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Paediatrics

Surgical pleth index in children younger than 24 months of age: a randomized double-blinded trial

J. Harju[1,*], M.-L. Kalliomäki[1], H. Leppikangas[1], M. Kiviharju[1] and A. Yli-Hankala[1,2]

[1]Department of Anaesthesia, Tampere University Hospital, PL2000, Tampere 33521, Finland, and [2]Medical School, University of Tampere, Tampere, Finland

*Corresponding author. Email: jarkko.harju@fimnet.fi

Abstract

Background: The surgical pleth index (SPI) is a measurement of intraoperative nociception. Evidence of its usability in children is limited. Given that the autonomic nervous system is still developing during the first years of life, the performance of the SPI on small children cannot be concluded from studies carried out in older age groups.

Methods: Thirty children aged <2 yr, planned for elective open inguinal hernia repair or open correction of undescended testicle, were recruited. The children were randomized into two groups; the saline group received ultrasound-guided saline injection in the ilioinguinal and iliohypogastric nerve region before surgery and ropivacaine after surgery, whereas the block group received the injections in the opposite order. The SPI was recorded blinded and was analysed at the time points of intubation, incision, and when signs of inadequate anti-nociception were observed.

Results: There was a significant increase in the SPI after intubation (P=0.019) and after incision in the saline group (P=0.048), but not at the time of surgical incision in the block group (P=0.177). An increase in the SPI was also seen at times of clinically apparent inadequate anti-nociception (P=0.008). The between-patient variability of the SPI was large.

Conclusions: The SPI is reactive in small children after intubation and after surgical stimuli, but the reactivity of the SPI is rather small, and there is marked inter-individual variability in reactions. The reactivity is blunted by the use of ilioinguinal and iliohypogastric nerve block.

Clinical trial registration: NCT02045810.

Key words: monitoring, intraoperative; nociception; paediatrics

Editor's key points

- The surgical pleth index (SPI) has been developed as a measure of nociception in adults.
- It is calculated from analysis of the heart beat interval and plethysmographic pulse wave amplitude.
- The value of the SPI in small children, in whom the sympathetic system is not fully developed, is unknown.
- The authors found that the SPI did react to noxious stimuli in children younger than 2 yr.

Nociception during general anaesthesia can elicit significant autonomic, hormonal, and metabolic changes. Marked changes in heart rate, blood pressure, or patient movement during anaesthesia are considered signs of inadequate anaesthesia. A variety of opioids are used during surgery in order to prevent these changes.[1] The use of opioids can lead to significant postoperative respiratory depression, especially in small children.[2]

Traditionally, the signs of inadequate anti-nociception have guided opioid administration. The surgical pleth index (SPI, formerly surgical stress index) was originally introduced in 2007.

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It is calculated from normalized photoplethysmographic waveform analysis and normalized analysis of the heart rate.[3]

The SPI has been used to study opioid administration during surgery,[4–7] but evidence of its efficacy in paediatric populations is scarce. Only two studies have been conducted in paediatric populations, and the children were older than 3 yr in both.[8 9]

Development of the nervous system continues after birth,[10] and heart rate is an age-dependent parameter in children.[11] As the heart rate is higher when compared with adults, and the scientific background on the behaviour of the plethysmographic waveform as a function of age is very limited, evidence from adult populations cannot be directly adapted to children.

In this prospective, randomized, double-blinded study, we wanted to test the performance of the SPI to detect nociception in small children at the time of intubation, surgical incision, and at signs of inadequate anti-nociception.

Methods

The study was registered at ClinicalTrials.gov (NCT02045810). After receiving approval from the local ethics committee (ETL R13137), 30 patients were randomized into the study groups (Fig. 1). Written informed consent was obtained from both parents before enrolment. The study population consisted of children aged <2 yr, with ASA classification I–III. They were undergoing surgery for inguinal hernia repair or correction of undescended testicles. Both uni- and bilateral procedures were included. Patients with cardiac problems or known ECG disturbances were excluded.

