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Original Article

A randomised controlled trial of intravenous dexmedetomidine added to dexamethasone for arthroscopic rotator cuff repair and duration of interscalene block

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Summary

Prolongation of peripheral nerve blockade by intravenous dexamethasone may be extended by intravenous dexmedetomidine. We randomly allocated 122 participants who had intravenous dexamethasone 0.15 mg.kg^{-1} before interscalene brachial plexus block for day-case arthroscopic rotator cuff repair to intravenous saline (62 participants) or intravenous dexmedetomidine 1 μg.kg^{-1} (60 participants). The primary outcome was time from block to first oral morphine intake during the first 48 postoperative hours. Fifty-nine participants reported taking oral morphine, 25/62 after placebo and 34/60 after dexmedetomidine, p = 0.10. The time to morphine intake was shorter after dexmedetomidine, hazard ratio (95%CI) 1.68 (1.00–2.82), p = 0.049. Median (IQR [range]) morphine doses were 0 (0–12.5 [0–50]) mg after control vs. 10 (0–30 [0–50]) after dexmedetomidine, a difference (95%CI) of 7 (0–10) mg, p = 0.056. There was no effect of dexmedetomidine on pain at rest or on movement. Intra-operative hypotension was recorded for 27/62 and 50/60 participants after placebo vs. dexmedetomidine, respectively, p < 0.001. Other outcomes were similar, including durations of sensory and motor block. In conclusion, dexmedetomidine shortened the time to oral morphine consumption after interscalene block combined with dexamethasone and caused intra-operative hypotension.

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Introduction

Intravenous and perineural dexamethasone prolong analgesia for about 8 h after peripheral nerve block [1–3]. Dexmedetomidine may also prolong peripheral nerve blockade by perhaps 6 h [4]. Intravenous dexamethasone may provide superior analgesia to perineural dexamethasone and perineural dexmedetomidine [5].

Intravenous dexmedetomidine may prolong analgesia provided by interscalene brachial plexus block for shoulder surgery [6]. We think that the 66-h duration of analgesia

reported in that trial cannot be explained by the individual pharmacokinetic properties of dexmedetomidine and dexamethasone, unless their combination exhibits synergy.

We aimed to test whether dexmedetomidine prolonged the time to postoperative oral morphine after interscalene block combined with intravenous dexamethasone used for arthroscopic rotator cuff repair.

Methods

We conducted and reported this prospectively registered randomised controlled trial as standard [7]. The Ethics Committee of the University Hospital of Clermont Ferrand approved the trial. We studied adults (aged ≥ 18 y), ASA physical status 1–3, scheduled for arthroscopic rotator cuff repair between October 2020 and December 2021. We did not study patients with coagulopathy, infection near the operative site, allergy to study drugs, patients prescribed opioids and pregnant women. Informed participants signed consent. A computer-generated randomisation sequence was used to block allocate participants, five to each group. Each allocation was sealed in an opaque envelope, opened on the day of surgery by the participant's anaesthetist. The control was 100 ml intravenous saline infused over 30 min, containing dexamethasone 0.15 mg.kg^{-1}, after the induction of general anaesthesia. The saline for the intervention group contained dexmedetomidine 1 μg.kg^{-1}, as well as dexamethasone 0.15 mg.kg^{-1}.

Participants were given sublingual midazolam 0.1 mg.kg^{-1} mg before the anaesthetist performed an interscalene block, with intravenous access and standard monitoring. Under sterile conditions, the interscalene brachial plexus was identified with a high-frequency linear array transducer (12–8 MHz, Logiq V2, General Electric, Boston, MA, USA). A 22-gauge 50-mm insulated short-bevel block needle (Vygon Echoplex, Vygon, Ecouen, France) connected to a nerve stimulator (Stimuplex-HNS II A; B. Braun Melsungen AG, Germany) was inserted in-plane with the ultrasound beam, in a lateral-to-medial direction, until the needle tip was positioned between the C5 and C6 roots [8, 9]. The needle was not repositioned during injection of 20 ml ropivacaine 0.75%, unless the participant complained of paraesthesia, or the nerve sheath expanded on injection or muscle contraction was stimulated with a current ≤ 0.6 mA at 1 Hz. A further 10 ml ropivacaine 0.75% was injected if there was residual motor or sensory function innervated by C5 and C6 nerve roots 30 min later.

General anaesthesia was induced with propofol 1.5–3 mg.kg^{-1} and sufentanil 0.05–0.15 μg.kg^{-1}. Cisatracurium 0.15 mg.kg^{-1} facilitated tracheal intubation. Participants' lungs were ventilated with air supplemented with oxygen. Anaesthesia was maintained with sevoflurane. Intravenous atropine, ephedrine, phenylephrine and sufentanil were used as necessary to maintain mean arterial pressure and heart rate within 20% of pre-operative values. Intravenous paracetamol, ketoprofen, nefopam and droperidol 1.25 mg were injected after induction. A surgeon (AG) performed all operations. Postoperatively, participants were given paracetamol 1 g and nefopam 20 mg every 6 h and ketoprofen 100 mg every 12 h, supplemented by oral morphine 10 mg as necessary every 6 h.

