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ORIGINAL RESEARCH

Efficacy of Dexamethasone as an Adjuvant for Scalp Nerve Blocks to Prolong Analgesia: A Prospective, Double-Blind, Randomized Controlled Study

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Background: Scalp nerve blocks (SNB) may significantly reduce post-craniotomy pain (PCP) but only for a short period of time. Dexamethasone, as an adjuvant to local anesthetics, was reported to prolong the analgesia duration of never block; however, the addition of dexamethasone to SNB is rare. We therefore tested the hypothesis that dexamethasone as an adjuvant to bupivacaine in SNB is positive after craniotomy.

Methods: Patients elective for craniotomy were randomly assigned to receive SNB with bupivacaine alone compared with dexamethasone and bupivacaine. The primary outcome was the duration of analgesia. The secondary outcomes include the cumulative amount of sufentanil consumption, the numeric rating scale (NRS), patient satisfaction score (PSS), the complications during the postoperative period, and SNB's relevant adverse events.

Results: There were 156 subjects included and 78 patients in each group (control and DEX group). The analgesia duration was significantly prolonged in the DEX group compared with the control group (660min (390,1005) vs 420min (314,504)) ($p<0.001$). The postoperative sufentanil consumption was lower in the DEX group compared with the control group at 12h ($P<0.001$), 24h ($P=0.014$), and 48h ($P=0.049$). The NRS scores were significantly lower in the DEX group compared with the control group at 8h ($P<0.001$) and 12h ($P=0.007$) after craniotomy. From 4h to 16h postoperative, the PSS in the control group was lower than the DEX group ($P < 0.05$).

Conclusion: Perineural dexamethasone as an adjuvant to bupivacaine without background glucocorticoid has the potential to improve the postoperative analgesic effect and patients' satisfaction without serious complications after craniotomy.

Keywords: post-craniotomy pain, scalp nerve block, peripheral dexamethasone, analgesia, postoperative

Introduction

Current evidence suggests that post-craniotomy pain (PCP) is more severe than expected[1,2] and usually occurs within 2 days after craniotomy.[3] PCP, if not properly managed, may elevate intracranial pressure, lead to intracranial hematoma, and even transit to chronic pain.[4] Therefore, PCP is a challenge for neurosurgeons, anesthetists, and pain management specialists.[3–5]

The ideal analgesic after craniotomy should provide adequate pain relief without serious side effects such as excessive sedation or respiratory depression, resulting in nausea and vomiting.[6] Traditional opioid had a limited role in PCP management because of their potential adverse effects and interferes with the assessment of neurological function.[3,7] Nonopioid analgesics alone are reported to be insufficient after craniotomy.[8] Up until now, there has been no consensus on the best agents after craniotomy. Pain that occurs within the first day after craniotomy has a pattern of superficial pain in 73% of the cases and both superficial and deep pain in 14% of the cases.[9] This suggests that PCP is

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more a somatic pain that arises from the muscles and soft tissues of the scalp than a visceral pain because the neural tissue of the brain does not contain any pain receptors.[1] Therefore, regional analgesia (scalp block or local wound infiltration) is an important means for multimodal analgesia to reduce the incidence and severity of PCP.[10]

Scalp nerve blocks (SNB) have been shown to effectively attenuate the intraoperative hemodynamic response[11,12] and is an easy and efficient method of keeping hemodynamics stabilized after craniotomy. However, the pain intensity was reduced after SNB with local anesthetics only in the first few hours after craniotomy. Even though SNB performed after skin closure using 0.5% bupivacaine with adrenaline, it could only achieve pain relief for a maximum of 6h.[13] Therefore, prolonging the duration of SNB is of great significance.

Adjuvants offer the available possibility to improve the pharmacodynamic profile of nerve blocks. Dexamethasone is one of the most investigated adjuvant drugs of this kind. Shrestha et al[14] firstly reported that the addition of dexamethasone as an adjuvant to local anesthetics significantly prolonged the analgesia duration of peripheral nerve block compared with local anesthetics alone in 2003. In a systematic review and meta-analysis of peripheral nerve blocks, Albrecht et al[15] also reported that dexamethasone increased the mean duration of analgesia by 488min compared with local anesthetics alone. However, the addition of dexamethasone to SNB is rare and inconsistent with the above studies, Jose et al[16] reported that the addition of dexamethasone as an adjuvant to local anesthetics in SNB did not prolong the duration of the block, probably because all patients in their study received quite high doses of systemic dexamethasone to decrease cerebral edema.