Randomization

Randomization information was kept in opaque, sealed, numbered envelopes. Before the patient entered the operating room, an independent nurse, who was otherwise not involved in the study, opened the envelope and labelled two syringes based on the randomization. The syringes were marked as number one or two, indicating the order of usage. The saline group (SG) was given an injection of NaCl 0.9% into the ilioinguinal and iliohypogastric nerve region before surgery and an injection of levobupivacaine 2.5 mg ml^{-1} (Abbvie, Helsinki, Finland) after surgery, before extubation. The block group (BG) received the injections in the opposite order. The order of the injections was blinded to the patient and the study personnel.

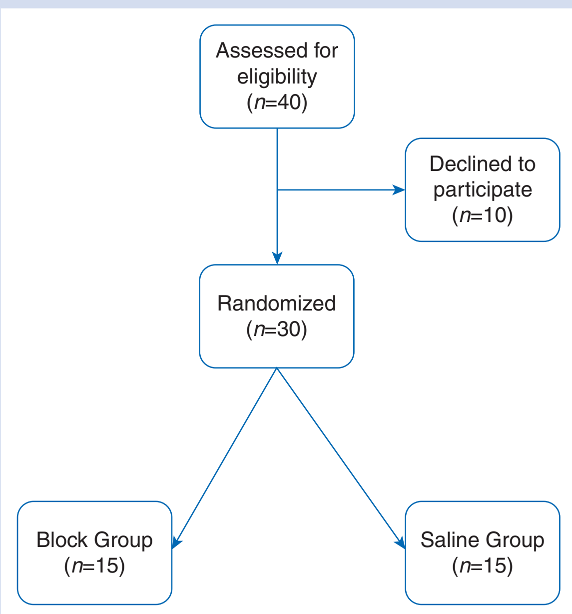

Fig 1 Flowchart.

Induction of general anaesthesia

Fentanyl 2 μg kg^{-1} i.v., glycopyrrolate 5 μg kg^{-1} i.v., and thiopental 4–5 mg kg^{-1} i.v. were used for induction of general anaesthesia and to enhance tracheal intubation. When clinically necessary, succinylcholine 1–1.5 mg kg^{-1} i.v. was also given.

Delivery of local anaesthesia

Patients received an ilioinguinal and iliohypogastric nerve block under ultrasound guidance (Sonosite S-nerve; Sonosite Inc., Bothell, WA, USA) during anaesthesia, before and after surgery. One author (J.H.) performed all of the preoperative blocks and most of the postoperative blocks. A visual assessment with ultrasound was used to ensure the necessary amount of local anaesthesia to produce an effective block. However, the maximal amount of levobupivacaine (1.5 mg kg^{-1} for children <6 months or 3 mg kg^{-1} for children >6 months) was not exceeded.

Maintenance of anaesthesia

Anaesthesia was continued with sevoflurane (2–5% end tidal) and additional fentanyl boluses of 0.5–1.0 μg kg^{-1} i.v., if clinically necessary. As the concentration of sevoflurane was considered sufficient, any additional medication was at the discretion of the practising anaesthetist. In most instances, a bolus of fentanyl was given in the event of movement or a rapid 15% increase in heart rate (HR) or non-invasive blood pressure (NIBP) during a 5 min period if clinically necessary. A fentanyl bolus was not judged as mandatory treatment in all episodes of movement or changes in haemodynamics. The delivery of sevoflurane was adjusted based on clinical decision and primarily not as a reaction to the signs of inadequate anti-nociception. Tracheal extubation was performed in children aged <6 months when fully awake, and in older children after the return of spontaneous breathing. Monitoring ended in all patients upon leaving the operating theatre.

