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REPORTS OF ORIGINAL INVESTIGATIONS

Low dose intravenous dexamethasone (4 mg and 10 mg) significantly prolongs the analgesic duration of single-shot interscalene block after arthroscopic shoulder surgery: a prospective randomized placebo-controlled study

La dexaméthasone intraveineuse à des doses de 4 mg ou de 10 mg prolonge significativement la durée analgésique du bloc interscalénique simple suite à une chirurgie arthroscopique de l'épaule: une étude prospective, randomisée et contrôlée avec placebo

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Abstract

Background *Although intravenous dexamethasone prolongs the analgesic duration of interscalene brachial plexus block, it is uncertain whether this effect can be observed using lower doses of dexamethasone. This study evaluated the impact of intravenous dexamethasone (4 mg and 10 mg) on the analgesic duration of single-shot interscalene block after arthroscopic shoulder surgery. We hypothesized that both doses would prolong the analgesic duration compared with placebo.*

Methods *This was a prospective double-blind randomized placebo-controlled study in patients undergoing elective arthroscopic shoulder surgery under regional anesthesia with a single-shot interscalene block (0.5% ropivacaine 20 mL). Patients received dexamethasone 4 mg (D4), dexamethasone 10 mg (D10), or a placebo (normal saline [NS]) intravenously at the time of block completion. The primary outcome was the duration of analgesia, defined as the time from the onset of sensory blockade to the first analgesic request. The primary outcome was first analyzed with a Kruskal-Wallis test and then with a Mann-Whitney test for pairwise between-group comparison.*

Results *Sixty-nine patients completed the study. The median [interquartile range] duration of analgesia was significantly different between the three groups (D4, 19.7 [16.9-23.3] hr; D10, 19.1 [11.5-22.8] hr; and NS, 11.8 [9.3-14.0] hr; $P = 0.001$). This difference was statistically significant for D4 and D10 compared with placebo (median difference [MD], 7.8 hr; 95% confidence interval [CI], 4.6 to 11.1 hr; $P < 0.001$; and MD, 7.4 hr; 95% CI, 4.2 to 10.5 hr; $P = 0.001$, respectively) but not for D4 compared with D10 (MD, 0.5 hr; 95% CI, −2.8 to 3.7 hr; $P = 0.38$).*

Conclusions *Low doses of intravenous dexamethasone (4 mg and 10 mg) significantly prolong the analgesic duration of interscalene block. This trial was registered at ClinicalTrials.gov (NCT02412657).*

Résumé

Contexte *La dexaméthasone intraveineuse prolonge la durée analgésique du bloc interscalénique du plexus*

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brachial, mais il n'est pas certain que cet effet soit reproduit avec de plus faibles doses. Le but de cette étude était d'évaluer l'impact de deux doses différentes de dexaméthasone (4 mg et 10 mg) sur la durée analgésique du bloc interscalénique simple suite à une chirurgie arthroscopique de l'épaule. Nous avons testé l'hypothèse selon laquelle les deux doses prolongent cette durée analgésique, comparativement au placebo.

Méthode *Cette étude prospective, randomisée et contrôlée à double insu avec placebo a été réalisée auprès de patients qui se présentaient pour une chirurgie arthroscopique de l'épaule sous bloc interscalénique (20 mL de ropivacaïne 0,5%). Les patients ont reçu en intraveineux soit: dexaméthasone 4 mg (D4), dexaméthasone 10 mg (D10) ou un placebo [normal salin (NS)]. Le critère d'évaluation principal était la durée analgésique du bloc interscalénique, définie par le temps écoulé entre l'amorce du bloc sensitif et la première prise de médication analgésique orale, et a premièrement été analysé avec un test de Kruskal-Wallis suivi d'un test de Mann-Whitney pour la comparaison des groupes.*

Résultats *Soixante-neuf patients ont complété l'étude. La durée analgésique médiane [écart interquartile] était significativement différente entre les trois groupes (D4: 19,7 [16,9-23,3] h, D10: 19,1 [11,5-22,8] h, et NS: 11,8 [9,3 -14,0] h; P = 0,001). Cette différence était statistiquement significative lorsque les groupes D4 et D10 étaient comparés au placebo (différence médiane, 7,8; intervalle de confiance [IC] 95%, 4,6 à 11,1 h; P < 0,001; et 7,4; IC 95%, 4,2 à 10,5 h; P = 0,001, respectivement) mais pas lorsque les groupes D4 et D10 étaient comparés entre eux (différence médiane, 0,5 h; IC 95%, −2,8 à 3,7 h; P = 0,38).*

Conclusion *Les doses de 4 et de 10 mg de dexaméthasone intraveineuse prolongent toutes deux significativement la durée analgésique du bloc interscalénique. Cette étude a été enregistrée au ClinicalTrials.gov (NCT02412657).*

Postoperative pain after arthroscopic shoulder surgery can be very severe during the first 48 hr. Interscalene brachial plexus block (ISB) is widely accepted as the method of choice in the management of acute pain after shoulder surgery,[1] but it is often insufficient because postoperative pain frequently outlasts its analgesic duration.