So far, no studies have reported the analgesic effect of single dexamethasone as a local anesthetic adjuvant for SNB without the background of perioperative glucocorticoid. Therefore, in the absence of perioperative systemic dexamethasone, we performed a prospective double-blinded randomized trial to assess the role of dexamethasone as an adjuvant to bupivacaine in SNB compared with bupivacaine alone for patients undergoing craniotomy.

Materials and Methods

Study Design and Registration

This is a prospective, single-center, parallel-group randomized double-blind controlled study, and it was approved by the ethics committee of Beijing Tiantan Hospital, Capital Medical University (KY 2018-034-02-9, July 20, 2018). Our study complies with the Declaration of Helsinki and all patients/guardians signed informed consent. The clinicians, patients, and researchers responsible for follow-up were blinded to treatment allocation. This study has been registered at ClinicalTrials.gov (NCT04648358, https://clinicaltrials.gov/study/NCT04648358, November 30, 2020). The study protocol (REDUCE trial) was published on TRIALS in 2021.[17] This manuscript adheres to the applicable CONSORT guidelines.

Eligibility and Exclusion Criteria

Eligibility criteria were patients aged from 18 to 64 years, male or female, with an American Society of Anesthesiology (ASA) status of I to III and Glasgow Coma Scale (GCS) score of 15/15, who were undergoing elective supratentorial craniotomy under general anesthesia (GA).

Exclusion criteria were history of chronic headache or chronic pain syndrome, psychiatric disorders, uncontrolled epilepsy, inability to understand the pain scales, excessive alcohol or drug abuse, chronic opioid use (more than 2 weeks or 3 days per week for more than 1 month), use of drugs with confirmed or suspected sedative or analgesic effects, use of any painkiller within 24h before surgery, request of oral/intravenous glucocorticoid within 1 week before surgery, pregnancy or breastfeeding, extreme body mass index (BMI) (<15 or >35), participation in another interventional trial, refusal or inability of the patient and/or legal guardian to provide informed consent, coagulopathy, infection around the puncture site, history of allergies to any of the study drugs.

Withdrawal criteria included patients who could not complete the trial for any reasons; oral/intravenous glucocorticoid administration intraoperatively or postoperatively; the planned craniotomy was delayed; or serious adverse events (AE) forced patients to withdraw from the study.

Randomization and Blinding

The patients were randomized into the control group or dexamethasone group (DEX group) using a computer-generated list. After opening the envelope containing the treatment allocation, the study solutions were prepared by an independent researcher in a separate room. In the control group, 0.5% bupivacaine 21mL with epinephrine at 1:200,000, plus normal saline 1mL, while in DEX group, 0.5% bupivacaine 21mL with epinephrine at 1:200,000, plus dexamethasone 0.8mL (4mg) and normal saline 0.2mL were prepared. After induction, the assigned solutions were used for SNB by the anesthesiologist who was blinded to the group allocations.

Anesthesia Protocol

Standard monitoring (5-lead electrocardiogram, heart rate (HR), pulse oximetry, and noninvasive arterial blood pressure (BP)) were performed. Induction was carried out with 2–3mg.kg^{-1} propofol, 0.3–0.5μg.kg^{-1} sufentanil, and 0.6mg.kg^{-1} rocuronium. Anesthesia was maintained with 4–8mg.kg-1.hour^{-1} propofol, and 0.1–0.3μg.kg-1.min^{-1} remifentanil. Remifentanil was adjusted according to the surgical stimulation to maintain BP and HR within 20% of baseline value or treated with nicardipine or dopamine if necessary. No additional sufentanil was used intraoperatively. After surgery, ondansetron (8mg) as an antiemetic prophylaxis were intravenously administered.

Scalp Nerve Blocks

The anesthesiologist performed SNB 10min before the insertion of cranial pins according to the technique previously described by Pinosky et al.[18] The following nerves were blocked bilaterally: the supraorbital and supratrochlear nerves (2mL); the zygomaticotemporal nerves (2mL); the auriculotemporal nerves (3mL); the postauricular branches of the greater auricular nerves (2mL); the greater, lesser, and third occipital nerves (2mL). The total volume of the solution used for SNB was 22 mL in all participants.