Monitoring

The ECG and the photoplethysmography were continuously monitored. For ECG monitoring, a standard three-lead ECG was used. Measurement of the SPI was performed from a finger on the side opposite to the NIBP measurement, with a TS-PAW adhesive saturation sensor™ (GE Healthcare, Helsinki, Finland). The NIBP measurement was set to 5 min intervals. The SPI and the entropy values were kept hidden from the personnel during surgery. An anaesthesia nurse or attending anaesthetist simultaneously recorded the time points of interest and the concentrations of sevoflurane throughout the study. The numerical values of HR, NIBP, entropy, and SPI were monitored with a Carescape B850 or B650 monitor (GE Healthcare) and recorded using the S5 Collect software (GE Healthcare) at 10 s intervals. The plethysmographic waveform was continouously recorded, and the manufacturer reanalysed the curve to produce data for the components of the SPI, normalized pulse plethysmographic amplitude (PPGAnorm), and normalized RR interval (RRInorm).[3]

Power analysis

The power analysis was based on the results of a previous study comparing the surgical stress index in a group of adult female patients, with or without epidural analgesia at skin incision.[12] The primary outcome measure of our study was the change in SPI value at the time of the surgical incision. Assuming similar responses [20 units difference (Δ) in SPI and standard deviation (SD) of 14.4], nine patients per group would be needed to reach a power of 0.80 ($P<0.05$). However, given that the physiology of small children differs from that of adults, and because previously there was no knowledge of the magnitude of SD in small children, the study size was increased to 15 patients in each group.

Statistical analysis

The results were analysed using IBM SPSS statistics version 23 (IBM, Armonk, NY, USA). Two-tailed *P*-values <0.05 were considered significant. The data were found to be scattered and are reported as the median and quartiles Q_1 and Q_3 (IQR). Between-group differences were analysed using Wilcoxon signed rank tests.

Our primary outcome measure was the difference in the SPI at the time of incision. As a secondary outcome measure, the SPI values were also compared at the time of intubation or when the signs of inadequate anti-nociception [movement, somatic arousal (coughing, grimacing etc.), 15% elevation in NIBP or HR] were observed. Our special interest was in instances when the patient received fentanyl in association with a reaction. Additionally, the components of the SPI, PPGAnorm, and RRInorm were analysed at the time points of intubation and incision. To prevent inaccuracy in the choice of analysed time windows, the median value within a selected time window of 30 s before and 30 s after the point of interest was used for the statistical calculations of SPI, RRInorm, and PPGAnorm values. The signs of inadequate anti-nociception were analysed only between the time of intubation and the end of surgery. In the event of several signs of inadequate anti-nociception occurring within 10 min intervals, only the first was included in the analysis.

Results

Data were collected between January 2014 and March 2015. The patient characteristics and relevant intraoperative data are shown in Table 1. A significant increase in the SPI was observed at the time of intubation and at the time of incision in the SG. At the time of incision in the BG, and when the signs of inadequate anti-nociception were present, no significant changes in the SPI were observed (Fig. 2 and Table 2). The PPGAnorm changed significantly at the times of intubation and incision in the BG, and the RRInorm at the time of incision in the SG (Fig. 3 and Table 2). Eighteen patients experienced 26 events of inadequate anti-nociception, fulfilling the predetermined criteria.

As a reaction to the operation, fentanyl was administered 12 times; six times in both groups (in nine instances soon after incision). The main reason for administration was movement (five times) or heart rate and blood pressure reaction (seven times). A significant change in the SPI from a median (IQR) of 56 (45, 67) to 78 (67, 84; $P=0.008$) was observed (Fig. 2).

At the time of tracheal intubation, the sevoflurane end-tidal concentration was between 1.8 and 5.3%. No correlation between the ΔSPI and age was found (data not presented).

The changes in heart rate, response entropy (RE), NIBPsys, and NIBPmean after the incision are shown in Table 3. There were no significant differences between the groups.

The mean amount of local anaesthetic used was 0.2 (SD 0.1) ml kg^{-1} for each block.