Intravenous administration of dexamethasone 8-10 mg significantly increases ISB analgesic duration after arthroscopic shoulder surgery.[2,3] Nevertheless, these doses of dexamethasone may induce undesirable side effects such as hyperglycemia and perineal pruritus.[4,5] A lower dose of dexamethasone might minimize these events, but its efficacy remains uncertain. Indeed, Kawanishi *et al.*[6] found that intravenous dexamethasone 4 mg did not extend the analgesic duration of an ISB performed with 0.75% ropivacaine 20 mL. Nevertheless, their finding might have resulted from a lack of power due to their small sample size and from differences in outcome measurements. Even so, their results were in accordance with a meta-analysis that concluded that dexamethasone at doses < 0.1 mg·kg^{-1} had no effect on postoperative analgesia and opioid consumption.[7]

In contrast, one recently published study showed that intravenous dexamethasone in doses of 2.5 mg and 10 mg significantly prolong the analgesic duration of ISB performed with 0.5% ropivacaine 30 mL when compared with placebo and dexamethasone 1.25 mg.[8] Nevertheless, this study was the only one to suggest that smaller doses of dexamethasone can increase the analgesic duration of ISB, and these results need to be confirmed by other studies.

We conducted a prospective randomized-controlled study to evaluate the effect of intravenous dexamethasone 4 mg and 10 mg on the analgesic duration of ISB after arthroscopic shoulder surgery when compared with placebo. A 4-mg dose was chosen because it is frequently used in anesthetic practice. Our primary outcome was the analgesic duration of ISB, defined as the time from onset of ISB sensory blockade to the first analgesic request. We hypothesized that both doses would significantly increase the analgesic duration compared with placebo. Secondary outcomes included differences in pain scores and cumulative opioid consumption (at 12, 24, 36, and 48 hr postoperatively), sleep disruption on the first and second postoperative nights, residual motor weakness at 24 and 48 hr postoperatively, patient satisfaction, differences in blood glucose levels, and the incidence of perineal pruritus after intravenous dexamethasone injection.

Methods

This study was approved by the Institutional Review Board of Hôpital Maisonneuve-Rosemont, Montréal, QC, Canada (MP-HMR-14-002, October 7 2014). This was a multicentre prospective double-blind randomized placebo-controlled study conducted at three different sites (Hôpital Maisonneuve-Rosemont, Hôtel-Dieu de Sorel, and Hôpital Pierre-Boucher).

Inclusion criteria were patients with American Society of Anesthesiologists (ASA) physical status I-III, aged 18-80 yr, and scheduled for elective ambulatory arthroscopic shoulder surgery (rotator cuff repair, Bankart repair, or subacromial decompression) performed under regional anesthesia with single-shot ISB. Exclusion criteria

included patients with contraindications to interscalene block (coagulopathies, severe bronchopulmonary disease, contralateral diaphragmatic paralysis, prior contralateral pneumonectomy, preexisting neuropathy involving the surgical limb), preference for general anesthesia, allergy or intolerance to one or more medications of the study protocol (dexamethasone, acetaminophen, morphine, or hydromorphone), chronic pain syndrome, chronic opioid use, chronic systemic corticosteroid use, weight < 50 kg, or pregnancy, and patient refusal.

The research nurse contacted all eligible patients by phone a few days before their surgery to inform them about the study protocol. An information and consent form was sent by e-mail to those interested in participating in the study. On the morning of surgery, patients signed the informed consent form and received instructions about the pain numeric rating scale (NRS) from 0 to 10 (0 = no pain at all; 10 = worst pain imaginable).

Randomization, blinding, and study drug preparation

A computer-generated list with random block size was used[9] to randomize patients into three groups: dexamethasone 4 mg (D4), dexamethasone 10 mg (D10), or placebo (normal saline [NS]). A research nurse prepared and numbered 75 sealed opaque envelopes according to this list. Arthroscopic shoulder surgeries were performed on different days at each hospital site. Skilled anesthesiology residents performed the blocks at all three sites under the direct supervision of attending anesthesiologists experienced with the ISB technique. Each recruiting day, the anesthesiology resident scheduled to perform the blocks brought a number of sealed envelopes corresponding to the number of patients expected to enrol. Immediately before each ISB was performed, a dedicated assistant otherwise uninvolved with the study opened an envelopes and prepared the medication according to the assigned group. The study drug was diluted with NS to a final volume of 20 mL (group D4: dexamethasone 4 mg with NS 19 mL; group D10: dexamethasone 10 mg with NS 17.5 mL; group NS: NS 20 mL). Patients, study staff, and clinical personnel were blinded to group allocation.

