A comparison study of 2 mg versus 4 mg of dexamethasone combined with local anesthetic drug in increasing the analgesic duration of a single-shot supraclavicular brachial plexus block

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Abstract

Background: Addition of dexamethasone to local anesthetic can prolong the analgesic duration in peripheral nerve block. However, the proper adding dose of dexamethasone for brachial plexus block can not be concluded. ***Objectives:*** To compare the analgesic duration of dexamethasone 2 versus 4 mg added to local anesthetic drugs following supraclavicular brachial plexus block. ***Methods:*** This study was a double-blinded randomized controlled trial. Fifty seven patients undergoing upper extremity surgery were randomly assigned to 3 groups. All patients received 20 ml of 2% lidocaine with adrenaline 5 mcg/ml and 10 ml of 0.5% bupivacaine for supraclavicular brachial plexus block. Same volume of normal saline, dexamethasone 2 mg and dexamethasone 4 mg were added to local anesthetics in C group, Dex2 group and Dex4 group, respectively. ***Results:*** Median and 95% CI of analgesic duration in Dex2 and Dex4 group were 620(440-837), 894(652-960) minutes which were longer than C group [335(259-491)] significantly (p-value 0.001). Analgesic duration in Dex4 group was longer than Dex2 group (p-value < 0.05). Both of dexamethasone groups had longer duration of motor block than C group [Dex2 group 525(441-720), Dex4 group 518(467-840), C group 420(310-483) minutes, p-value 0.0028). However, there was no difference in duration of motor block between Dex2 and Dex4 group. Morphine consumption in C group was more than both of dexamethasone groups. No adverse events were noted in all groups. ***Conclusion:*** Adding dexamethasone 4 mg in supraclavicular BPB has longer duration of analgesia than dexamethasone 2 mg with a comparable duration of motor block.

Keywords: *dexamethasone, supraclavicular, brachial plexus block, analgesia, duration*

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การศึกษาเปรียบเทียบการเพิ่มระยะเวลาการระงับความรู้สึกของยา dexamethasone ขนาด 2 และ 4 มิลลิกรัมร่วมกับยาชาในการระงับความรู้สึกเฉพาะส่วน supraclavicular brachial plexus block

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บทคัดย่อ

บทนำ: การให้ dexamethasone ร่วมกับยาชาสามารถเพิ่มระยะเวลาการระงับปวดในการฉีดยาชาที่เส้นประสาทส่วนปลาย (peripheral nerve block) ได้ แต่ยังไม่ทราบขนาดยา dexamethasone ที่เหมาะสมสำหรับการทำ brachial plexus block (BPB) ผู้วิจัยจึงศึกษาเปรียบเทียบระยะเวลาการระงับความรู้สึกของ dexamethasone ขนาด 2 และ 4 มก. ร่วมกับยาชาในการระงับความรู้สึกเฉพาะส่วน supraclavicular BPB ***วิธีการศึกษา:*** เป็นการศึกษาแบบ double-blinded randomized controlled trial ในผู้ป่วยที่เข้ารับการผ่าตัดบริเวณแขน 57 คน โดยสุ่มแบ่งเป็น 3 กลุ่ม ผู้ป่วยทุกรายจะได้รับการทำ supraclavicular BPB ด้วย 2% lidocaine with adrenaline 20 มล. ร่วมกับ 0.5% bupivacaine 10 มล. โดยผู้ป่วยกลุ่มควบคุม (C group) จะได้ normal saline ส่วนกลุ่ม Dex2 และกลุ่ม Dex4 จะได้ dexamethasone 2 และ 4 มก. ผสมในยาชาตามลำดับ ***ผลการศึกษา:*** ค่ามัธยฐานและค่า 95% CI ของระยะเวลาการระงับปวดในกลุ่ม Dex2 และ Dex4 มีค่าคือ 620(440-837) และ 894(652-960) นาที ซึ่งมีระยะเวลานานกว่ากลุ่มควบคุม [335(259-491)] อย่างมีนัยสำคัญทางสถิติ (p-value 0.001) และระยะเวลาของกลุ่ม Dex4 นานกว่ากลุ่ม Dex2 (p-value <0.05) กลุ่มที่ได้รับ dexamethasone มีกล้ามเนื้อแขนอ่อนแรงนานกว่ากลุ่มควบคุม [Dex2 group 525 (441-720), Dex4 518(467-840), C group 420 (310-483) นาที, p-value 0.0028) แต่ระหว่างกลุ่มที่ได้รับ dexamethasone มีระยะเวลาที่กล้ามเนื้อแขนอ่อนแรงไม่แตกต่างกัน จำนวนผู้ป่วยในกลุ่มควบคุมต้องยาแก้ปวด morphine มากกว่ากลุ่มที่ได้รับ dexamethasone ภายในเวลา 24 และ 48 ชม. ไม่มีภาวะแทรกซ้อนเกิดขึ้นในผู้ป่วยทุกกลุ่ม ***สรุป:*** การให้ dexamethasone ขนาด 4 มก. ร่วมกับยาชาในการระงับความรู้สึกเฉพาะส่วน supraclavicular BPB เพิ่มระยะเวลาการระงับปวดได้นานกว่าเมื่อเทียบกับขนาด 2 มก. โดยไม่มีความแตกต่างของเวลาในการทำให้กล้ามเนื้อหย่อนตัว

