Original Article

The Effect of 0.5% Levo-Bupivacaine Scalp Block during Craniotomy: A Double-Blind Randomized Placebo Controlled Trial

Manee Raksakietisak MD[1], Pajongjit Suwansukroad MD[1],
Taschan Uengkajornkul MD[1], Pranee Rushatamukayanunt MD[1]

[1] Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Objective: The objectives of the present study are to evaluate the scalp block efficacy in term of perioperative use of analgesic (fentanyl), awakening time, hemodynamic stability and postcraniotomy pain control.

Materials and Methods: One hundred and thirty (18 to 75 years old) patients were enrolled and allocated into 2 groups by computer-generated randomization. Group N received scalp block with 0.9% Normal saline solution [NSS] and group L received scalp block with 0.5% levo-bupivacaine 10 to 15 mL. Both groups also received pre-incisional local anesthetic infiltration from neurosurgeons due to their routine practice (a mixture of 0.5% bupivacaine 10 mL and 1% lidocaine with epinephrine 1: 200,000 10 mL) and intravenous fentanyl for intra-operative pain control. The assessed outcomes were intra-operative total fentanyl consumption, hemodynamic stability, awakening time, pain scores, postoperative morphine consumption, nausea and vomiting.

Results: One hundred and twenty-eight patients were analyzed with 64 patients in each group. There were no differences in patient demographics, fentanyl consumption, and awakening time. In group L, the median postoperative pain score was significantly lower at 4th hour (group L 5 (3, 6) vs. group N 6 (4, 8), $p = 0.029$). However, group L had higher incidence of hypotension (group L 84.4% vs. group N 68.7%, $p = 0.037$).

Conclusion: The scalp block with 0.5% levo-bupivacaine, added up to intravenous fentanyl and local infiltration, provided slightly better postoperative pain control for craniotomy.

Keywords: Scalp block, Craniotomy, Pain, Hypotension

J Med Assoc Thai 2018; 101 (Suppl. 9): S59-S65
Website: http://www.jmatonline.com

More than two-thirds of the patients reported moderate to severe pain after craniotomy[1,2]. During craniotomy, procedures such as pinning, incision, removal of skull bone and dura cause painful stimuli and lead to increasing heart rate and blood pressure, alter in physiologic and neuro-hormonal responses. Fentanyl, a short-acting and strong systemic opioid is widely used during craniotomy for providing pain relief for these procedures. However, fentanyl has undesirable side effects such as delayed emergence, delayed neurological assessment which lead to delayed detection of postoperative intracranial complications. Therefore, the use of regional scalp block combined with general anesthesia may be beneficial over general anesthesia alone. The regional scalp block may lower the doses of anesthetic agents and provide better hemodynamic control[1,3-7]. The scalp block is supposed to prevent or reduce the incidence of post-surgical pain syndrome[8].

Although several observational and randomized studies of scalp block have been published, different conclusions have been drawn regarding scalp block and the amount of intra-operative fentanyl used. Accordingly, the primary aim of the present study was

Correspondence to:
Rushatamukayanunt P. Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: +66-2-4197989; **Fax:** +66-2-4113256
E-mail: pnrusha@gmail.com, pnrusha@hotmail.com

How to cite this article: Raksakietisak M, Suwansukroad P, Uengkajornkul T, Rushatamukayanunt P. The Effect of 0.5% Levo-Bupivacaine Scalp Block During Craniotomy: A Double-Blind Randomized Placebo Controlled Trial. J Med Assoc Thai 2018;101;Suppl.9: S59-S65.

to investigate the effect of 0.5% levo-bupivacaine scalp block vs. 0.9% Normal saline solution [NSS] scalp block on intra-operative fentanyl requirement during craniotomy. The secondary objective was to study block efficacy in terms of hemodynamic stability, awakening time, and post-craniotomy pain control.

Materials and Methods

Study design

This prospective randomized parallel study was conducted at Siriraj Hospital, Mahidol University, Thailand from September 2015 to August 2016. After being approved by the Siriraj Institutional Review Board (Si. 457/2015) at our institution, one hundred and thirty patients, given written informed consent, were randomized into 2 groups. Randomization was performed in blocks of 4 by computer-generated numbers. The sequence numbers and groups were placed inside concealed envelopes, which were opened before anesthetic induction. The researchers who enrolled the participants and prepared the drugs for scalp blocks did not take part in patient care and assessment. The patients, anesthesiologist in charge and ICU nurses who assessed pain scores were blinded to group allocation.