Interscalene brachial plexus block and study drug administration

Blocks were performed using a combined ultrasound and electrical nerve stimulation technique. Patients were premedicated with intravenous midazolam 1-2 mg and/or fentanyl 25-50 μg after standard ASA monitoring was installed. Patient positioning (supine or lateral) depended on the anesthesiologist's preference. After skin disinfection with chlorhexidine, ultrasound scanning with a high-frequency linear (10-15 Hz) transducer was performed to visualize the nerve roots and nerve trunks in the short-axis view at the level of the sixth cervical vertebra. Lidocaine 2% was infiltrated at the site of puncture and a 22G 50-mm insulated Stimuplex® needle (B.Braun, Canada Ltd, Mississauga, ON, Canada) was inserted and positioned between the fifth and sixth cervical nerve roots using an in-plane posterior approach. Appropriate needle position was confirmed with deltoid, biceps, or triceps muscle contraction at a threshold current of 0.4-0.6 mA. After careful aspiration, local anesthetic was injected. Initial spread was observed, and the needle was repositioned to obtain circumferential distribution of local anesthetic, if needed. In total, 20 mL of 0.5% ropivacaine were injected in a fractionated manner.

Right after ISB completion, an assistant administered the study drug intravenously. The injection was performed slowly over 30 sec to reduce the risk of dexamethasone-induced perineal pruritus.

The patients were then assessed every five minutes for 15 min for the development of sensory blockade using ice over the deltoid region. The ISB onset time was recorded as the time when loss of sensation to cold was achieved. After 15 min, patients with a failed ISB (no sensory blockade at all) or an incomplete ISB (some degree of sensory blockade but not enough to allow surgery without general anesthesia) were excluded from the study.

Surgeries were performed under regional anesthesia. A light-to-moderate sedation (midazolam 1-2 mg *iv* every 30 min and/or propofol 25-100 $\mu g \cdot kg^{-1} \cdot min^{-1}$) could be administered according to the patient's preference. No other analgesic medication (acetaminophen, nonsteroidal anti-inflammatory drugs, opioids, ketamine) was allowed. The need to administer any of these drugs or the need to convert to general anesthesia for any other reason led to patient exclusion from the study.

Postoperative pain management

Upon arrival and discharge in the postanesthesia care unit (PACU), patients were again taught about the NRS and instructed to delay any analgesics until their pain was $\geq 4/10$. Patients left the hospital with a prescription for acetaminophen (650 mg every six hours for seven days) and hydromorphone (1-2 mg) or morphine (5-10 mg) every four hours as needed for pain $\geq$ 4/10 despite regular acetaminophen intake.

When their pain reached a score of $\geq 4/10$, patients were instructed to start taking the acetaminophen with or without the opioid and then to continue this medication as prescribed. They were asked to record the date and time

at which this first analgesic request occurred as well as all further use of medication in the first 48 hr.

Data collection

Preoperative

The following preoperative data were recorded: patient characteristics, including age, sex, diabetes, smoking status, weight, and height, as well as clinical data such as hospital, surgeon, and procedure. The baseline blood glucose level was measured, and times of study drug administration and onset of ISB sensory blockade were collected. Any spontaneous report of pruritus at the moment of study drug administration was recorded.

Intraoperative

Time of skin incision and wound closure, total surgical time, and cumulative dose of midazolam and/or propofol were recorded.

Postoperative

A postoperative blood glucose level was measured at the patient's arrival in the PACU. All patients were given a diary in which to record their pain ratings using the NRS as well as the date, time, and dose of all analgesic medication used in the first 48 hr. The initial intent was to collect pain ratings every six hours until 48 hr postoperatively, but the resulting diary would have been dense and confusing. The authors predicted that this could lead to patients only partially completing their diary. Hence, before data collection began, they decided to collect patients' pain scores only at 12, 24, 36, and 48 hr after surgery. Patients also rated their sleep disruption on the first and second postoperative nights using a numeric sleep disruption scale from 0 to 10 (0 = no sleep disruption, and 10 = maximal sleep disruption) and the degree of motor blockade at 24 and 48 hr using a numeric strength scale from 0 to 2 (0 = complete motor blockade - no forearm/hand/finger movement at all; 1 = residual motor weakness (forearm/hand/finger movement, weaker than normal); 2 = normal strength (forearm/hand/finger movement, as normal). Upon completion of the study period, patients were asked to return their diary by mail using a prepaid envelope. In addition, a blinded research staff member contacted the patients by telephone on postoperative days 1 and 2 to remind them about the diary, inquire about the time of the first analgesic request, and assess patient's satisfaction about their anesthesia and analgesia. Patient satisfaction was a binary outcome (yes = satisfied - I would want exactly the same anesthesia and analgesia method if I had to undergo the same surgery; no = unsatisfied - I would prefer a different anesthesia and/or analgesia method if I had to undergo the same surgery).

