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Dexamethasone as an Additive to Low Volume Interscalene Plexus Blockade: A Randomized Controlled Study

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Abstract

Background: Interscalene Blockade is widely used to ensure analgesia in surgery involving the shoulder. Both i.v. and perineural dexamethasone seem to be able to prolong the block duration and can therefore be used to reduce the use of analgesics.

However most of the studies focusing on dexamethasone as an additive use large volumes (20 ml) of local anesthetic agent.

Larger volumes may be associated with a higher rate of complications.

Therefore the hypothesis of this study is to prove whether dexamethasone is also able to prolong the pain free time when given together with a low volume (10 ml) of anesthetic agent.

Methods: The study was conducted as a prospective, double-blinded randomized trial. Patients with arthroscopic surgery of the shoulder were included in our study. The blockade was performed using ultrasound guidance to ensure a low rate of block failure. We used eight milligrams of dexamethasone (free of preservative) and ten millilitres of ropivacaine in a concentration of 0.75%. The primary endpoint was analgesic duration defined as the time between performance of the block and first analgesic request. The primary variable was analyzed using a log rank test. Secondary endpoints were the assessment of the pain at the surgical site ten hours after operation at rest and movement.

Results: 104 patients were included in our study. The ethics committee of Lower Austria approved the study and patients signed an informed consent in order to participate in our study. During the study five patients were excluded due to block failure. Using a log-rank test, we observed a prolongation of pain free time of 310 minutes.

The analysis of the NRS-score ten hours after surgery yielded a significant difference between the control and active group at rest. Unexpectedly the NRS – score at movement does not differ between the control and active group.

Conclusion: Dexamethasone used in a low volume plexus brachialis blockade is able to prolong the pain free time.

Keywords: Analgesia; Anaesthetics local; Brachial plexus; Dexamethasone; Postoperative; Regional

Introduction

The use of plexus blockades to reduce postoperative pain in shoulder surgery is very common [1]. Proper management of postoperative pain can reduce economic costs and allows earlier discharge of patients [2,3].

A single shot blockade does not last long enough to help patients over the first night after surgery without analgesics. Therefore continuous blockades have become more popular, but they have their limitations; like the potential risk of infections or catheter dislocation [4,5]. In our experience, management of such catheters in a daily setting is difficult and laborious. Regular checking is required to ensure proper functioning and analgesia. Furthermore, consistent with the literature, the rate of catheter dislocation is high. Prolongation of a peripheral block might provide sufficient analgesia in the first phase after surgery without the limitations of catheter application. A nerve block is also very efficient against pain induced hyperalgesia and pain related neuronal plasticity [6].

Many substances have been investigated to circumvent the problem of limited analgesia after single-shot blockade [7-11], among them the synthetic glucocorticoid dexamethasone. Dexamethasone has been shown to prolong the duration of an interscalene block [12-14].

However, most studies investigating dexamethasone used large volumes of local anesthetics at a low concentration [15-17].

We believe that the usage of lower volumes can decrease the incidence of adverse events. A lower volume does not spread as far as a

high volume. Also the risk for systemic absorption is lower when using low volumes instead of high volumes.

Indeed, the incidence of phrenical nerve paresis and respiratory complications is reduced when using lower volumes [18,19]. Ultrasound guidance might further reduce the risk of adverse events [20]. Therefore one advantage of using lower volumes could lie in the lower rate of complications associated with interscalene plexus block.

Low volume blocks are well established for plexus block using the interscalene approach. We believe that low volume blocks are representing the current practice better than high volume blocks and therefore it is relevant to research the effects of dexamethasone on low volume blocks. Studies have proven that even volumes as low as 7 ml ensure proper plexus blockade.

Our hypothesis is that dexamethasone prolongs the analgesic effect of an interscalene plexus block when given with a low volume of local anesthetic agent.

Our primary endpoint was the analgesic duration defined as the time between performance of the block and first analgesic request.

Methods

The study was conducted as a prospective, controlled, randomized, double-blinded trial.