Postoperative Analgesia

On arrival in the post-anesthesia care unit (PACU), each patient received a patient-controlled analgesia (PCA) pump including 100μg sufentanil and 16mg ondansetron diluted to 100mL of 0.9% saline. When at the request or reported a numeric rating scale (NRS, 0=no pain and 10=worst imaginable pain) score ≥4, patients could press the PCA demand button for 2mL bolus, with a lockout interval of 10min, without continuous background infusion and a maximum of 8mL per hour. If patients' NRS were still over 4, Tylenol (combination of oxycodone hydrochloride and paracetamol) would be given as first rescue analgesic. Intravenous morphine was given as a second rescue analgesic if the NRS remained over 4. The type and doses of postoperative analgesic supplementation would be recorded in detail in the case report form (CRF).

Collection of Data

Baseline demographic was collected including each patient's gender, age, height, body weight, BMI, ASA status, and concomitant disease.

The primary outcome was the duration of analgesia, which was defined as the time between the performance of the SNB and the first press of the PCA demand button postoperatively. The secondary outcomes included the cumulative amount of sufentanil consumption by PCA at 4, 12, 24, and 48h postoperatively, the NRS score, GCS score, and patient satisfaction score (PSS, 0 for unsatisfactory to 10 for very satisfactory) at 2, 4, 8, 12, 16, 20, 24, and 48h after operation, the time in the PACU and the length of stay (LOS, the number of nights spent in the hospital after surgery) were collected.

The intraoperative HR and BP were collected in an aesthesia computerized record software before and after anesthetic induction, 5min after intubation, the insertion of cranial pins, skin incision, skull drilling, dura mater opening, and skin closure. Duration of surgery and anesthesia, size of surgical incision, and the intraoperative cumulative sufentanil and remifentanil administration had been closely recorded by the investigator. Any complications during the postoperative period such as postoperative nausea and vomiting (PONV), bradycardia, hypotension, and emergence delirium were noted for the first 48h.

Relevant adverse effects of SNB, such as local anesthetic toxicity or allergy, nerve injury, rhythm disorders, local hematoma (hematoma occurrence immediately after SNB) were recorded in the CRF.

Statistical Analysis

Based on previous studies,[13,19,20] we hypothesized that the duration of analgesia in the DEX group would be 30% longer than in the control group. We calculated those 70 patients per group for a power of 90% and an α error of 0.05. In consideration of an attrition dropout rate of about 10%, 78 patients were needed in each group, and the total sample size was 156 patients in this study.

We used a modified intention-to-treat (mITT) and a per-protocol (PP) analysis in this study for the primary and secondary outcome analysis. Patients who were randomized to receive at least one of the study interventions would be included in the mITT analysis and the conclusion was determined by the mITT principle. Sensitivity analysis would be performed as an additional evaluation with the PP analysis and patients who withdrew from the study would be excluded.

Statistical analyses were performed using SPSS Statistics version 20.0 (IBM Corporation, Armonk, NY). Normality and homogeneity of the data distribution were evaluated using the Shapiro–Wilk test. Baseline characteristics were described using the mean ± SD when they consist of descriptive variables with a normal distribution. Data with a skewed distribution were presented as the median with the 25th and 75th percentiles. Dichotomous and categorical data were described as frequencies and percentages. Group comparisons were performed by Student's *t*-test or the nonparametric Wilcoxon–Mann–Whitney test for quantitative variables, and Pearson's chi-squared test or Fisher's exact test for categorical variables. NRS score and GCS at different time points were analyzed using repeated measures analysis of variance (ANOVA) using time as the between-subjects factor. Details of statistical analysis were fixed, at the latest, in the statistical analysis plan that was prepared before the database is locked and analysis is commenced. The statistical tests were 2-tailed and P<0.05 will be considered statistically significant.

Results

Between December 13, 2020, and December 31, 2022, 210 patients scheduled for supratentorial craniotomy under GA were screened, and 54 were not eligible. A total of 156 patients were enrolled and included in mITT analysis for 78 patients in each group. Fourteen patients were withdrawn from the trials for several reasons and among them post-operative hematomas happened in a total of 3 patients, 1 patient (at 6h after craniotomy) in the control group and 2 patients (at 6 and 24h after craniotomy) in the DEX group. Finally, 71 patients in each group completed the trial. The recruitment and follow-up of all patients are presented in Figure 1.