Inclusion and exclusion

We included patients aged 18 to 75 years old, American Society of Anesthesiologists [ASA] physical status I to III, with single and small ($\leq$4 cm in tumor size) brain tumor. Patients with full Glasgow Coma Score (GCS = 15), and have good communication were scheduled for elective supratentorial craniotomy under general anesthesia. We included re-craniotomy cases if the patients were eligible to other inclusion criteria.

The exclusion criteria included patients with unstable hemodynamics such as uncontrollably high blood pressure or needed inotropic or vasopressor drugs, allergic to local anesthetics or opioids, coagulopathy or liver diseases, BMI $\geq$30 kg/m^2 or suspected brain herniation.

Intervention

The day before surgery, the study protocol and verbal numeric scale [VNS] for pain assessment were explained to all patients. No premedication was given and randomization was conducted before induction. The standard monitors (electrocardiogram, non-invasive blood pressure, pulse rate and pulse oximetry) were applied then invasive blood pressure was placed when patients asleep. The patients were induced with propofol (1.5 to 2.0 mg/kg), fentanyl (1 to 2 mcg/kg) and atracurium (0.5 to 0.6 mg/kg) or cisatracurium (0.15 mg/kg) to facilitate intubation.

Group N received scalp block with 0.9% Normal saline [NSS] and group L received 0.5% levo-bupivacaine prepared by the researchers. Both solutions (0.9% NSS and 0.5% levo-bupivacaine) looked similar. The scalp blocks were performed after induction by experienced anesthesiologists in charge. The target nerves were infiltrated with 2 to 3 mL of study drug at multiple sites according to surgical incision with a total volume of 10 to 15 mL. The scalp block technique is described in details by Papangelou et al[3]. The procedure involved injection to block the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, lesser occipital and greater occipital nerves. In the present study, only the related nerves were blocked. In addition, local anesthetics (a mixture of 0.5% bupivacaine 10 mL and 1% lidocaine with epinephrine 1: 200,000 10 mL) were infiltrated by the neurosurgeon routinely to reduce bleeding just before skin incision (about half an hour after scalp block) and before skin closure.

The anesthesia maintenance was standardized for all patients by continuous infusion of neuro-muscular blocking agent (atracurium 0.3 to 0.5 mg/kg/hr or cisatracurium 0.06 to 0.10 mg/kg/hr. Fentanyl (1 mcg/kg/hr) was infused before dural opening and then 0.5 mcg/kg/hr and desflurane up to 6%. In some cases, propofol was infused in the dosage of 2 to 6 mg/kg/hr to reduce intracranial pressure and/or reduce brain swelling (upon the anesthesiologists in charge's decision) and was discontinued after complete tumor removal.

If blood pressure increased greater than 20% from pre-operative measures, the desflurane concentration was increased to maximal end-tidal concentration of 6%. If the blood pressure remained high, an additional dose (25 mcg) of fentanyl was given but not more than two dosages (50 mcg) in a half an hour. If the blood pressure was still high, a titration dose, 0.2 to 0.4 mg of nicardipine was given as an antihypertensive drug. For hypotension, it was treated with fluid and vasopressor.

Fentanyl and neuromuscular blocking agent were stopped half an hour before finishing operation. At the end of the operation, the desflurane was turned off and neuromuscular blockage was reversed with glycopyrrolate 0.5 mg and neostigmine 2.5 mg and train of four was used for ensuring adequate reversal. The awakening time is defined as time from giving reversal

drugs until patient has adequate ventilation, eye opening, and purposeful responses. The extubation time is defined as time from giving reversal drugs to extubation.

Outcome measures

The primary outcome was intra-operative total fentanyl consumption. The secondary outcomes were awakening time, incidences of hypo or hypertension and postoperative pain scores. Other parameters recorded were blood loss, fluid, neurological complications and extubation time.