Participants

Participants (n=104) received either 8 mg dexamethasone (2 ml) with 10 ml (0.75%) ropivacaine (n=50) or 0.9% saline (2 ml) with 10 ml (0.75%) ropivacaine (n=49). The inclusion criteria for patients were the following: arthroscopy of the shoulder or repair of the rotatory cuff, Age>18 years and ASA I, II, III.

Exclusion criteria for patients included the following: patient is a fertile woman, opiates usage more than 30 mg oxycodon or equivalent a day, surgery involving bone structures, corticoid usage for more than 2 weeks in the past six months, Neuropathy or an injury of nerves in the upper limb, history of osteosynthesis or prosthesis. Fertile women were excluded from our study in order to spare expenses due to an otherwise needed pregnancy test.

The study protocol including off-label use of dexamethasone as an additive was approved by the Ethics committee of Lower Austria (GS4-EK-2/304-2013) and the local government and registered in the international registry for clinical trials (clinicaltrials.gov).

All participants were recruited at the University hospital of St. Polten, Austria and provided informed consent. We conducted a standardized anesthesia protocol. Patients received premedication of 3.5 to 7.5 mg midazolam.

The nerve block was performed either in a holding area or in the operating room. After the block was performed a general anesthesia was performed to optimize surgical conditions and to avoid patient's discomfort due to the beach chair position.

General anesthesia was performed using propofol 1.5 mg to 3 mg/kg, rocuronium 0.3 mg-0.5 mg/kg and fentanyl: 0.0075- 0.0125 mg/kg. After induction and airway management (endotracheal intubation), sevoflurane was used as maintenance anesthesia (MAC: 0.8-1).

The interscalene block was performed using ultrasound support with SonoSite Inc. M-Turbo devices. The probe used was an HFL38x (13-6 MhZ) linear probe. The tip of the needle was located at C6. Checking of local anesthetic spread over the anterior scalene muscle was not performed.

After performing nerve block, sensory discrimination between hot and cold and mobility of the shoulder was assessed. If the block failed the patient were excluded from the study. During surgery, vegetative reactions to incision were closely monitored. If any such reactions (increase of heart rate or blood pressure, sweating) occurred due to pain, the block was considered inefficient and the patient received additional analgesics (i.v.). If block failure occurred, the patient was excluded from the study.

Patients did not receive analgesics postoperatively unless demanded, ruling out bias due to use of analgesics. The time at which the patients demanded analgesia was documented. The primary endpoint was pain-free time after surgery, computed as the time point of request of drug be the patient subtracted by the time point of successful block.

Ten hours after nerve block, patients rated their pain at rest and movement on a numeric rating scale from zero to ten. This time point was chosen based on previous observations at our side concerning first analgesic request of patients. The standardized movement performed was abduction in the shoulder joint to a level of 45 degrees. Furthermore, possible side effects from the interscalene block were assessed. All variables were assessed by an anesthesiologist.

We decided to plan only one ward round, because further ward rounds would increase the overall overhead and the data they may be retrieve did not influence our primary endpoint. We tried to research a mean prolongation of the pain free time of two hours compared with the saline group considering a standard deviation of six hours.

Sample size was calculated using a standard deviation of 6 hours, a mean time of 10 hours prior to first analgesic request and a standardized effect size of 2 hours. The data needed to calculate the sample size was collected from observations of blocks performed prior to the trial and review of the data in literature [12,21].

The calculated sample size for our trial was 104 patients (assuming a block failure rate of 7%). The randomization sequence was created with the tool randomiser developed by the department of statistics at the University of Graz, Austria.

Patients were randomized at a block size of ten. Randomization lists were created by the dispensary of the hospital, making unblinding by the assessing anesthesiologist impossible. Randomization and production of the local anesthetics solution was performed by the dispensary, so all doctors and patients were unaware of the drug given. After inclusion the patient received an insurance contract and given an appointment for surgery.

The primary outcome was analyzed using the log rank test, with the assumption that the Kaplan-Meier curves would not intersect. Secondary outcome variables were analyzed using Mann-Whitney U test. Calculations were performed with SPSS [22]. Whiskers of box plots represents minimum and maximum NRS scores.