คำสำคัญ: *การระงับความรู้สึกเฉพาะส่วน, ยาชา, ระยะเวลาการระงับปวด, dexamethasone, brachial plexus block*

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Introduction

Moderate to severe postoperative pain following orthopedic surgeries can be reduced by regional neural blockade with local anesthetic (LA).[1] Interventions that increase the duration of local anesthetic action could prolong postoperative patient comfort.[2] Analgesic time depends on the pharmacological duration of the LA used including placement of indwelling perineural catheters to allow prolonged infusion or adding adjuvants such as epinephrine, clonidine, dexmedetomidine, midazolam, or dexamethasone.[3-5] Indwelling perineural catheter techniques are limited by technical challenges with placement, a higher incidence of catheter migration, inherent secondary failure rate, difficulties with catheter removal, or rarely infection.[6-8] So several additives have been trialed to prolong the duration of single-shot peripheral nerve blocks.

The results of many studies including meta-analysis support that the addition of dexamethasone to local anesthetic can prolong the analgesic duration.[3, 9,10,15,16] the doses of dexamethasone were vary from 4 to 10 mg but most researchers used 4 or 8 mg. There were no differences between 4 and 8 mg of dexamethasone on subgroup analysis.[10] in some papers, the investigators suggested that a smaller dose of dexamethasone should be used.

The objective of this study was to compare the effect of dexamethasone 2 and 4 mg adding to local anesthetics drug in increasing the analgesic duration following supraclavicular brachial plexus block in upper extremity surgery.

Methods

The study protocol was approved by Khon Kaen Hospital Institute Review Board in Human Research (KIRB) and registered on clinical trials. Fifty seven ASA I-II patients aged between 18 and 75 undergoing upper extremity surgery were included after an informed consent was obtained. Exclusion criteria included patients' refusal, allergies to local anesthetics or dexamethasone, diabetes mellitus, coagulation disorders, morbid obesity, infection in the injection site, any chronic pain with opioid usage, any internal brain, mental or physical illness which could interfere with evaluation of Numerical Rating Scale (NRS), using of systemic corticosteroids and systemic infection such as tuberculosis or viral infection.

Patients' fasting blood sugar were checked and they were instructed how to assess pain by using NRS from zero to ten before surgery. The patients were randomized by using a computer generator (STATA 10) into three-treatment groups. All groups received same local anesthetic drugs that used in general practice (2% lidocaine with adrenaline 1:200000 7 mg/kg [maximum dose 20 ml] with 0.5% bupivacaine 10 ml)

Group 1 Control (Gr. C): receiving local anesthetic drugs with normal saline 1 ml

Group 2 Dexa2 (Gr. Dex2): receiving local anesthetic drugs with dexamethasone 2 mg (0.5 ml) + normal saline 0.5 ml

Group 3 Dexa4 (Gr. Dex4): receiving local anesthetic drugs with dexamethasone 4 mg (1 ml)

A sealed opaque envelope with the study group allocation would be opened before the block was

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performed. Medication was prepared by a staff member who was not involved in the study and delivered in unidentifiable syringes. Anesthesiologist who performed supraclavicular brachial plexus block and nurses who evaluated the patient did not aware of patient's group.