Discussion

The main finding in our study was that the SPI was able to detect nociceptive stimuli in children aged younger than 24 months. A significant increase in the SPI was seen in both groups at the time of intubation and at the time of incision in the SG. In the BG, the SPI did not change significantly at the time of incision, indicating a blunted reaction with ilioinguinal and iliohypogastric block. Moreover, a significant change in the SPI was also seen when the decision to administer fentanyl was made.

Table 1 Patient characteristics and details of anaesthesia and type of surgery presented as numbers or means (SD or range). The *P*-values were calculated using Student's unpaired *t* test

Characteristic	Block group	Saline group	P-value
Age (weeks)	21.6 (6–78)	23.7 (7–80)	
Gestational age (weeks)	57.1 (38.7–117)	61.3 (40–120)	
Sex (*n*)			
Female	2	2	
Male	13	13	
Height (cm)	58.0 (11.9)	63.0 (2.2)	
Weight (kg)	5.8 (3.1)	6.8 (2.2)	
ASA I/II/III (*n*)	2/12/1	5/10/0	
Surgery (*n*)			
Inguinal hernia	14	13	0.559
Undescended testicle	1	2	
Type (*n*)			
Unilateral	13	10	0.208
Bilateral	2	5	
Intubation attemps (*n*)	1.6 (1.0)	1.5 (0.9)	0.849
Time from block to incision (min)	23:33 (7:40)	18:57 (4:41)	0.057
Fentanyl (μg kg^{-1})	3.0 (0.8)	2.4 (0.64)	0.386
Sevoflurane at incision (end-tidal %)	2.9 (0.4)	2.9 (0.4)	0.930