The baseline data with respect to gender, age, height, body weight, BMI, ASA status, and concomitant disease were similar between the two groups (p>0.05) (Table 1).

Surgical characteristics, intraoperative sufentanil, and cumulative remifentanil administration, duration in PACU and lOS were similar among the 2 groups (p>0.05) (Table 2).

The intraoperative HR and MAP (Figure 2) before and after anesthetic induction, 5 min after intubation, at insertion of cranial pins, skin incision, the skull drilling, dura mater opening, and skin closure were similar between the two groups (p>0.05).

Analgesia duration was significantly prolonged in the DEX group compared to the control group via mITT analysis (660min (390min, 1005min) VS 420min (314min, 504min)) (p<0.001) (Table 3), which was similar in the PP analysis (eTable 1 in Supplement 1).

The cumulative sufentanil consumption at 4h after craniotomy was similar between the two groups (P=0.574) but was lower in the DEX group at 12h (p<0.001), 24h (p=0.014) and 48h (P=0.049). There were no differences in NRS scores at 2h and 4h after craniotomy (P>0.05); however, the NRS scores were lower in the DEX group compared to the control group at 8h (P<0.001) and 12h (P=0.007) postoperatively; from 16h after surgery, the differences were insignificant. The median NRS score in the two groups was less than 3 during the first 48h postoperatively. There were no differences in GCS scores between the two groups within 48h postoperatively (P>0.05). PSS score in the control group was lower than the DEX group at 4h, 8h, 12h, 16h (P<0.05). There were no differences in the incidence PONV, bradycardia,