Statistical analysis

The sample size was calculated to detect a significant difference in total fentanyl consumption. From our pilot study, to detect a difference of fentanyl consumption between the groups (group N, fentanyl 250±50 mcg. vs. group L, fentanyl 200±50 mcg) with 80% power at an alpha value of 0.05, a sample size of 12 per group was required. While considering awakening time (group N, 20±10 min. vs. group L, 15±10 min), we needed 64 patients per group. No interim analysis.

The qualitative data were presented as number and percentage. The parametric quantitative data were presented as mean and standard deviation. The nonparametric quantitative data, such as pain score was presented with median and interquartile range. Comparison between groups were analyzed by using Chi-square test or Fisher exact test for qualitative data, unpaired t-test for parametric quantitative data and Mann-Whitney U test for nonparametric quantitative data. All statistical analysis was performed using SPSS software (version 21). The *p*-value of less than 0.05 was considered statistically significant.

Results

We assessed for eligibility in all craniotomy patients the day before surgery and excluded more than half of the cases due to exclusion criteria. One hundred thirty patients were enrolled but only 128 patients followed the protocol with complete follow-up at 24 hours after operation and were analyzed. One patient in each group was excluded due to protocol violation (Figure 1). There was no statistically significant difference in the demographic data (Table 1) respect to sex, age, body weight, BMI, ASA physical status and pre-operative provisional diagnosis. The average ages in both groups were 48.9±12.2 and 47.5±11.8 years, respectively. The main diagnosis was meningioma.

From intra-operative data, fentanyl consumption was slightly lower in group L but did not reach statistical significance (group N 314±108 mcg vs. group L 291±122 mcg, $p = 0.267$). The awakening (group N 7.9±7.9 min vs. group L, 6.2±6.2 min) and extubation time (group N 9.67±9.67 min vs. group L 8.6±8.1 min) did not differ between groups. However, in group L, the incidence of hypotension was higher (group N 68.7% vs. group L 84.4%, $p = 0.037$) but lower incidence of hypertension (group N 64.1% vs. group L 51.5 %, $p = 0.152$) (Table 2).

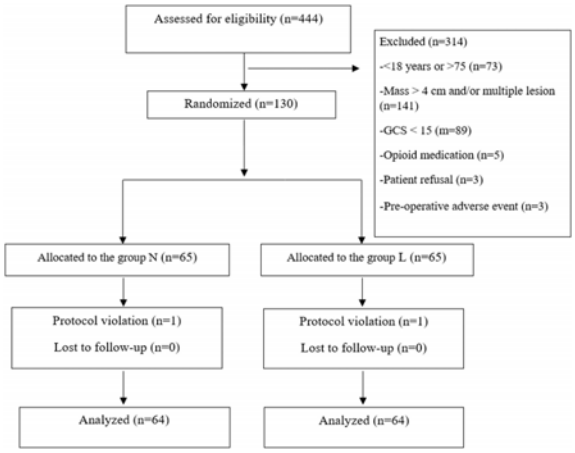

Figure 1. Consort flow diagram of the study. Group N indicates control group that received 0.9% NSS, group L indicated study group that received 0.5% levo-bupivacine.

Most of the patients were fully awake and met extubation criteria, however 6 patients (9.4%) in group N and 5 patients (7.8%) in group L remained intubated and transferred to ICU for some reasons such as prolonged operative time, excessive blood loss and large amount of fluid administration, brain edema, and emergence seizure.

From post-operative data, the median pain score in group L was significantly lower at 4 hours after operation (group L 5 (3, 6) vs. 6 (4, 8), $p = 0.029$). Although median pain scores during the first 12 hours post-operatively tended to be lower in group L than in group N, the differences were not statistically significant. Some patients had altered consciousness and could not give pain scores (Figure 2).