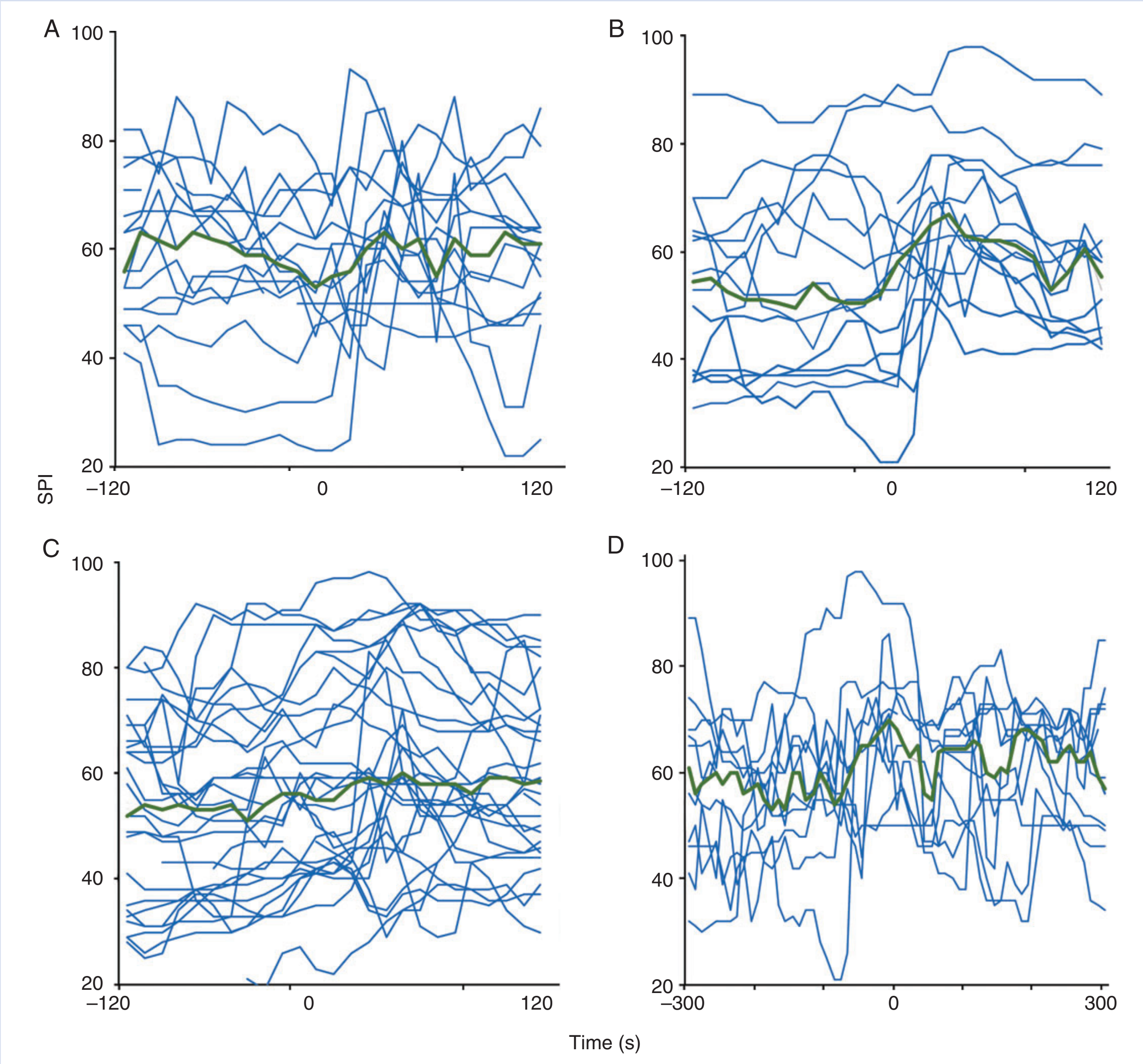

Fig 2 The median value of the surgical pleth index (SPI) at incision in the block group (A), the saline group (B), at intubation (C), and at times when fentanyl was administered (D). Blue lines represent each individual, and the green line shows the median of all measurements. The time point of interest is located at the middle of the x-axis (0). The total time line is 240 s (A–C) and 600 s (D).

The heart rate and NIBP changed at all measured points when defined by maximal change within a reasonable time frame. Although traditionally used as measurement of nociception, these have not been very specific markers for nociception.[13 14] This also applies to RE, which is known to reflect muscle activity at the forehead. The RE reaction is lost with the use of neuromuscular block,[15] and entropy has shown unreliable values in infants.[16] In contrast to earlier methods, the SPI has also proved to be a promising method for monitoring intraoperative nociception in older paediatric patients.[9] However, the paediatric data are inconsistent and controversial.[8] The SPI has not been studied in children younger than 24 months of age. To our knowledge, this is the first study conducted in children aged <2 yr.

Although significant changes in the SPI were seen, a large inter-individual difference was observed in our study (Figs 2 and 3). There also seemed to be a large variance in the baseline of the PPGAnorm, and the duration of the reactions was short. Interestingly, the PPGAnorm decreased in all groups at the times of both intubation and incision, but the change was not significant in the SG at the time of incision. This might be because of the wide IQR found with PPGAnorm. Although not statistically significant, the rate of change was almost the same as found at intubation. The RR interval, which is the inverse of the HR, increased at intubation, indicating decreasing HR, and decreased (i.e. HR increased) at incision. This is consistent with an earlier study in adults, where the RR interval reacted to tracheal intubation and a standardized tetanic stimulus.[17] The strong vagal stimulus caused by intubation might explain why the heart rate decreased as a reaction to intubation, but increased in association with surgical stimulation, which is known to provoke a sympathetic reaction.