The primary outcome was the difference in the duration of ISB analgesia between groups, defined as the time from onset of ISB sensory blockade to the time of the first analgesic request. First analgesic request occurred when patients rated their pain $\geq$ 4/10. This applied for patients both at home or in the PACU. Secondary outcomes included differences in NRS pain scores and cumulative opioid consumption (at 12, 24, 36, and 48 hr postoperatively), sleep disruption on the first and second nights after surgery, residual motor weakness at 24 and 48 hr postoperatively, patient satisfaction, differences in the variation of blood glucose levels, and the incidence of perineal pruritus after intravenous dexamethasone injection. Total opioid doses were converted to oral hydromorphone equivalents according to the conversion rates given by the American Pain Society.[10]

Statistical analysis

Sample size calculation

Based on our clinical experience and on work by Fredrickson *et al.*,[11] the median [interquartile range (IQR)] duration of analgesia obtained with 0.5% ropivacaine 20 mL was set at 11.5 [10.0-16.8] hr. According to the method for Cochrane reviews,[12] this IQR was converted to a standard deviation (SD) of five hours. Sample size calculation (powerandsamplesize.com) revealed that three groups of 21 patients would provide a power of 90%, with an alpha = 0.05, to detect a 50% difference in analgesic duration with dexamethasone.[13] To allow for loss to follow-up and exclusion after randomization, we allocated 25 patients in each of the three arms of the study for 75 patients in total.

Data analysis

Data were analyzed using IBM SPSS® Statistics, Version 20.0 (IBM Corp. Armonk, NY, USA). All continuous variables were analyzed with a one-sample Kolmogorov-Smirnov test to assess for normality. Demographic data are presented as mean (SD). Time to first analgesic request, cumulative opioid consumption (at 12, 24, 36, and 48 hr), and sleep disruption scores are presented as median [IQR]. Numeric rating scale pain scores at 12, 24, 36, and 48 hr and blood glucose variations are presented as mean (SD). Data for number of patients, including residual motor weakness at 24 and 48 hr, incidence of perineal pruritus, and patient satisfaction are presented as *n* (%), as appropriate.

Demographic and perioperative continuous and categorical data were analyzed using one-way analysis of variance (ANOVA) or Kruskal-Wallis and Chi square tests, respectively. The primary outcome, median ISB analgesic duration, was analyzed with a Kruskal-Wallis test, and the difference between groups was analyzed using a Mann-Whitney U test with a Bonferroni's correction for multiple testing. A sensitivity analysis, including patients with failed or incomplete blocks and those who converted to general anesthesia, was also performed for the primary outcome using the same tests. These patients were given an analgesic duration of zero hour. All secondary outcomes were analyzed using a Kruskal-Wallis test, except for pain scores at 12, 24, 36, and 48 hr and variations in blood glucose levels, which were analyzed using a one-way ANOVA, and incidence of perineal pruritus, which was analyzed using a Fisher's exact test. A $P < 0.05$ was considered significant, except for the Mann Whitney U test used for between group differences. For that comparison, a P value < 0.0167 (= 0.05/3) was considered significant.

Results

From October 2014 to October 2015, 103 patients were assessed for eligibility and 75 patients were randomized. Six patients were excluded after randomization: two patients had a failed ISB, two patients had an incomplete ISB, and two patients' procedures were converted to general anesthesia upon the surgeon's request because of agitation and anxiety that could not be controlled with propofol. Sixty-nine patients (22 in group NS, 23 in group D4, and 24 in group D10) completed the study (Fig. 1).

Baseline demographics and surgical characteristics were comparable between groups (Table 1).

Primary outcome

The median [IQR] duration of analgesia was significantly different between the three groups (NS, 11.8 [8.7-13.8] hr; D4, 19.6 [16.0-22.2] hr; and D10, 19.1 [11.5-22.8] hr; $P = 0.001$) (Fig. 2). Comparison between groups showed that