Results

Between March 2014 and April 2015, 104 patients were enrolled. Five patients were excluded due to failure of nerve block, resulting in

an effective sample size of 99 patients (Figure 1). Table 1 provides baseline characteristics of the patients.

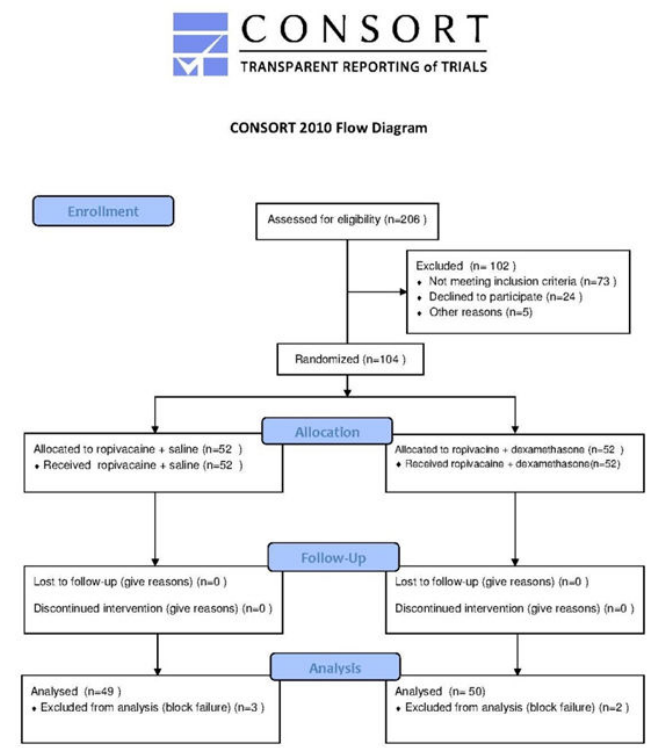

Figure 1: Patient flow through the study; provides an overview over the patient flow through our study. The figure adheres to the consort standard.

	Control (n=49)	Active Group (n=50)
Age mean (SD)	53.46 (SD:12.08)	49.7 (SD:15.53)
BMI mean (SD)	29.78 (SD:6.45)	27.06 (SD:4.38)
Sex (n)	Female:13, Male:36	Female:39, Male:11
Surgery duration (SD) minutes	75.94 (SD:44.83)	79.52 (SD:37.31)
ASA (n)	I:37,II:11,III:1	I:38,II:11,III:1
Type of surgical procedures performed (all athroscopical)		
Plain arthroscopy (n)	11	10
Arthroscopicrotatory cuff reconstruction (n)	18	22
Arthroscopic decompression (n)	18	13
Arthroscopic labrumrefixation (n)	2	5

Table 1: An overview about the descriptive data collected during the study.

Primary outcome

Mean pain-free time in the control group was 656.14 min with a standard error of 50.17 min. In contrast, in the active group, mean pain-free time was 966.80 min with a standard error of 60.30 min, resulting in a prolongation of pain-free time of 310.66 min by dexamethasone ($p<0.001$, Figure 2).

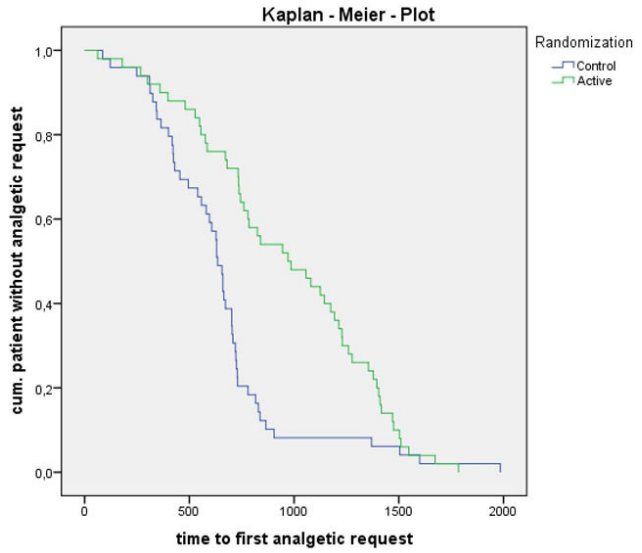

Figure 2: Kaplan-Meier-Plot; provides the graphical analysis of the survival times of the two trial arms in our study.