In operating room, the patient was monitored with standard monitoring. Supraclavicular brachial plexus block was performed by experienced staff anesthesiologists or anesthetic residents who have had experience at least 2 years for brachial plexus block (perineural technique) under ultrasound guidance with medication following patient's group. After the block, pinprick sensation loss and motor power loss would be test. If the patients felt uncomfortable or anxious during operation, they would receive midazolam 0.05-0.1 mg/kg or/and morphine 0.05-0.1 mg/kg. Postoperative rescue analgesia with morphine 0.05-0.1 mg/kg was administered upon patient's request or NRS was more than 3 with the time interval of 4 hours. All patients received paracetamol 500 mg every 6 hours orally. Number of patients who use morphine for postoperative pain control in 24 and 48 hours, blood sugar (preoperative, postoperative at hour 2, 4, 8), postoperative adverse events and patients' satisfaction were recorded.

Statistics analysis

Sample size was calculated by using the different analgesic time from pilot study between group Dex2 and Dex4. Power for the primary outcome was 0.9 and $P<0.05$ was considered statistically significant. Dropout rate from previous study was about 10% (partial block 6.6% and failure block 3.33%[14]). The sample size was finally adjusted to 19 per group. The primary outcome was duration of sensory block and secondary outcomes were duration of motor block, time to complete sensory and motor block, number of patients who use morphine for postoperative pain control in 24 and 48 hours, postoperative morphine consumption, level of blood sugar, occurrences of adverse events and patients' satisfaction. SPSS version 17 was used to analyse the data. Continuous variables were presented as mean (SD) or median where appropriate. Shapiro-Wilk test was used for normality test. Standard hypothesis test (t-test, ANOVA, Mann–Whitney U-test, Kruskal-Wallis, Chi-square or Fisher's exact) were used to compare the data. The duration of sensory and motor block were analyzed by Kaplan–Meier survival analysis with a log-rank test and Wilcoxon-Mann-Whitney.

Results

Fifty seven patients were included in this study but 4 patients were excluded during analysis because of no pain after surgery (two patients in Dex2 group and one patient in Dex4 group and C group). Patients' characteristics in each group were not different. (Table 1)

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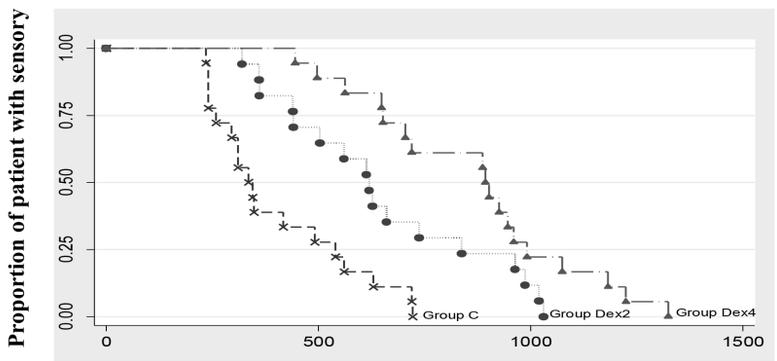
Table 1. Patient and procedure characteristics

	Group C (n=18)	Group Dex2 (n=17)	Group Dex4 (n=18)	p-value
Male; n(%)	11 (61.1)	14 (82.4)	14 (77.8)	0.392
Age (yr)	42.5±13.9	36.8±15.2	35.7±13.2	0.307
Body weight (kg)	61.0±7.7	63±12.0	59.3±8.4	0.530
Body mass index (kg/m^2)	22.9±2.8	22.8±3.5	22.5±2.3	0.912
ASA class I; n(%)	14 (77.8)	14 (82.4)	16 (88.9)	0.745
Type of injury; n(%)				
Fracture	12 (66.7)	8 (47.1)	10 (55.6)	
Laceration wound, tear tendon, others	6 (33.3)	9 (52.9)	8 (44.4)	0.106
Preoperative blood sugar (mg/dl)	101.7±14.3	99.6±19.0	91.4±18.4	0.182
Anesthetic time (min); median (IQR)	73.5 (32)	77 (42)	71 (60)	0.51
Operation time (min); median (IQR)	41 (26)	54 (39)	60 (58)	0.45

Data are mean+SD unless otherwise specified, ASA = American Society of Anesthesiologists, IQR = interquartile range