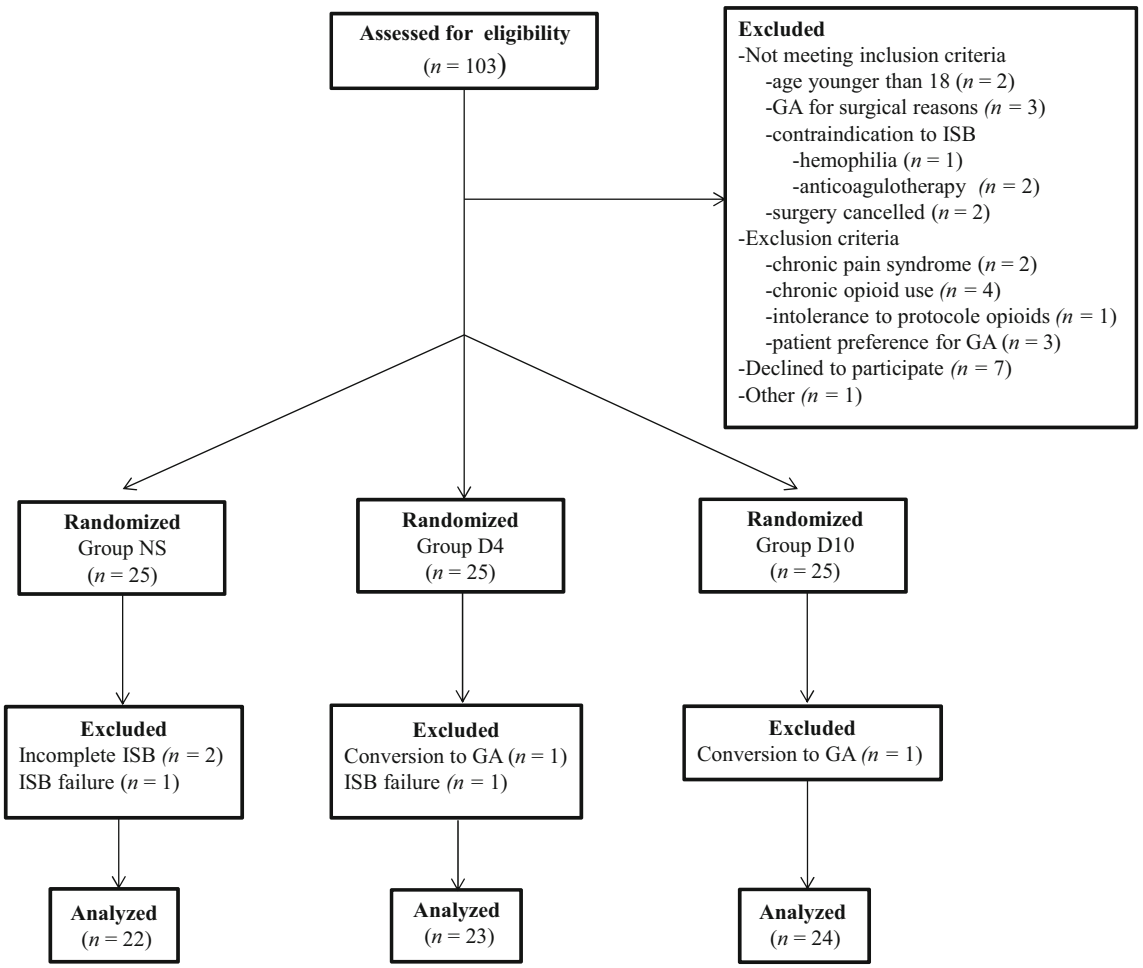

Fig. 1 Patient flow diagram. GA = general anesthesia; ISB = interscalene brachial plexus block

Table 1 Characteristics of the study population (n = 69)

	NS (n = 22)	D4 (n = 23)	D10 (n = 24)
Age (yr)	54.7 (7.4)	54.7 (10.5)	48.8 (12.4)
Sex (male)	11 (50%)	12 (52%)	17 (70%)
Weight (kg)	74.6 (9.1)	80.3 (14.1)	81.9 (20.0)
Height (cm)	165 (8)	168 (10)	173 (9)
BMI ($kg \cdot m^{-2}$)	27.4 (3.5)	28.7 (4.9)	27.1 (5.2)
BMI > 35	1 (5%)	4 (17%)	3 (13%)
Diabetes	0 (0%)	1 (4%)	0 (0%)
Smoking	3 (14%)	4 (17%)	3 (13%)
Type of surgery			
Rotator cuff repair	14 (64%)	14 (61%)	10 (42%)
Bankart repair	0 (0%)	0 (0%)	2 (8%)
Decompression	8 (36%)	9 (39%)	12 (50%)
Surgery duration (min)	32 (23)	24 (22)	32 (24)
Hospitals			
HMR	4 (57%)	1 (14%)	2 (29%)
HDS	7 (24%)	11 (38%)	11 (38%)
HPB	11 (33%)	11 (33%)	11 (33%)
Surgeons			
1	2 (40%)	1 (20%)	2 (40%)
2	2 (100%)	0 (0%)	0 (0%)
3	19 (31%)	22 (36%)	20 (33%)
4	0 (0%)	0 (0%)	1 (100%)
Delay between block and incision (min)	53 (28)	53 (26)	69 (44)
Total midazolam (mg)	1.5 (1.3)	1.5 (1.3)	1.5 (1.3)
Total propofol (mg)	137 (205)	94 (107)	165 (228)
Baseline blood glucose level ($mMol \cdot L^{-1}$)	5.3 (0.6)	5.4 (0.9)	5.0 (0.7)

Data are presented as mean (SD) or absolute number (%), as appropriate. BMI = body mass index; HDS = Hôtel-Dieu de Sorel; HMR = Hôpital Maisonneuve-Rosemont; HPB = Hôpital Pierre-Boucher; D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline; SD = standard deviation

the median difference (MD) was statistically significant for D4 and D10 compared with placebo (MD, 7.8 hr; 95% confidence interval [CI], 4.6 to 11.1 hr; $P < 0.001$; and MD, 7.4 hr; 95% CI, 4.2 to 10.5 hr; $P = 0.001$, respectively) but not for D4 compared with D10 (MD, 0.5 hr; 95% CI, -2.8 to 3.7 hr; $P = 0.38$).