The incidence of postoperative nausea and vomiting was quite high, about half of the patients suffered from nausea and vomiting (43.7% in group N vs. 46.8% in group L, $p = 0.723$). Postoperative nausea and vomiting frequently occurred after intravenous

Table 1. Patient data

	Group N (n = 64)	Group L (n = 64)	*p*-value
Age (yr)	48.9±12.2	47.5±11.8	0.530
Sex: Male	16 (25)	17 (26.6)	0.861
ASA I/II/III	11/40/13	11/38/15	0.907
Weight (kg)	61.6±11.1	61.2±10.6	0.796
BMI (kg/m^2)	24.3±3.4	24.2±3.5	0.881
Underlying (n)			
Hypertension	21 (32.8)	18 (28.1)	0.565
Diabetes Mellitus	8 (12.5)	7 (10.9)	0.783
Dyslipidemia	9 (14.1)	9 (14.1)	1.000
Coronary Artery Disease	1 (1.6)	1 (1.6)	1.000
Others	7 (10.9)	8 (12.5)	0.783
Diagnosis			0.693
Meningioma	44 (68.8)	45 (70.3)	
Neurocytoma	2 (3.1)	2 (3.1)	
Arteriovenous malformation	3 (4.7)	4 (6.3)	
Glioma&Glioblastoma	8 (12.5)	5 (7.8)	
Metastasis	1 (1.6)	4 (6.3)	
Others	6 (9.4)	4 (6.3)	

The data are presented as mean ± standard deviation or n (%).
*$p<0.05$ indicates statistical significance
Group N receiving scalp block with NSS and Group L receiving scalp block with 0.5%levo-bupivacaine

Table 2. Intraoperative data

	Group N (n = 64)	Group L (n = 64)	*p*-value
Fentanyl (mcg)	314±108	291±122	0.267
Fentanyl (mcg/kg/hr)	1.0±0.3	0.9±0.3	0.152
Awakening time (min)	7.9±7.9	6.2±6.2	0.117
Extubation time (min)	9.7±9.7	8.6±8.1	0.635
Total propofol (mg)			
Induction only (mg)	164±43	175±51	0.254
Induction + infusion (mg)	845±485 (n = 21)	1,004±565 (n = 17)	0.357
Atracurium(mg)	146±66	132±52	0.199
Anesthetic time (min)	342±160	320±109	0.375
Operative time (min)	269±153	251±108	0.451
Estimated blood loss (mL)	515±422	525±537	0.901
Urine output (mL)	1,598±773	1,529±631	0.584
Crystalloid (mL)	2,387±1,117	2,158±998	0.225
Hypotension	44 (68.7)	54 (84.4)	0.037*
Hypertension	41 (64.1)	33 (51.5)	0.152

The data are presented as mean ± standard deviation or n (%)
* $p<0.05$ indicates statistical significance
Group N receiving scalp block with NSS and Group L receiving scalp block with 0.5% levo-bupivacaine

morphine administration and postoperative morphine consumption in both groups did not differ (7.8±3.8 mg in group N vs. 8.1±3.9 min group L, $p = 0.574$) (Table 3). There were no reports of infection or hematoma at puncture sites or other complications related to scalp block such as nerve injury or facial nerve palsy.

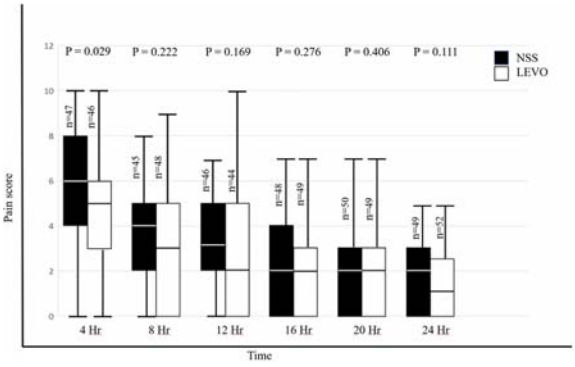

Figure 2. Box plot chart of median pain score levels during each 4 hr interval in control (NSS) and study (Levo) group. Comparison of pain score levels between two groups was performed by the Mann-Whitney U Test and *p*-values are presented above the box plots. The error bars represent the interquartile ranges. Immediate 4 hr post-operative pain score difference between two group was significant (p = 0.029) and almost all of the pain score at each time point was lower in study group than in control group.

Only 4 patients (2 patients form each group) developed post-operative neurological deficits such as alteration of consciousness, limb weakness, blurred vision. However, all of those symptoms were improved before being discharged. No hypotension, malignant arrhythmia or any major adverse cardiac events were recorded in either group.

Discussion

The craniotomy procedure causes several pain stimuli during operation and the perioperative pain management has not been standardized[9]. The short-acting opioid, such as fentanyl, is widely used intra-operatively but it can cause delayed recovery especially in geriatric patients[10]. The regional scalp block alone[9,10] or combination with other analgesics has been widely used for perioperative pain control with great successes[1,3-8].