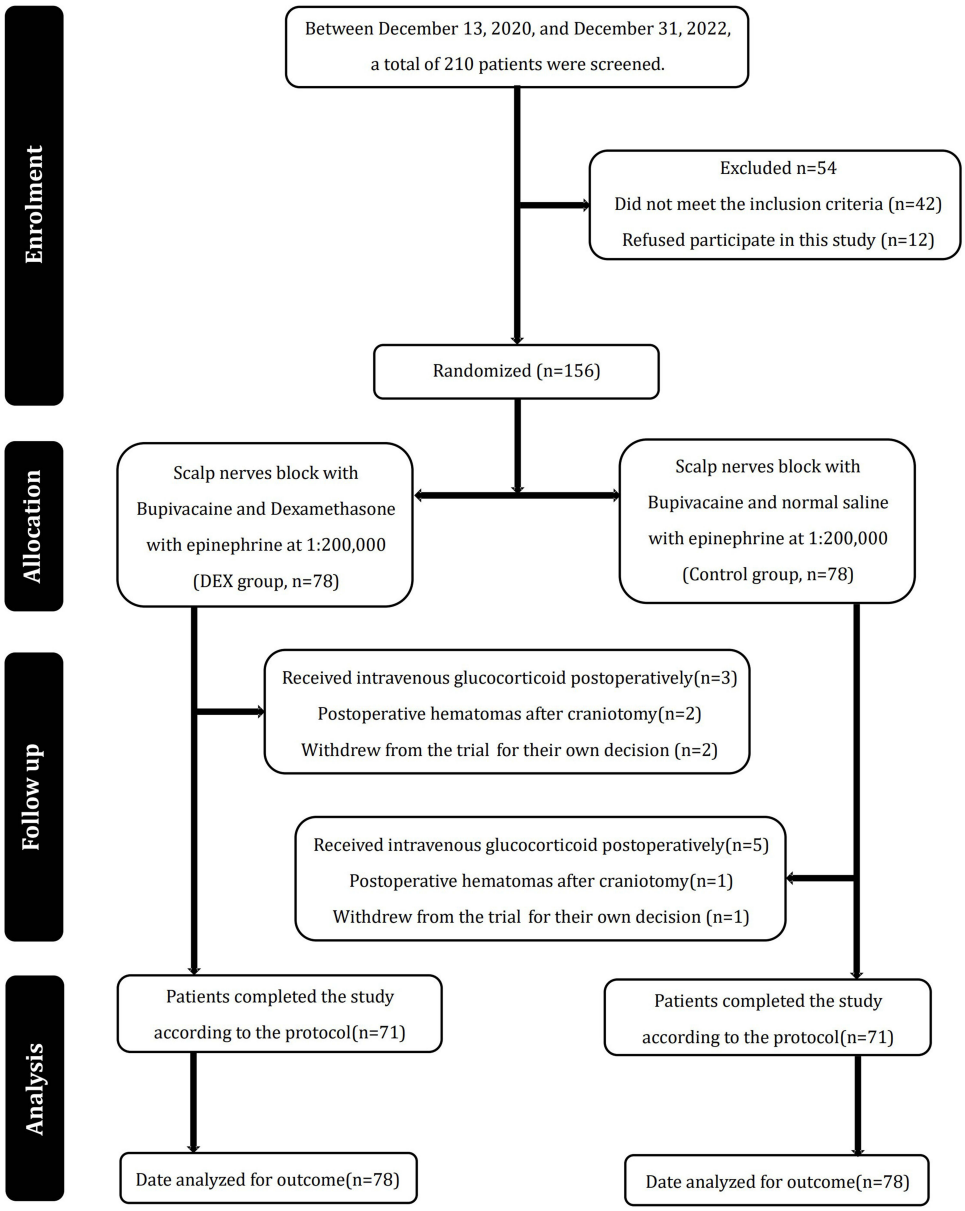

Figure 1 Consort flow diagram.

hypotension, and emergence delirium within 48h after surgery between the two groups (P>0.05). The incidence of local hematoma at the nerve block site was similar between the two groups, and other SNB associated AEs were not observed in our study (Table 3).

Discussion

In this randomized controlled trial, we first compared the effects of dexamethasone as an adjuvant to bupivacaine with bupivacaine alone for SNB in patients scheduled for supratentorial craniotomy under GA, without the background of perioperative glucocorticoid. The main finding of our research is that perineural dexamethasone prolongs the analgesic duration of SNB without serious compilations.

The median duration of analgesia was 660min in the DEX group when 4mg dexamethasone was added to bupivacaine for SNB. Our finding is largely consistent with that of Maagaard et al[21] who reported that perineural 4mg dexamethasone when used as an adjunct to bupivacaine increases the duration of an ulnar nerve block compared to bupivacaine alone,

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Table 1 Patient Characteristics of the mITT Population

	DEX Group (n=78)	Control Group (n=78)	P
Female/male ratio	0.46	0.40	0.518
Age (years, mean ± SD)	47.08±12.20	49.72±12.36	0.188
Height (cm, mean ± SD)	166.52±8.09	167.40±9.13	0.523
Body weight (kg, mean ± SD)	63.20±9.97	65.31±11.16	0.215
BMI (kg/m^2, mean ± SD)	22.71±2.50	23.27±3.19	0.221
ASA status (I/II/III, n)			0.183
I	35	44	
II	41	30	
III	2	4	
Concomitant disease (n)			0.107
Hypertension	13	21	
Coronary disease	8	14	
Diabetes mellitus	19	17	
Cerebrovascular disease	6	9	

Abbreviations: BMI, Body mass index; ASA, American Society of Anesthesiologists.

Table 2 Surgical Characteristics and Cumulative Opioids Administration Intraoperative of the mITT Population

	DEX Group (n=78)	Control Group (n=78)	P
Duration of surgery (min, mean ± SD)	245.88±70.53	232.19±62.82	0.483
Duration of anesthesia (min, mean ± SD)	343.59±84.33	332.88±88.17	0.202
Size of surgical incision (cm, mean ± SD)	18.09±4.42	19.00±4.82	0.221
Cumulative remifentanil dose (mg, mean ± SD)	1.85±0.70	1.69±0.53	0.113
Sufentanil dose (μg, mean ± SD)	31.44±7.63	32.27±8.67	0.525
Surgical site			0.147
Right	38	45	
Left	35	26	
Median	5	7	
Site of incision			0.267
Frontal	23	19	
Frontotemporal	17	26	
Temporal	2	1	
Temporoparietal	19	24	
Parietal	11	5	
Other	6	3	
Tumor types			0.741
Benign	47	50	
Malignancy	31	28	
Duration in PACU (min, mean ± SD)	105.62±56.07	100.85±52.43	0.584
LOS (day, mean ± SD)	8.40±1.92	8.45±2.16	0.876

Abbreviations: PACU, postoperative care unit; LOS, length of stay.

with a mean sensory block duration of 651±120mins. In a review article, Albrecht et al[15] reported that, dexamethasone increased the mean duration of analgesia by 488min, with long-acting local anesthetics in peripheral nerve blocks in upper or lower limbs. The analgesia duration was only prolonged by about 240min in our study, and the difference may be due to the difference in dose of dexamethasone, volume of local anesthetics, type of local anesthetics, and sites of nerve block. Each of the factors mentioned above may contribute to the substantial heterogeneity observed in the duration of analgesia.