The primary outcome was the time from the block to the first morphine dose, recorded by the participant in a diary after hospital discharge. Secondary outcomes were: time from injection to first shoulder paraesthesia; time from injection to first movement; pain scores (0–10) at rest and on movement 4 h, 12 h, 24 h and 48 h after surgery; cumulative oral morphine dose at 48 h; satisfaction with analgesia, measured with a Likert scale at 96 h; and events such as bradycardia, hypotension, infection, neuropathic pain, paraesthesia and muscle weakness up to 96 h. Participants were discharged home with a diary once recovered. We telephoned participants 24 h, 48 h and 96 h after surgery to ask them the times for these outcomes. An independent organisation (Euraxi Pharma, Joué-lès-Tours, France) verified electronic case records, consent signatures and peri-operative measurements.

We calculated that 49 participants in each group would provide 80% power to reject the null hypothesis at α 0.5 for a 20% increase by dexmedetomidine of mean (SD) time to first morphine intake, from 20.8 (7.5) h in participants without dexmedetomidine (unpublished data). We planned to recruit 61 participants to each group to account for drop-out and protocol violation. We analysed results on an intention-to-treat basis. We used the log-rank test for time to first oral morphine. We used mixed-effects linear models for pain and satisfaction, with group, time and their interactions as fixed effects and the participant as a random effect. We used Student t-test, Wilcoxon rank test, chi-squared test and Fisher's exact test as appropriate. We declared non-zero effect for differences with two-tailed $p < 0.05$. We used Stata for analyses (version 16.1, StataCorp, College Station, TX, USA).

Results

We recruited 122 participants (Table 1 and Fig. 1). Fifty-nine participants reported taking oral morphine: 25/62 after placebo and 34/60 after dexmedetomidine, $p = 0.10$. The time to morphine intake was shorter after dexmedetomidine, hazard ratio (95%CI) 1.68 (1.00–2.82), $p = 0.049$ (Fig. 2). Median (IQR [range]) morphine doses were 0 (0–12.5

Table 1 Characteristics for participants allocated to pre-operative saline (control) or dexmedetomidine. Values are number or mean (SD).

	Control n = 62	Dexmedetomidine n = 60	p value
Sex; male	22	23	
Age; y	57.1 (7.2)	57.5 (7.7)	
Weight; kg	78.2 (19.0)	79.7 (16.4)	
Height; cm	170.3 (8.7)	170.0 (8.6)	
BMI; $kg.m^{-2}$	26.7 (5.2)	27.5 (5.3)	
ASA physical status; 1/2	39/23	29/31	
Duration of surgery; min	52.7 (14.3)	49.0 (16.5)	0.18

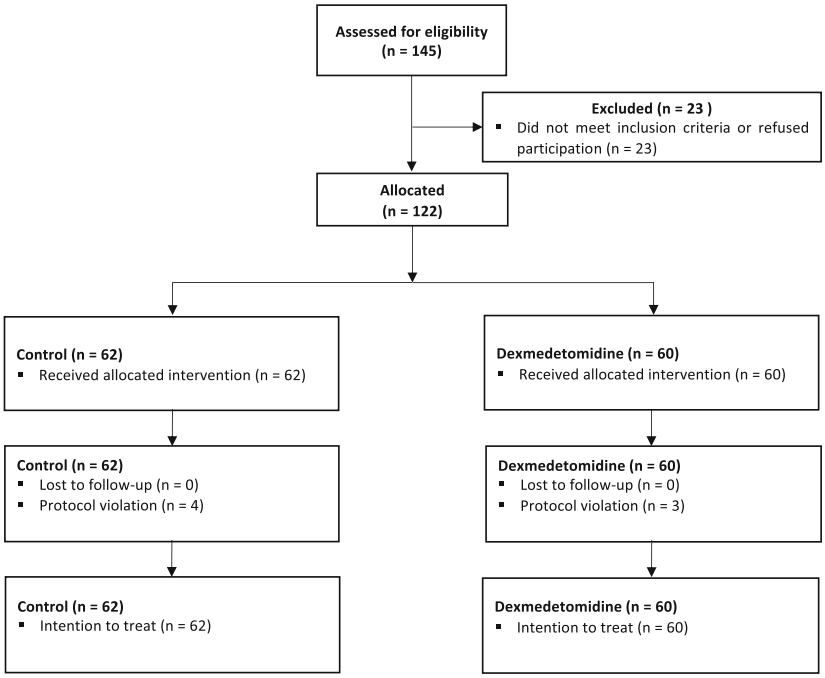

Figure 1 Study flow diagram.