Table 2 Surgical pleth index, normalized pulse plethysmographic amplitude, and normalized RR interval values at different time points. Each A and B represents a Median value of a time window of 30 s length. The time window was taken ending about 20 s before (A) and starting about 20 s after (B) each time point (like SPI at intubation). For signs of inadequate anti-nociception, the median value at the time point (B) and 5 min before (A) is presented. Δ describes the median magnitude of change at each value. The *P*-values were calculated with the Wilcoxon signed rank test. Values are presented as median (interquartile range). *$P<0.05$. PPGAnorm, normalized pulse plethysmographic amplitude; RRInorm, normalized RR interval; SPI, surgical pleth index

Parameter	*n*	A	B	Δ	*P*-value
SPI					
Intubation	30	52.5 (40.5–69.5)	58.5 (50.5–58.5)	5.8 (−1.5 to 20.3)	0.019*
Incision in saline group	15	49.00 (37.6–67.2)	62.8 (53.0–69.9)	10.7 (−6.1 to 24.1)	0.048*
Incision in block group	15	58.0 (44.9–60.6)	57.3 (51.8–68.8)	2.8 (−4.1 to 13.9)	0.177
Signs of inadequate anti-nociception	28	56.0 (47.6–68.9)	60.0 (52.8–76.0)	1.3 (−3.9 to 12.5)	0.148
PPGAnorm					
Intubation	30	522.0 (273.0–713.2)	426.6 (157.1–595.9)	1.3 (−3.8 to 12.5)	0.003*
Incision in saline group	15	521.0 (252.5–635.5)	349.4 (214.8–520.6)	−68.3 (−245.1 to 127.7)	0.397
Incision in block group	15	396.0 (274.0–493.0)	323.9 (178.4–440.7)	−98.1 (−175.5 to −27.1)	0.009*
RRInorm					
Intubation	30	263.3 (97.0–518.0)	293.3 (129.0–405.5)	2.3 (−189.3 to 89.0)	0.387
Incision in saline group	15	587.3 (480.3–690.5)	481.5 (186.4–543.3)	−120.9 (−355.1 to −10.1)	0.007*
Incision in block group	15	667.0 (564.8–690.0)	631.3 (243.4–715.3)	−38.0 (−176.1 to 16.4)	0.087

Table 3 The maximal change of systolic (NIBPsys), mean (NIBPmean) pressures and Response Entropy (RE) within a selected timeline (max2min and max5min). Values are presented as median (interquartile range). *$P<0.05$. BG, block group; HR, heart rate; SG, saline group

Parameter	At incision	After incision	P-value
$HR^{max2min}$			
BG	135.0 (130.0–150.0)	145.0 (130.0–160.0)	0.008*
SG	138.0 (130–160.0)	155 (145.0–160.0)	0.001*
$RE^{max2min}$			
BG	26.0 (17.50–38.8)	30.0 (22.0–62.0)	0.008*
SG	26.0 (17.50–50.0)	30.0 (22.0–69.0)	0.001*
$NIBPsys^{max5min}$			
BG	73.70 (49.0–80.0)	76.0 (54.3–90.0)	0.003*
SG	67.0 (48.0–76.0)	72.0 (54.0–82.0)	0.001*
$NIBPmean^{max5min}$			
BG	52.0 (37.5–58.3)	54.0 (40.5–69.3)	0.002*
SG	47.0 (37.0–58.0)	56.0 (41.0–61.0)	0.001*

These findings suggest that the rapid change seen in the SPI at intubation was most probably caused by a change in PPGAnorm.

The SPI was developed by combining two parameters, RRInorm and PPGAnorm, which were found to describe the surgical nociception best.[3] To our knowledge, these components have not been studied in detail thereafter, in relation to surgical nociception. Nobody really knows how these components behave in small children. In the present study, the change in PPGAnorm was significant in the block group, but not in the saline group, which is paradoxical. The SPI response was nevertheless significant in the saline group and not in the block group. This might be because of a higher basal heart rate in small children when compared with adults.