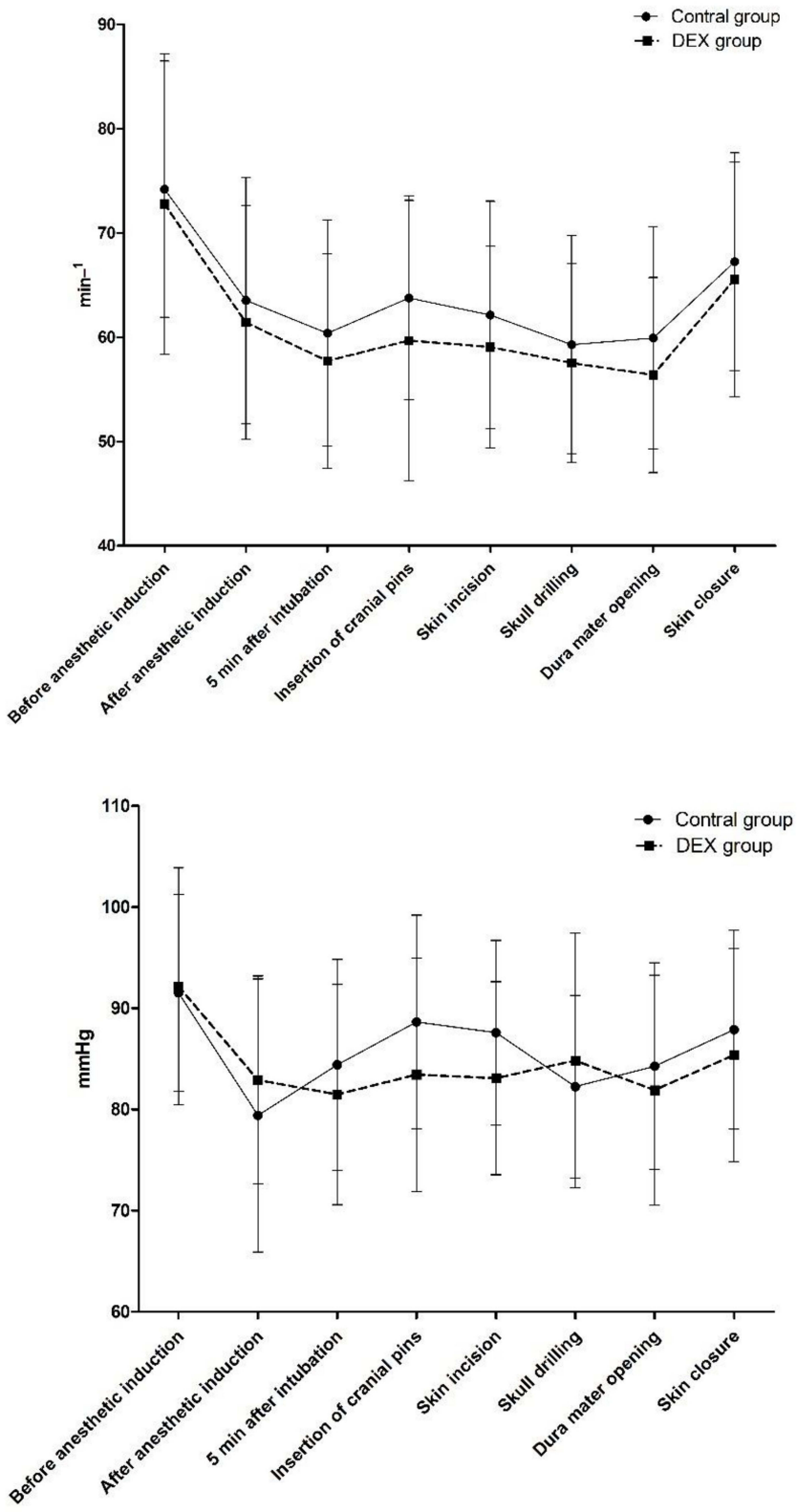

Figure 2 The intraoperative heart rate at each time points and the intraoperative mean arterial blood pressure at each time point.