From the present study, 128 patients were enrolled with the mean age around 48 years. The intra-operative fentanyl consumption was slightly lower in scalp block with 0.5% levo-bupivacaine but not statistical significance. The awakening and extubation time did not differ between groups. These finding could be explained by our protocol, which consists of local wound infiltration by the surgeon and adequate continuous fentanyl infusion so scalp block, was only an additive analgesic on top of two analgesics. Abbass et al used either fentanyl or scalp block with 0.5% bupivacaine for perioperative pain control and they found that scalp block provided better hemodynamic control and faster recovery[10]. The study of Tuchinda et al[12] showed that intra-operative fentanyl requirement was significantly greater in control group (NSS group) compared with study groups (0.5% bupivacaine or 0.25% bupivacaine with 1: 200,000 adrenaline). The results were different from our study because we used continuous fentanyl infusion and local infiltration by surgeon due to their routine practice whereas the study of Tuchinda et al used intermittent fentanyl administration.

For hemodynamic control, both groups experienced hypotension but in the scalp block group (group L) the incidence was higher (group N 68.7% vs. group L 84.4%, p = 0.037). Too deep an anesthesia could be a cause of hypotension. There was no difference in the incidence of hypertension. Many studies[7,10,12,13] reported less hypertension with scalp block during painful stimuli such as pinning which was in accordance with this study. The regional scalp block with levo-bupivacaine undoubtedly reduced stress responses during surgery. The present study showed significant incidence of hypotension in scalp block with 0.5% levo-bupivacaine so intra-operative fluid optimization is very important to prevent significant hypotension.

Nevertheless, the present study showed slightly better postoperative pain control in scalp block with 0.5% levo-bupivacaine. The median pain score was significantly lower at 4 hours postoperative in the group L (5 (3, 6) vs. 6 (4, 8), p = 0.029). This result is in accord with the meta-analysis in 2013[1] from 7 randomized controlled trials [RCTs] with 4 pre-operative scalp block, they found that pain scores were lower at 1, 2, and 4 hours after operation. The recent meta-analysis in 2016[9] included only 1 additional RCTs showed that the scalp block provided better recovery profiles with lower pain scores, less opioid consumption with less nausea and vomiting[14]. The other methods for craniotomy pain control were maxillary nerve block[15], pre-emptive local scalp infiltration[16], intravenous NSAIDs and dexmedetomideine[9]. The pain assessment was limited in some patients due to alteration of consciousness, agitation and/or remained intubation. Current research shows that the two tools best validated for patients unable to self-report pain are the Behavioral Pain Scale [BPS] and the Critical Care Pain Observation Tool [CPOT]. Although

international guidelines recommend the use of these validated tools for pain evaluation[17], these tools were not used in our neuro-critical care unit.

The present study has some limitations. Firstly, we used scalp block as an adjunct to intravenous fentanyl and local anesthetic infiltration so the perioperative pain control was already covered by the two methods but the add-up scalp block might provide extra benefit. Secondly, the continuous fentanyl infusion might be too much so there was no need for extra dose. Thirdly, around one-third of the patients could not give pain scores despite being taught before operation; nevertheless, the pain scores during first 4 hours were still slightly lower in scalp block with 0.5% levo-bupivacaine.

Further researches should focus on pre and postoperative scalp block alone without the use of continuous fentanyl infusion or focus on special patient groups such as obese, geriatric or hypertensive patients who might have greater benefit from scalp block.

Conclusion

The scalp block with 0.5% levo-bupivacaine added up to intravenous fentanyl and local infiltration provided slightly better postoperative pain control for craniotomy.

What is already known on this topic?

The scalp block provide better recovery profiles with lower pain scores, less opioid consumption with less nausea and vomiting.

What this study adds?

The scalp block together with systemic fentanyl and local anesthetic infiltration can provide slightly better pain control for craniotomy in early postoperative period.

Acknowledgements

The authors would like to thank Julaporn Pooliam for her statistical assistance, Nichapat Thongkaew and Chusana Rungjindamai for their great help with administrative work.

Trial registration

Clinical Trials.gov registration as NCT0255 8569.