Our patients were very young, especially when defined by gestational age. The infants were still immature, which might explain the difference in reactions when compared with adults.[10] The individual differences in the values of PPGAnorm at the time of skin incision were large. Several patients in both groups reacted strongly, but others had almost no reaction. The baseline values of SPI and PPGAnorm were also variable. The reasons for this variability remain unknown.

The median SPI value seems to be much higher in our study (52.5) compared with the mean SPI value before intubation in adults (44.2)[18] and older children (43.3),[9] perhaps because of a higher HR in the younger age group. At the time of incision, the HR increased in both of our study groups. The SPI consists of HR (33%) and change in the pulse plethysmographic amplitude (67%). It combines the information as one number from 0 to 100, indicating surgical nociception.[3] In other words, the higher baseline HR in small children compared with that of adults results in a higher baseline value of SPI in children. For example, a 20 unit change in HR in paediatric patients has a smaller relative effect on the SPI as compared with adults. All in all, the role of plethysmography is major in the calculation of the SPI.

A recent study[8] attempted to show the usefulness of SPI in guiding intraoperative fentanyl administration in children aged 3–10 yr undergoing adenotonsillectomy. The study showed that the use of SPI was associated with adequate intraoperative anaesthesia and anti-nociception. Unfortunately, patients had more pain, nausea, and emergence agitation during the postoperative period, which was interpreted as a failure of the SPI. This underlines the fact that the effect of perioperative treatment during the postoperative period should not be underestimated. In addition, this unsatisfactory result may have been a consequence of trying to transpose reference adult values directly to children, as discussed above.

The SPI has mostly been studied with propofol–remifentanil anaesthesia.[4 7 19] The SPI guidance in propofol–remifentanil anaesthesia compared with standard monitoring resulted in more stable anaesthesia and lower consumption of remifentanil.[4] It has also been shown to be similarly reactive during sevoflurane–fentanyl anaesthesia[20] and sevoflurane–sufentanil-based anaesthesia.[6] However, using such anaesthesia, SPI guidance did not show any benefits when compared with standard of care. Although the reactivity of the SPI to noxious stimulation has been found to be present with all opioids in the adult population, it remains to be determined whether such reactivity is present in small children when other opioids are used.