Our results are different from those reported by Jose et al,[16] who were the first to report that, the addition of dexamethasone as an adjuvant to local anesthetics for SNB did not prolong the duration of analgesia in patients who received 24mg of dexamethasone perioperatively to decrease cerebral edema. Previous studies have indicated that

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Table 3 Primary Outcome and Secondary Outcomes of the mITT Population

	DEX group(n=78)	Control group(n=78)	P
Primary outcome			
Duration (min, median (interquartile range))	660 (390,1005)	420 (314,504)	**0.000**
Secondary outcomes			
Cumulative of sufentanil consumption by PCA(μg)			
4h	0.51±1.46	0.64±1.39	0.574
12h	2.69±5.15	5.62±4.85	**0.000**
24h	4.67±7.11	7.45±6.90	**0.014**
48h	5.49±8.71	8.13±7.90	**0.049**
NRS score (median (interquartile range))			
2h	1(0–1)	1(0–1)	0.762
4h	1(0–1)	1(0–1)	0.087
8h	1(0–1)	1(1–3)	**0.000**
12h	1(1–2)	2(1–4)	**0.007**
16h	2(1–2)	2(1–3)	0.198
20h	1(1–2)	1(1–2)	0.333
24h	1(0–2)	1(0–2)	0.283
48h	1(0–1)	1(0–1)	0.814
GCS score (median (interquartile range))			
2h	15(15–15)	15(14–15)	0.465
4h	15(15–15)	15(15–15)	0.768
8h	15(15–15)	15(15–15)	0.985
12h	15(15–15)	15(15–15)	0.561
16h	15(15–15)	15(15–15)	0.156
20h	15(15–15)	15(15–15)	0.317
24h	15(15–15)	15(15–15)	1.000
48h	15(15–15)	15(15–15)	1.000
PSS score (median (interquartile range))			
2h	9(9–10)	9(8–10)	0.425
4h	9(9–10)	9(8–9.25)	**0.002**
8h	9(9–10)	7(7–9)	**0.000**
12h	8(8–9)	8(7–9)	**0.009**
16h	9(8–9)	8(8–9)	**0.027**
20h	9(8–10)	9(8–9)	0.468
24h	9(9–10)	9(9–10)	0.454
48h	10(9–10)	9.5(9–10)	0.884
Postoperative observation			
PONV (n, %)	11 (14.10%)	15 (19.23%)	0.520
Bradycardia (n, %)	3 (3.85%)	1 (1.28%)	0.620
Hypotension (n, %)	1 (1.28%)	1 (1.28%)	1.000
Emergence delirium (n, %)	6 (7.69%)	4 (5.13%)	0.746
Hematoma at SNB puncture site (n, %)	3 (3.85%)	5 (2.56%)	0.719
Postoperative intracranial hematoma (n, %)	2 (2.56%)	1 (1.28%)	1.000

Abbreviations: PCA, patient control analgesia; NRS, numeric rating scale; GCS, Glasgow coma scale; PSS, patient satisfaction score; PONV, postoperative nausea and vomiting; SNB, scalp nerve blocks. Significant differences are emphasized by bolding.

intravenous dexamethasone at a dose of only 0.1–0.2mg.kg-1 can have a comparable analgesic effect.[22–24] Gaudray et al[25] reported that SNB with 0.75% ropivacaine, when administered with 8mg of i.v. dexamethasone provides adequate analgesia and decreases the requirement of rescue analgesics over first 48h after supratentorial craniotomies. Therefore,

we speculated that the high doses of systemic dexamethasone may have masked the analgesic effect of nerve block in Jose et al's study. Nonetheless, in this study, we excluded the patients who received glucocorticoid perioperatively to suppress the interference of systemic dexamethasone.