[0–50]) mg after control vs. 10 (0–30 [0–50]) mg after dexmedetomidine, a difference (95%CI) of 7 (0–10) mg, p = 0.056. Control and intervention median (IQR [range]) durations of sensory block were 18 (15–21 [4–31]) h vs. 17 (14–20 [5–31]) h, respectively, p = 0.49. The equivalent durations of motor block were 21 (18–23 [7–43]) h vs. 20 (18–22 [8–48]) h, respectively, p = 0.33. Pain scores at rest and on movement were unaffected by dexmedetomidine, p = 0.68 and p = 0.40, respectively (Fig. 3). The median (IQR [range]) satisfaction level was 3 (2–3 [0–3]) in both groups, p = 0.52.

We recorded intra-operative bradycardia for 1/62 and 3/60 participants after placebo vs. dexmedetomidine, respectively, p = 0.36, and intra-operative hypotension for 27/62 and 50/60 participants after placebo vs. dexmedetomidine, respectively, $p < 0.001$. We did not report any other adverse events.

Discussion

We found that dexmedetomidine shortened rather than prolonged time to oral morphine intake and might have increased morphine dose. Dexmedetomidine did not affect the duration of interscalene sensory or motor blockade. Intra-operative hypotension was more frequent after dexmedetomidine.

We conducted this trial because dexmedetomidine has been reported to prolong the analgesia provided by interscalene blockade combined with intravenous

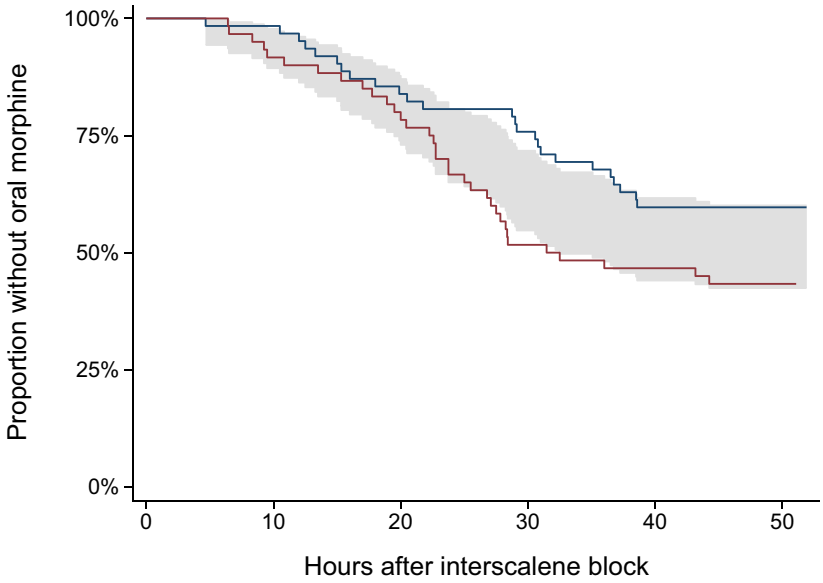

Figure 2 Kaplan–Meier estimates of time from interscalene block to first oral morphine intake in the first 48 h after day-case arthroscopic rotator cuff repair, after pre-operative intravenous saline (blue line) vs. intravenous dexmedetomidine (red line). Line lengths outside the grey shaded area differ at the 95%CI level.