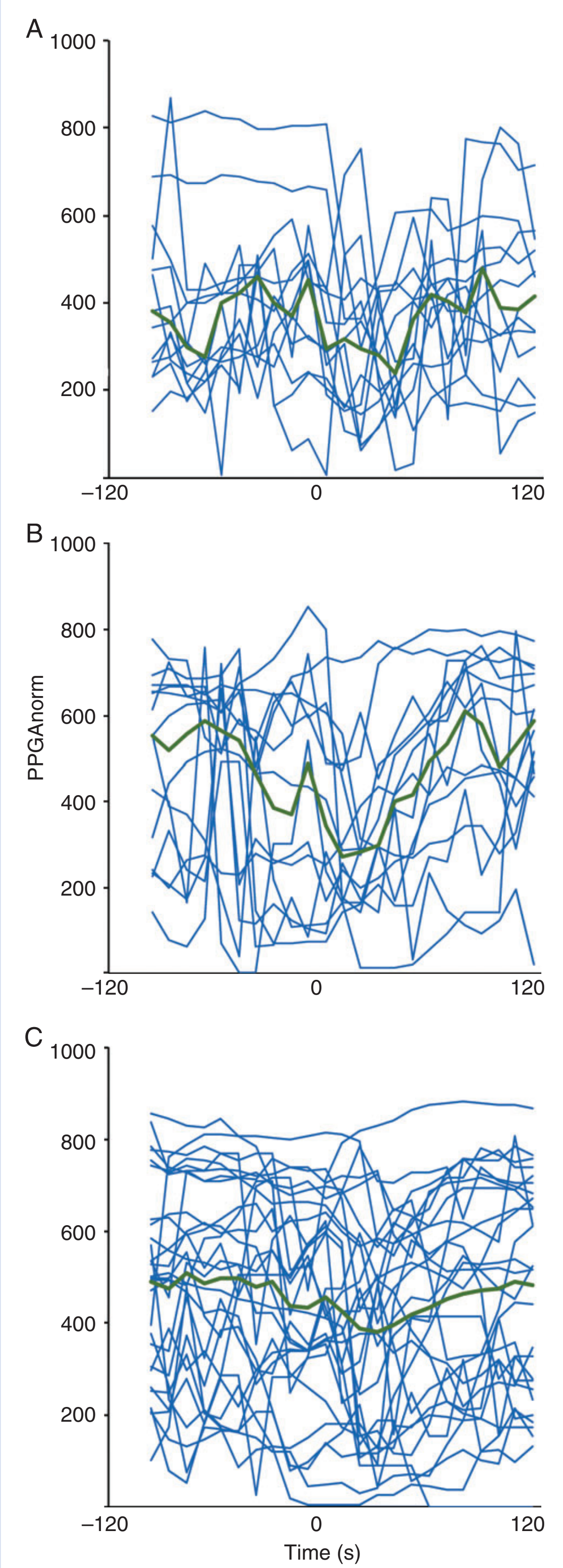

Fig 3 The median value of the normalized pulse plethysmographic amplitude (PPGAnorm) at incision in the block group (A), the saline group (B), and at intubation (C). Blue lines represent each individual, and the green line shows the median of all measurements. The time point of interest is located at the middle of the x-axis (0). The total time line is 240 s.

The ilioinguinal and iliohypogastric block has been shown to be an effective aid for inguinal hernia repair.[21] With ultrasound guidance, it has shown a 95% success rate in inguinal hernia repair, orchidopexy, or hydrocoele repair for postoperative pain.[22] Placing the block before the surgery is common practice at our hospital, and surgeons have not argued about interference with the surgical site when it is placed before surgery. In our study, no difference in the amount of fentanyl used in micrograms per kilogram or the number of administrations during the intraoperative period were found between the two study groups. These results are also in line with the findings of a study that found ilioinguinal and iliohypogastric nerve block unable to block all reactions during inguinal hernia repair.[23]

A number of confounding factors can be found in our study. Firstly, all patients were intubated, with relatively high amounts of opioid administered. This might have blunted the effect of relatively minor noxious stimulus, namely the surgical incision. Secondly, the patients were also administered a relatively high sevoflurane concentration. Thirdly, the innervation of the testicles and abdominal wall comes from pelvic plexus and thoracic nerve routes, which are not necessarily affected by the block.[23 24] This might explain why the fentanyl consumption did not differ between the groups, even though the ilioinguinal and iliohypogastric block should be effective during the incision for both types of surgeries. In relation to this, the groups are only comparable up to the time of incision and the time interval briefly afterward. Fourthly, all patients received glycopyrrolate in order to block possible side-effects caused by succinylcholine. Glycopyrrolate has anticholinergic effects, which might block part of the reactions used in the calculation of the SPI.[25] However, all the anaesthetics and anaesthesia methods used in this study are typical in paediatric anaesthesia practice; thus, our findings describe the typical performance of the SPI in this patient group.

Conclusions

Our study shows that the SPI has the potential to detect nociception in small children, and an (blinded) increase in the SPI was associated with the clinical decision to administer fentanyl. However, the duration of the reaction was very short, and there were large inter-individual differences among children, which might have interfered with the clinical usefulness of the SPI. This indicates that one should be cautious when considering using the SPI in clinical practice in this age group.

Authors' contributions

Study design, writing, and analysis: J.H., M.-L.K., H.L., A.Y.-H.
Conduct of the study measurements and blocks: J.H., M.K.
Analysis of the results: J.H., M.-L.K., H.L., A.Y.-H.
Writing the manuscript: J.H., M.-L.K., H.L., A.Y.-H., M.K.

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Declaration of interest

None declared.

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