The sensitivity analysis, including patients with failed or incomplete blocks and those who converted to general anesthesia, also showed that the median [IQR] duration of analgesia was significantly different between the three groups (NS, 10.8 [8.2-13.7] hr; D4, 19.2 [15.8-22.1] hr; and D10, 19.1 [11.1-22.5] hr; $P < 0.001$). Similarly, this difference was statistically significant for D4 and D10 compared with placebo (MD, 8.4 hr; 95% CI, 5.3 to 11.5 hr; $P < 0.001$; and MD, 8.3 hr; 95% CI, 5.2 to 11.4 hr; $P =$

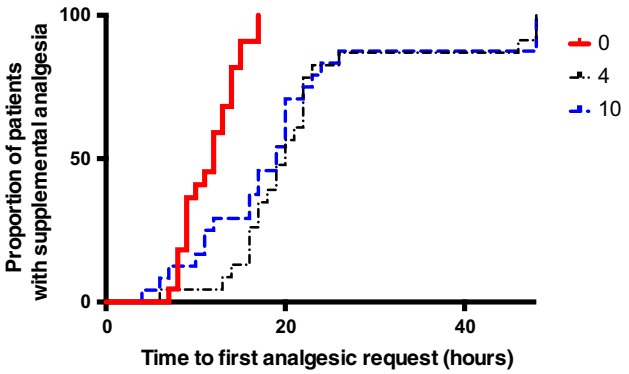

Fig. 2 Depiction of primary outcome (analgesic duration of ISB defined as the time from the onset of ISB sensory blockade to the first analgesic request), according to study group (red = group NS; black = group D4; blue = group D10). Median duration of analgesia (Kruskal-Wallis test), $P = 0.001$. Between-group comparisons (Mann-Whitney U test): D4 compared with NS, D10 compared with NS, and D4 compared with D10 ($P < 0.001$; $P = 0.001$; and $P = 0.38$, respectively). ISB = interscalene brachial plexus block; D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

0.001, respectively) but not for D4 compared with D10 (MD, 0.1 hr; 95% CI, -3.0 to 3.2 hr; $P = 0.57$).

Secondary outcomes

Mean NRS pain scores at 12, 24, 36, and 48 hr postoperatively revealed pain of moderate intensity at 24, 36, and 48 hr, though not significantly different between groups (Table 2). Cumulative hydromorphone use was significantly different between groups at 12, 24, and 36 hr postoperatively, but not at 48 hr (Table 3) (Fig. 3).

Compared with placebo, groups receiving dexamethasone experienced less sleep disruption on the first postoperative night, but this difference was not found on the second postoperative night (Table 4).

At 24 and 48 hr after surgery, a small proportion of patients reported residual motor weakness (score of 1/2), but no patient reported complete motor block (score of 0/2). There was no difference between groups (Table 5). Overall, patient satisfaction was excellent in all three groups: NS, 21/22 (95%); D4, 23/23 (100%); D10, 24/24 (100%) ($P = 0.33$).

Dexamethasone caused a significant increase in mean (SD) variation in blood glucose level compared with placebo [NS, 0 (0.8) $mMol \cdot L^{-1}$; D4, 0.8 (0.9) $mMol \cdot L^{-1}$; D10, 0.7 (0.7) $mMol \cdot L^{-1}$; $P = 0.001$]. This difference was significant only when comparing group NS with groups D4 and D10 ($P = 0.003$ and $P = 0.004$, respectively) but not when comparing groups D4 and D10 ($P = 1.00$). There was only one diabetic patient in the study (group D4) whose blood glucose level was not increased by dexamethasone

Table 2 Pain scores at 12, 24, 36, and 48 hr postoperatively, according to study group

	NS (n = 22)	D4 (n = 23)	D10 (n = 24)	P value
12 hr	1 (0 to 4)	0 (0 to 2)	0 (0 to 4)	0.32
24 hr	5 (4 to 6)	4 (3 to 5)	3 (2 to 4)	0.12
36 hr	5 (4 to 6)	4 (3 to 5)	4 (3 to 5)	0.30
48 hr	4 (3 to 5)	4 (3 to 5)	4 (3 to 5)	0.64

Numeric rating scale from 0-10: 0 = no pain at all; 10 = worst imaginable pain

Data are presented as mean (95% confidence interval). D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