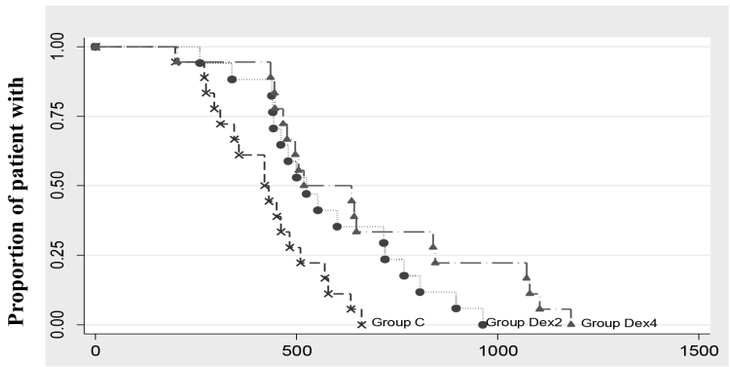
Duration of sensory block in Dex2 and Dex4 group [median (95%CI), 620(440-837), 894(652-960) minutes] were longer than C group [335(259-491)] significantly (p-value 0.001). (Figure 1) The analgesic duration in Dex4 group was longer than Dex2 group significantly (p-value < 0.05). Similarly, both of dexamethasone groups had longer duration of motor block than C group [Dex2 group 525(441-720), Dex4 518(467-840), C group 420(310-483) minutes, p-value 0.0028]. However, there was no difference in the duration of motor block between Dex2 and Dex4 group. (Figure 2)

Figure 1. Kaplan-Meier analysis for duration of sensory block (time from patients feel no pain to the time when their NRS were more than three). Analgesic duration in dexamethasone groups were longer than C group significantly (p-value 0.001)



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Figure 2. Kaplan-Meier analysis for duration of motor block (duration from the time that patients could not abduct the arm to the time when they were able to abduct their arm at least 2 inches away from the body)



Secondary outcomes were shown in Table 2. Number of patients who needed morphine for postoperative pain control in C group was more than Dex2 and Dex4 group in 24 and 48 hours. No adverse events such as nausea-vomiting, somnolence, and adverse drug reaction were noted in all groups. Blood sugar level increased in dexamethasone groups at 4th and 8th hour after operation but no clinical symptoms were noted. All patients were satisfied with the postoperative pain control.

Table 2. Secondary outcomes

	Group C (n=18)	Group Dex2 (n=17)	Group Dex4 (n=18)	p-value
Duration of sensory block (min); median (IQR)	335 (281)	620 (396)	894 (340)	0.001*
(95% CI)	(259-491)	(440-837)	(652-960)	
Duration of motor block (min); median (IQR)	420 (200)	525 (277)	518 (378)	0.0028*
(95% CI)	(310-483)	(441-720)	(467-840)	
Onset of sensory loss (min)	7.4±5.7	6.8±4.3	5.3±3.4	0.541
(95% CI)	(4.7–10.2)	(4.7–8.8)	(3.7-6.9)	
Onset of motor loss (min)	5.7±7.0	3.5±4.7	3.6±2.9	0.479
(95% CI)	(2.4-9.0)	(1.2–5.7)	(2.2-4.9)	
Number of patients who received intraoperative medication; n (%)				
Morphine	1 (5.5)	2 (11.8)	3 (16.7)	0.676
Midazolam	4 (22.2)	0 (0)	1 (5.6)	0.113
Intraoperative morphine consumption (mg)	6.0±0	5.0±2.8	3.7±0.6	0.570
Intraoperative midazolam consumption (mg)	1.75±0.5	0±0	2.0±0	0.617
Number of patient who use morphine in 24 hrs; n(%)	16 (89)	6 (35.3)	10 (55.6)	0.005*
Number of patient who use morphine in 48 hrs; n(%)	16 (89)	6 (35.3)	11 (61.1)	0.005*

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Table 2. Secondary outcomes (con.)

	Group C (n=18)	Group Dex2 (n=17)	Group Dex4 (n=18)	p-value
Morphine consumption in 24 hrs (mg); median (IQR)	5 (4.5)	3 (0)	3.5 (1)	0.37
(95% CI)	(3.0–7.45)	(2.1–11.1)	(3–5.35)	
Morphine consumption in 48 hrs (mg); median (IQR)	6 (6)	3 (0)	4 (3)	0.32
(95% CI)	(3.0–9.0)	(2.1–13.8)	(3–6.57)	
Blood sugar (mg/dl) (95% CI)				
2^{nd} hr	96.6±13.2	102.8±18.3	103.4±23.4	0.476
	(90.4–102.8)	(93.9–111.7)	(124.2–182.6)	
4^{th} hr	133.4±44.5	171.7+56.4	153.4±61.8	0.049*
	(112.4–154.4)	(144.2–199.1)	(124.2–182.6)	
8^{th} hr	119.9±24	142.9±46.2	160.9±36.6	0.003*
	(108.0–131.27)	(120.5–165.4)	(143.6–178.2)	

