *et al*. Gender differences in the anatomy of the distal femur. *J Bone Joint Surg Br* 2011; **93**: 357–63

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