Table 3 Cumulative hydromorphone use during the first 48 hr postoperatively, according to study group (mg)

	NS (n = 22)	D4 (n = 23)	D10 (n = 24)	P value
12 hr*	0.0 [0.0-0.0]	0.0 [0.0-0.0]	0.0 [0.0-0.0]	0.04
24 hr	2.5 [2.0-5.0]	0.0 [0.0-2.0]	2.0 [0.0-2.5]	< 0.01
36 hr	6.5 [3.0-8.0]	2.0 [0.5-4.0]	2.0 [1.0-5.5]	0.04
48 hr	8.5 [3.0-12.0]	3.0 [2.0-7.0]	4.0 [1.0-8.0]	0.22

Data are presented as median [interquartile range]

*Range of cumulative hydromorphone use (mg): NS (0-2); D4 (0-2); D10: (0-3). D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

(pre and postoperative blood glucose levels, 8.7 and 8.1 mMol·L^{-1}, respectively). Four patients spontaneously reported perineal pruritus at the time of dexamethasone injection. All were in group D10 (P = 0.02).

Discussion

This study evaluating intravenous dexamethasone (4 mg and 10 mg) showed that both doses significantly prolong the analgesic duration of ISB after arthroscopic shoulder surgery. This confirms the Desmet study[8] that smaller doses of dexamethasone significantly prolong the analgesic duration of ISB after arthroscopic shoulder surgery when compared with placebo. This also confirms that the study by Kawanishi *et al*. showing a non-significant increase in ISB analgesic duration with dexamethasone 4 mg was likely underpowered.[6] In their study, Desmet *et al.* showed that all doses of intravenous dexamethasone extended ISB analgesia, and higher doses prolonged analgesia more than lower doses, suggesting a dose-effect relationship.[8] When all studies are considered together, the median ISB analgesic durations reported after arthroscopic shoulder surgery using 0.5% ropivacaine 30 mL with intravenous dexamethasone 2.5, 8, and 10 mg are 17.4, 18.2, 20.1, and 21.2 hr, respectively, which also suggests a dose-effect relationship.[2,3,8] Our study did not result in a longer duration of analgesia when increasing the dose from 4-10 mg. Considering the small differences in ISB analgesic durations observed by increasing the dexamethasone dose, our study was likely underpowered to detect any difference. Although it is important to understand the dexamethasone dose-effect relationship, its relevance and clinical importance for patients is uncertain. Indeed, patients from all three groups in this study expressed a high degree of satisfaction despite great differences in analgesic duration between the control and the dexamethasone groups.

The ISBs in this study were performed with 0.5% ropivacaine 20 mL, which is a lower dose than used by

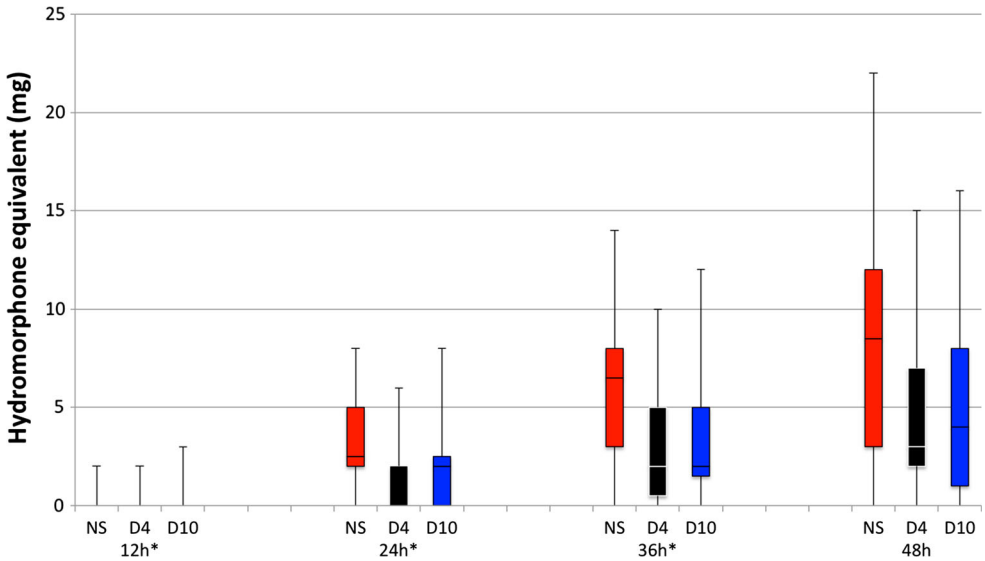

Fig. 3 Cumulative hydromorphone use during the first 48 hr postoperatively, according to study group (red = group NS; black = group D4; blue = group D10). Median cumulative hydromorphone use (Kruskal-Wallis test) at 12, 24, 36, and 48 hr (P = 0.04; P < 0.01; P = 0.04; and P = 0.22, respectively). D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