Therefore our trial showed that dexamethasone is able to prolong the pain-free time of the patients to around 310.66 minutes.

Post-hoc analyses were performed to assess the influence of gender, weight and age on primary outcome. We did not observe any correlations between these variables and pain-free time.
Figure 2 shows the kaplan-meier plot for the control and the active group.

Secondary outcome

In the active group, the NRS score at rest after ten hours was significantly lower compared to the control group ($p=0.016$, Table 2 and Figure 3), whereas no difference of NRS score at movement was observed ($p=0.451$, Table 2 and Figure 4).

Group	NRS-Score-Type	Mean, minimum, maximum, range
Active	NRS at rest	1.88, 0, 8, 8
Active	NRS at movement	2.44, 0, 8, 8
Control	NRS at rest	2.98, 0,10,10
Control	NRS at movement	3.51, 0, 8, 8

Table 2: An overview about mean, minimum, maximum and range of the NRS-scores at rest and movement.

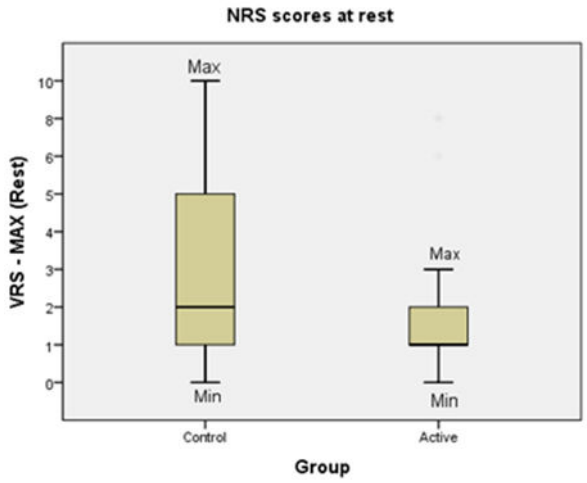

Figure 3: NRS-at rest; provides a box plot diagram showing the nrs values at rest of the two trial arms.

Concerning incidence of adverse events, no differences between groups were observed (Table 3).

Adverse Event	Active (n=50) or Control Group (n=49)	
Hoarseness	7 (14%)	9 (18%)
Horner Syndrom	11 (22%)	10 (20%)
Bezold-Jarisch-Reflex	0 (0%)	0 (0%)
Damage of nerves	0 (0%)	0 (0%)

Table 3: Shows the adverse events observed in the study population.

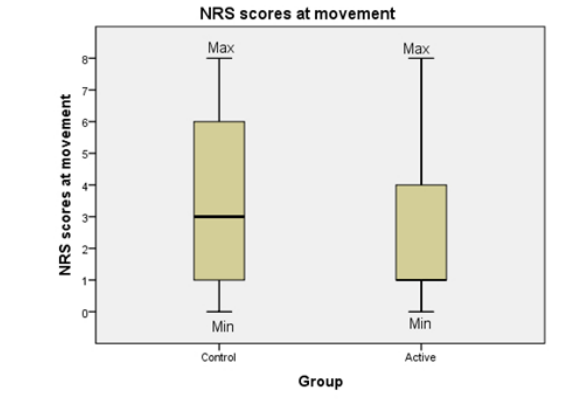

Figure 4: NRS-at movement; provides a box plot diagram showing the nrs values at movement of the two trials arms.

Discussion

In our study, dexamethasone used together with low-volume ropivacaine prolonged pain-free time compared to control.

The optimal dosage of dexamethasone as an analgesic additive is controversial. Liu et al. compared 1, 2, and 4 mg of dexamethasone given together with 30 ml bupivacaine (0.25%) [23]. In this study, no dose-dependent prolongation of pain-free time was observed. Woo et al. used a lower volume of ropivacain (12 ml) with 2.5, 5 mg or 7.5 mg dexamethasone and showed that there is a dose dependent prolongation of pain-free time [13].