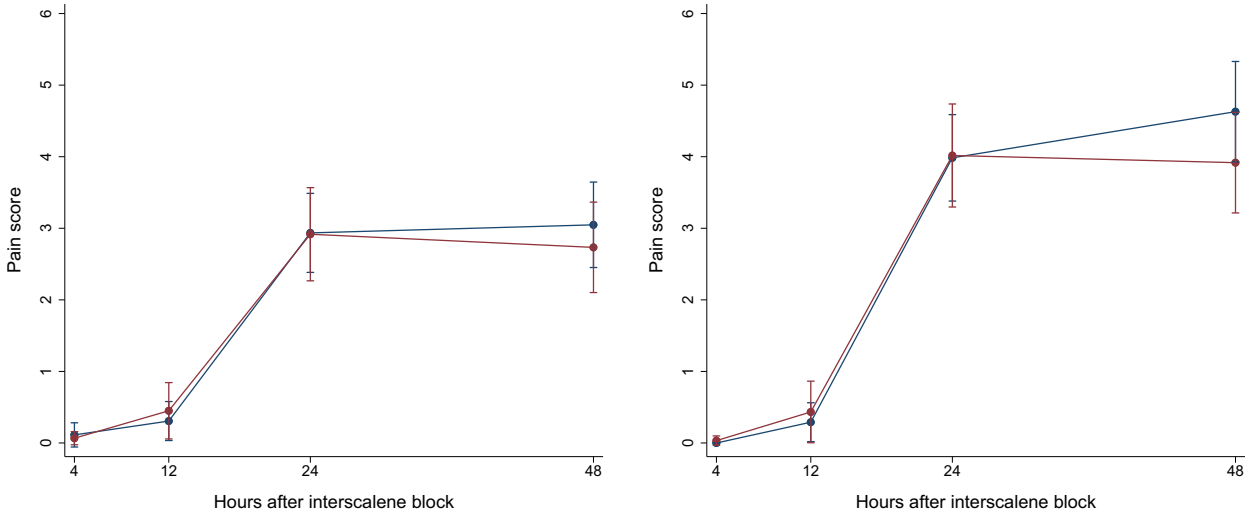

Figure 3 Postoperative pain scores (a) at rest and (b) on movement. Values are mean (95%CI). There were no significant effects of dexmedetomidine on pain at rest, p = 0.68, or on movement, p = 0.40.

dexamethasone [6]. We cannot explain the discrepancies between that trial and our results, given the similarities in participants and interventions. Trials in different populations with different routes of administration have reported conflicting results [10–12]. We did not blind the anaesthetist to the intervention, which could have systematically biased the results. Observations recorded by participants at home were not independently verified.

In conclusion, we think that dexmedetomidine is unlikely to benefit patients after arthroscopic rotator cuff repair when interscalene blockade is combined with other analgesics and its duration is extended by intravenous dexamethasone.

Acknowledgements

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References

1. Albrecht E, Kern C, Kirkham KR. A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. *Anaesthesia* 2015; **70**: 71–83.
2. Kirkham KR, Jacot-Guillarmod A, Albrecht E. Optimal dose of perineural dexamethasone to prolong analgesia after brachial plexus blockade: a systematic review and meta-analysis. *Anesthesia and Analgesia* 2018; **126**: 270–9.
3. Baeriswyl M, Kirkham KR, Jacot-Guillarmod A, Albrecht E. Efficacy of perineural vs systemic dexamethasone to prolong analgesia after peripheral nerve block: a systematic review and meta-analysis. *British Journal of Anaesthesia* 2017; **119**: 183–91.
4. Albrecht E, Vorobeichik L, Jacot-Guillarmod A, Fournier N, Abdallah FW. Dexamethasone is superior to dexmedetomidine as a perineural adjunct for supraclavicular brachial plexus block: systematic review and indirect meta-analysis. *Anesthesia and Analgesia* 2019; **128**: 543–54.
5. Sehmbi H, Brull R, Ceballos KR, et al. Perineural and intravenous dexamethasone and dexmedetomidine: network meta-analysis of adjunctive effects on supraclavicular brachial plexus block. *Anaesthesia* 2021; **76**: 974–90.
6. Kang RA, Jeong JS, Yoo JC, et al. Improvement in postoperative pain control by combined use of intravenous dexamethasone with intravenous dexmedetomidine after interscalene brachial plexus block for arthroscopic shoulder surgery: a randomised controlled trial. *European Journal of Anaesthesiology* 2019; **36**: 360–8.
7. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *PLoS Medicine* 2010; **7**: e1000251.
8. Albrecht E, Kirkham KR, Taffe P, et al. The maximum effective needle-to-nerve distance for ultrasound-guided interscalene block: an exploratory study. *Regional Anesthesia and Pain Medicine* 2014; **39**: 56–60.
9. Palhais N, Brull R, Kern C, Jacot-Guillarmod A, Charmoy A, Farron A, Albrecht E. Extrafascial injection for interscalene brachial plexus block reduces respiratory complications compared with a conventional intrafascial injection: a randomized, controlled, double-blind trial. *British Journal of Anaesthesia* 2016; **116**: 531–7.
10. Chassery C, Marty P, Rontes O, et al. Total knee arthroplasty under quadruple nerve block with ropivacaine 0.32%: effect of addition of intravenous dexmedetomidine to intravenous dexamethasone on analgesic duration. *Regional Anesthesia and Pain Medicine* 2021; **46**: 104–10.
11. Zhang P, Liu S, Zhu J, Rao Z, Liu C. Dexamethasone and dexmedetomidine as adjuvants to local anesthetic mixture in intercostal nerve block for thoracoscopic pneumonectomy: a prospective randomized study. *Regional Anesthesia and Pain Medicine* 2019; **47**: 554–9.
12. Aliste J, Layera S, Bravo D, et al. Randomized comparison between perineural dexamethasone and combined perineural dexamethasone-dexmedetomidine for ultrasound-guided infraclavicular block. *Regional Anesthesia and Pain Medicine* 2022; **47**: 554–9.