Table 4 Sleep disruption during the two first postoperative nights, according to study group

	NS (n = 22)	D4 (n = 23)	D10 (n = 24)	P value
First night	7 [5-8]	2 [0-5]	3 [0-5]	< 0.01
Second night	3 [1-5]	3 [1-6]	2 [0-6]	0.96

Numeric sleep disruption scale from 0 to 10: 0 = no sleep disruption; 10 = maximal sleep disruption. Data are presented as median [interquartile range]. D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

Table 5 Patients reporting residual motor weakness at 24 and 48 hr postoperatively, according to study group

	NS (n = 22)	D4 (n = 23)	D10 (n = 24)	P value
24 hr	3 (14%)	5 (22%)	5 (21%)	0.70
48 hr	4 (18%)	3 (13%)	3 (13%)	0.23

Data are presented as absolute number (%). D4 = dexamethasone 4 mg; D10 = dexamethasone 10 mg; NS = normal saline

others. In our experience, 20 mL provide excellent surgical anesthesia for all arthroscopic shoulder surgeries. Despite using a smaller total dose of local anesthetic, we obtained analgesic durations that are similar to those reported with 30 mL. Our study thus shows that ISB performed with lower doses of ropivacaine can still allow for both excellent surgical anesthesia and prolonged postoperative analgesia when combined with a low dose of dexamethasone. This has the potential to increase patient safety by reducing the potential risks of local anesthetic toxicity and avoiding general anesthesia in the beach chair position.[14-17]

Patients in this study reported pain of moderate intensity at 24, 36, and 48 hr after surgery, underscoring the need to prolong postoperative analgesia. An outpatient continuous ISB catheter allows prolonging the analgesia beyond 24 hr.[1] Nevertheless, this more invasive procedure is costly, necessitates a more extensive follow-up and requires good patient collaboration and understanding. The costs and benefits of this procedure would be worth comparing with those of single-shot ISB supplemented with intravenous dexamethasone.

Postoperative pain scores were similar between the three groups, but there was a significantly lower cumulative opioid consumption at 24 hr and 36 hr postoperatively in groups receiving dexamethasone. This difference was not statistically significant at 48 hr, although opioid use in groups receiving dexamethasone was less than half that in the placebo group. Similarly, patients receiving dexamethasone experienced less sleep disruption in the first postoperative night. Opioid avoidance and quality of sleep are very important issues in improving patient care in the postoperative period and can have a considerable impact on overall patient satisfaction.[18]

The mechanism by which intravenous dexamethasone extends the analgesic duration of peripheral nerve blocks is still unclear, but it likely involves peripheral and central anti-inflammatory effects.[19-23] Nevertheless, prolonging the local anesthetic effect could also play a role because extensions in the duration of both sensory and motor blocks have been reported with intravenous dexamethasone[3,24,25] —although these studies were not designed for that purpose. The present study did not show prolongation of the motor block but its assessment was limited by the design of the study. A recent study that specifically addressed the duration of motor block showed increased duration of motor and sensory block with perineural *vs* intravenous dexamethasone, but there was no control group.[26]

Dexamethasone caused a small but statistically significant increase in blood glucose concentration, but this augmentation was not related to the dose of dexamethasone. As this study was not powered for secondary outcomes and included only one diabetic patient, no conclusion can be drawn regarding the impact of the dexamethasone dose on the variation of blood glucose in diabetic and non-diabetic patients.

Perineal pruritus after intravenous dexamethasone injection is a known side effect that can be quite uncomfortable for patients.[27] Despite adequate dilution and slow injection,[28] this side effect occurred significantly more frequently in group D10.

Limitations

Whereas Desmet *et al.* found a 15% difference in analgesic duration between dexamethasone 2.5 mg and 10 mg,[8] our study did not have sufficient power to detect a difference between groups D4 and D10. A study aimed at showing the superiority of dexamethasone 10 mg over 4 mg would contribute to knowledge about dexamethasone's dose-effect relationship, although its clinical importance for patients is uncertain. Another limitation is that this study did not objectively assess the duration of sensory and motor blocks. These evaluations would allow better understanding of intravenous dexamethasone's mechanism of action. Sensory and motor blocks are difficult to assess without a neurological exam, which is logistically difficult to conduct in an ambulatory setting.

In conclusion, this present study shows that intravenous dexamethasone in either a 4 mg or 10 mg dose significantly extends the analgesic duration of a single-shot ISB after arthroscopic shoulder surgery when compared with NS. Interscalene brachial plexus block performed with only 20 mL of 0.5% ropivacaine provided both excellent surgical

anesthesia and prolonged postoperative analgesia. Dexamethasone is also associated with significantly less sleep disruption during the first postoperative night and with significantly less cumulative opioid use during the first 36 hr after surgery. Reducing the dexamethasone dose from 10 mg to 4 mg reduced the incidence of perineal pruritus.

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