The contradictor results might be due to the fact Liu performed a supraclavicular block and Woo a interscalene block. Another explanation might be that Woo used a low volume approach. The volume of local anesthetic could have an influence on the block enhancing capabilities of the additive. Another influence factor could be the use of different local anesthetic agents.

Using lower amounts of dexamethasone could be interesting, because only few data is available on adverse events originating from perineurally applied dexamethasone.

We overlooked different meta studies reporting on adverse events from dexamethasone. There was no case of nerval injury reported but long term adverse events with low frequency are possible. Also our trial does not discover any adverse events indicating potential damage to nerves due to the application of dexamethasone, but we only monitored the patients over a short time window of 24 hours. This window does not allow drawing conclusions about long term adverse events. The observation period in many of the studies researching dexamethasone as additive is too short to detect long term adverse events. A follow up after three to six months would be more appropriate to detect such adverse events.

Williams researched the effect of different additives in a rat model so the data cannot be extrapolated on humans [24].

Ropivacaine is more neurotoxic than dexamethasone and shows a time- and concentration-dependent effect [24]. High concentrations of ropivacaine, as used in this study, might increase the risk of neurotoxicity. However, we chose a high concentration to enhance duration and density of nerve block. Future studies to evaluate efficacy and safety of ropivacaine are warranted.

The incidence of phrenic nerve paralysis was not evaluated via ultrasound in our study. Although no patient experienced dyspnea after the procedure, this does not rule out nerve paralysis. Therefore, we cannot prove that a lower volume is associated with a decreased incidence of this side effect. However, current research indicates that lower volumes are associated with lower rates of phrenic nerve paralysis [18-20].

The effect of lower volumes on adverse events like hoarseness, Horner syndrome or vegetative disturbances is poorly described. In our study, the total rate of hoarseness was 16% which was lower compared to a study using 30 ml [23]. The incidence of Horner syndrome in our study was 21%, which was also lower. Furthermore, no difference in the occurrence of these adverse events between the active and control groups were observed. Our data therefore indicate that lower volumes may reduce side effects of interscalene plexus blockade. But when comparing two different studies precaution must be taken because different baseline characteristics and study methods can have an influence on the results.

We did not monitored vegetative disturbances as reaction to the block, because hemodynamic reactions to general anesthesia which was performed after nerve block could obscure the overall rate of side effects.

Despite randomization, sex, weight and age in the two groups was heterogeneously distributed. The difference in weight between active and control groups was significant. Weight might bias our results as the literature indicates that obese patients have a higher risk of block failure, probably due to difficulties locating the plexus, whereas relatively lower dosage of local anesthetics in relation to body weight does not appear to have an influence [25]. Ultrasound guidance helps to minimize risk of block failure in obese patients. In order to exclude a potential influence of these variables on our findings, we performed correlation analyses. This, however, did not yield any negative or positive correlations.

We could observe a significantly lower NRS (numerical rating scale) score ten hours after blockade in the dexamethasone group compared to control. However, the NRS score at movement did not differ between the groups. As early recovery of pain-free movement is of paramount importance post operatively, future studies might include additional time points of assessment during the first 24 h after surgery.

The ideal volume and concentration of local anesthetic agent for prolongation of the effect of dexamethasone remains elusive. Some studies favor a larger volume of local anesthetic over a higher concentration [26]. Another study implied that the higher volumes of ropivacaine not only enhance the effect of dexamethasone but also increase the effect of ropivacaine [27].

In conclusion, our study proved that dexamethasone (8 mg) used as an additive in a low volume (10 ml), high concentration (0.75%) single shot interscalene plexus blockade, is able to prolong the pain-free-time.

Acknowledgments

Author's contribution

A. L.: Patient recruitment, Study design and data collection

B. S.: Study design, Data analysis and writing up the first draft of the paper

C. F.: Patient recruitment and data collection

I. Z.: Patient recruitment and data collection

S. O.: Patient recruitment and data collection

H. S.: Patient recruitment and data collection

C. H.: Review and correction of the paper, Head of Department, Study design

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Declaration of Interests

The authors declared that there are no conflicts of interest.

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