Data are mean±SD unless otherwise specified, *P-value < 0.05, IQR = interquartile range, CI = confidence interval

Discussion

The results of this study showed that duration of sensory loss in Dex4 group was longer than Dex2 group significantly [median (95% CI), 894(652-960), 620(440-837) minutes, p-value < 0.05] but there was no difference in duration of motor block [518(467-840), 525(441-720) minutes]. Albrecht et al. eported in a systematic review and meta-analysis that duration of analgesia with the use of dexamethasone 4 mg and local anesthetics of short or medium-term action was 200(51-350) minutes and of long term action was 461(240-682) minutes.[10] On the other hand, De Oliveira et al. reported in another meta-analysis that analgesic duration and motor block duration were 473(264-682) and 500(154-846) minutes, respectively.[16] Analgesic duration of this study was longer than those of systematic review and meta-analysis study but shorter than the study of Choi et al. Their meta-analysis showed that dexamethasone prolonged the analgesic duration for intermediate local anesthetics from 168 to 343 minutes [mean difference 175, 95% CI 73-277], for long-acting from 730 to 1306 minutes [mean difference 576 minutes, 95% CI 522-631], and for motor block from 664 to 1102 minutes [mean difference 438 minutes, 95% CI 89-787].[9] Onset time of sensory and motor block in this study were not different between control group and dexamethasone group which were similar to De Oliveira et al. but different from Albrecht et al.[10,16] The varying analgesic duration and onset time may be due to different techniques of brachial plexus block, methods of assessment, dose and type of local anesthetics and using of adjuvant like adrenaline.

The mechanism of dexamethasone for analgesia may stem from attenuating the release of inflammatory mediators, reducing ectopic neural discharge, and inhibiting potassium channel-mediated discharge of nociceptive C-fibers.[11-13] The block effect may be due to its local action and not a systemic one.[17] The mechanism may be from its local action on

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nociceptive C fibers mediated via membrane associated glucocorticoid receptors[13] and the up-regulation of the function of potassium channels in excitable cells.[11,18] In vivo study, the rat sciatic nerve block-prolonging effect of dexamethasone could be eliminated by co-administration of the glucocorticoid-receptor antagonist cortexolone.[19] However, Albrecht et al. reported that intravenous dexamethasone at dose of 0.1-0.2 mg/kg could have comparable analgesic effect with perineural injection.[10]

The patients who needed postoperative opioids in dexamethasone group in 24 and 48 hours were fewer than control group significantly. However, doses of morphine for patient who needed morphine were not different because each patient requested morphine only one or two times and dose of morphine per time was the same protocol, and this was a limitation of our study. The systematic review and meta-analysis could not find a significant difference in opioid consumption because the analgesic protocols varied and opioid consumption time (72 hrs) was longer than time frame in the context of the intervention.[9]

The safety of dexamethasone use in a nerve sheath may raise some concerns. Corticosteroid mediated neurotoxicity seems to be related to the vehicle polyethylene glycol and the preservative benzyl alcohol in steroid preparations as well as the presence of insoluble steroid particulate matter in the injectate.[20] However, dexamethasone sodium phosphate is a non-particulate steroid and does not contain either polyethylene glycol or benzyl alcohol so it is safe for using in peripheral nerve block.[20] No adverse events such as nausea-vomiting, somnolence, adverse drug reaction were reported in all groups. Blood sugar level increased in dexamethasone group at 4th and 8th hour after operation but less than 200 mg/dl. Desmet et al. reported that mean of postoperative blood sugar concentrations (within 24 hrs) increased in both intravenous and perineural dexamethasone groups but with no serious clinical symptom.[21]

Conclusion

Adding dexamethasone 2 and 4 mg to 20 ml of 2% lidocaine with adrenaline 5 mcg/ml mixed with 10 ml of 0.5% bupivacaine prolonged analgesic duration in supraclavicular brachial plexus block. Since adding dexamethasone 4 mg prolongs the duration of analgesia more than dexamethasone 2 mg with comparable duration of motor block. So we recommend touse dexamethasone 4 mg with local anesthetic for supraclavicular brachial plexus block.

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