Watkins et al[26] describe the effect of incompatibility of ropivacaine with alkaline solutions and how combination with dexamethasone would have an effect of crystallization. A network meta-analysis suggests that dexamethasone as an adjunct can prolong the durations of analgesia and the differences in block-related characteristics following perineural compared with i.v. dexamethasone is not clinically important, but existing evidence suggests that perineural dexamethasone may offer an advantage over i.v. for reducing 24h opioid consumption.[27] Therefore, perineural dexamethasone with long-acting bupivacaine would be the more appropriate choice for SNB.

In a review study, Baeriswyl et al[28] reported that perineural dexamethasone combined with bupivacaine could slightly prolong the duration of analgesia when compared to systemic administration of the same dose of dexamethasone. A meta-analysis demonstrated that perineural dexamethasone resulted in a more prolonged duration of motor block, decreased pain scores, and reduced opioid consumption, compared to i.v. dexamethasone.[29] In this study, the perineural dose of dexamethasone administered was only 4mg (0.06mg.kg^{-1}, based on average body weight) and the systemic effect of this extremely low dose of dexamethasone can be ignored, which is consistent with the conclusions of Maagaard et al.[21] From this, we inferred that dexamethasone prolonging the analgesic duration of SNB can be considered a local effect.

Moreover, we found that cumulative sufentanil consumption and NRS scores both decreased in the DEX group. Although the median NRS score in both groups was less than 3 within the first 48h, there were about a quarter of patients (25.6%) in the control group and only 5 patients (6.4%) in the DEX group had moderate-to-severe pain at 12h after surgery (Table 3), which indicated that SNB with bupivacaine and dexamethasone can contribute to better acute pain control than bupivacaine alone. Besides, patients in the DEX group had a higher PSS score from 4h to 16h than the control group. We could infer that patients in the DEX group may have had a more stable hemodynamic and to avoid discomfort. As the technique of GA and SNB were standardized between the two groups, any advantage of additional analgesia in the DEX group can be attributed to the addition of dexamethasone.

The mechanism of perineural dexamethasone prolonging the duration of analgesia and quality of peripheral nerve block includes a possible initiation of vasoconstriction,[30] that reduces the release of inflammatory mediators, decreasing the activity of C fibers through their direct effect on glucocorticoid receptors, thereby hindering the potassium channel.[31] Thus, dexamethasone can possibly improve the pharmacodynamic profile of nerve blocks. Without doubt, the mechanism of low dose perineural dexamethasone prolonging the duration of analgesic is not clear and may not be explained by the aforementioned mechanism, which still needs further exploration in future studies.

There was no difference in the duration of stay in the PACU and LOS between the 2 groups. Local hematoma was reported in a total of 8 patients after SNB and fortunately, the hematoma was absorbed within 2 days after surgery and none of them suffered from nerve injury. The overall incidence of PONV in our study was about 16.7% lower than what Lazt et al[32] reported.

Limitation

Our results should be interpreted within the context of several limitations. First, we enrolled a specific surgical patient population, and the generalizability of our findings must be verified in future studies. Second, the anesthesiologists performed SNB without ultrasound guidance; therefore, the possibility of SNB failure is undeniable. Third, the addition of dexamethasone to local anesthetics may have improved the effects of local anesthetics for a longer period; however, our study follow-up only lasted for 48h. Whether dexamethasone as an adjuvant to bupivacaine can prevent chronic pain after craniotomy needs further evaluation. Finally, 4mg of dexamethasone was used in our study because this dose seems to be safe in adults; we did not administer it separately based on body weight. In the future, multicenter research with a larger sample size is needed to obtain higher levels of evidence-based results.

Conclusion

In this study, patients in the DEX group only received 4mg perineural dexamethasone. We neither observed any neurotoxicity after SNB nor did we find any systemic side effects, perhaps because of the minimal dose of

dexamethasone used. Perineural dexamethasone as an adjuvant to bupivacaine without background glucocorticoid has the potential to improve the postoperative analgesic effect and patients' satisfaction without serious complications after craniotomy. Therefore, the dose of perineural 4mg dexamethasone has the potential of becoming an excellent method of preventing PCP. In the future, multicenter research with a larger sample size is needed to obtain higher levels of evidence-based results to verify the efficacy and safety.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author (Fang Luo, email: 13611326978@163.com). The data is not publicly available due to privacy or ethical restrictions.

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Disclosure

All authors declared no conflict of interest. The work described has not been submitted elsewhere for publication, in whole or in part, and all the authors listed have approved the manuscript that is enclosed.

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