Funding

This research project was supported by Faculty of Medicine Siriraj Hospital, Mahidol University, Grant Number (IO) R015831080.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Guilfoyle MR, Helmy A, Duane D, Hutchinson PJ. Regional scalp block for postcraniotomy analgesia: a systematic review and meta-analysis. Anesth Analg 2013;116:1093-102.
2. Suksompong S, Chaikittisilpa N, Rutchadawong T, Chankaew E, von Bormann B. Pain after major craniotomy in a university hospital: a prospective cohort study. J Med Assoc Thai 2016;99:539-48.
3. Papangelou A, Radzik BR, Smith T, Gottschalk A. A review of scalp blockade for cranial surgery. J Clin Anesth 2013;25:150-9.
4. Chaki T, Sugino S, Janicki PK, Ishioka Y, Hatakeyama Y, Hayase T, et al. Efficacy and safety of a lidocaine and ropivacaine mixture for scalp nerve block and local infiltration anesthesia in patients undergoing awake craniotomy. J Neurosurg Anesthesiol 2016;28:1-5.
5. Bebawy JF, Bilotta F, Koht A. A modified technique for auriculotemporal nerve blockade when performing selective scalp nerve block for craniotomy. J Neurosurg Anesthesiol 2014;26:271-2.
6. Pardey Bracho GF, Pereira de Souza NE, Grousson S, Mottolese C, Dailler F. Opioid consumption after levobupivacaine scalp nerve block for craniosynostosis surgery. Acta Anaesthesiol Taiwan 2014;52:64-9.
7. Lee EJ, Lee MY, Shyr MH, Cheng JT, Toung TJ, Mirski MA, et al. Adjuvant bupivacaine scalp block facilitates stabilization of hemodynamics in patients undergoing craniotomy with general anesthesia: a preliminary report. J Clin Anesth 2006;18:490-4.
8. Batoz H, Verdonck O, Pellerin C, Roux G, Maurette P. The analgesic properties of scalp infiltrations with ropivacaine after intracranial tumoral resection. Anesth Analg 2009;109:240-4.
9. Tsaousi GG, Logan SW, Bilotta F. Postoperative pain control following craniotomy: a systematic review of recent clinical literature. Pain Pract 2017;17:968-81.
10. Abbass OW, Hussien GZ, Aboeldahab HA, Othman S, Fareed M. Does scalp block with general anesthesia in craniotomy affect the intraoperative course and outcome in geriatric patients? Ain-Shams J Anesthesiol 2015;8:25-30.

11. Burnard C, Sebastian J. Anaesthesia for awake craniotomy. Cont Educ Anaesth Crit Care Pain 2014;14: 6-11.
12. Tuchinda L, Somboonviboon W, Supbornsug K, Worathongchai S, Limutaitip S. Bupivacaine scalp nerve block: hemodynamic response during craniotomy, intraoperative and post-operative analgesia. Asian Biomed 2010;2:243-51.
13. Geze S, Yilmaz AA, Tuzuner F. The effect of scalp block and local infiltration on the haemodynamic and stress response to skull-pin placement for craniotomy. Eur J Anaesthesiol 2009;26:298-303.
14. Hwang JY, Bang JS, Oh CW, Joo JD, Park SJ, Do SH, et al. Effect of scalp blocks with levobupivacaine on recovery profiles after craniotomy for aneurysm clipping: a randomized, double-blind, and controlled study. World Neurosurg 2015;83: 108-13.
15. Jayaram K, Srilata M, Kulkarni D, Ramachandran G. Regional anesthesia to scalp for craniotomy: Innovation with innervation. J Neurosurg Anesthesiol 2016;28:32-7.
16. Song J, Li L, Yu P, Gao T, Liu K. Preemptive scalp infiltration with 0.5% ropivacaine and 1% lidocaine reduces postoperative pain after craniotomy. Acta Neurochir (Wien) 2015;157:993-8.
17. Kotfis K, Zegan-Baranska M, Szydlowski L, Zukowski M, Ely WE. Methods of pain assessment in adult intensive care unit patients - Polish version of the CPOT (Critical Care Pain Observation Tool) and BPS (Behavioral Pain Scale). Anaesthesiol Intensive Ther 2017;49:66-72.