Emergence agitation in paediatric day case surgery: A randomised, single-blinded study comparing narcotrend and heart rate variability with standard monitoring

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ORIGINAL ARTICLE

Emergence agitation in paediatric day case surgery

A randomised, single-blinded study comparing narcotrend and heart rate variability with standard monitoring

Line Gry Larsen, Marie Wegger, Sebastian Lé Greves, Liv Erngaard and Tom G. Hansen

BACKGROUND Postoperative emergence agitation remains a significant challenge in paediatric anaesthesia. Although short-lived, it may cause harm to the patient and negative experiences for all. Differentiating agitation, delirium and pain is difficult. Electroencephalography allows precise titration of anaesthetic depth, and heart rate variability monitoring permits immediate intervention regarding nociception and pain. We examined if one of these measures could be used to reduce postoperative agitation in an unselected paediatric day surgical population.

OBJECTIVE The primary outcome was postoperative agitation with a Richmond Agitation-Sedation Scale greater than 0. Secondary outcomes were: length of stay, postoperative nausea and vomiting, fentanyl and propofol consumption, pain scores and use of postoperative analgesics.

DESIGN A randomised, single-blinded study constituting children aged 1 to 6 years, undergoing minor general day surgical procedures.

SETTING Paediatric day surgical department 29th March 2019 to 12th June 2020.

PATIENTS Ninety-eight children (ASA 1 or 2) were enrolled, and 93 children were included in the final analysis.

INTERVENTIONS Children received standard monitoring ($n=31$), standard monitoring plus either Narcotrend ($n=31$), or Anaesthesia Nociception Index monitoring ($n=31$). Sevoflurane or fentanyl was titrated immediately according to monitor thresholds.

RESULTS Kaplan–Meier analysis yielded a statistically significant difference between the groups ($P=0.016$) with the lowest agitation levels in the Anaesthesia Nociception Index group, intermediate levels in the control group and the highest agitation levels in the Narcotrend monitored group. Intergroup pairwise comparison however, showed no difference. The Anaesthesia Nocioception Index group received slightly more fentanyl ($P=0.277$). The control group patients had the highest pain scores despite receiving more caudal blocks and the Narcotrend group had more sevoflurane adjustments. Other secondary outcomes were comparable.

CONCLUSION Children in the Anaesthesia Nociception Index group were the least agitated with the highest fentanyl doses, without increasing the length of stay in the PACU or postoperative nausea and vomiting.

CLINICAL REGISTRATION The study was registered in RedCAP online trial database 1/11/2018 trial registration nr. OP720. https://open.rsyd.dk/OpenProjects/openProject.jsp?openNo=720&lang=da.

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KEY POINTS

- Paediatric emergence agitation may be reduced with increased and immediate nociceptive control.

Introduction

Paediatric postoperative emergence agitation and delirium remains a significant challenge in paediatric anaesthesia. Mental confusion, irritability, disorientation and inconsolable crying characterise this phenomenon. The

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terms emergence delirium and emergence agitation have previously been used interchangeably, even though delirium as such does not necessarily include motor activity. Assessing behaviour in children emerging from anaesthesia is difficult, and separating emergence agitation from delirium and pain is challenging as many symptoms overlap.[1,2]

Emergence agitation may result in unnecessary harm to the child, cause parental concern, and disturb the general atmosphere of the Postoperative Anaesthesia Care Unit (PACU). Furthermore, emergence agitation has been associated with an increased risk of transient postoperative maladaptive behaviour.[2,3] Emergence agitation usually occurs during the first 30 min after anaesthesia, resolves spontaneously and disappears within 10 to 45 min but may occasionally be more prolonged. Overall, the incidence of emergence agitation is approximately 5%[4] but is far more common in young children with a reported incidence ranging between 10 and 80%.[4,5] Predisposing factors are inhalational (sevoflurane) anaesthesia, age of the child (preschool children), preoperative anxiety, male sex and certain specific surgical procedures.

Traditional assessments of the depth of anaesthesia have been based on clinical signs and haemodynamic and respiratory responses. Technological advances during the last 20 years have led to the development of electroencephalography (EEG)-based depth of anaesthesia monitors.[6]

Recently the interest in the evaluation of nociception and pain has increased. Measuring nociceptive signals allows more precise dosing of drugs aimed at blocking these, for example opioids. One such measure for nociception is heart rate variability (HRV), which expresses the natural physiological irregularity of heartbeats, adjusted by increased or decreased vagal tone.[7,8] HRV data are obtained from an ECG signal and the variability analysis is then performed using mathematical modelling of R-R intervals. HRV analysis is an instant and noninvasive measure with a well examined basis in cardiology. It has been used as a marker for cardiac mortality, and also in the context of chronic pain, stress and epilepsy.[8,9]

Similar to EEG monitoring, the number of studies on HRV monitoring in children has risen within the last decade but so far no studies focusing on the impact of such monitoring on emergence agitation have been published.

Thus, the purpose of this study was to investigate if general anaesthesia guided by either EEG or HRV could reduce postoperative emergence agitation compared with traditional assessments of anaesthesia in an unselected outpatient paediatric population. The primary outcome was agitation as measured using a Richmond Agitation-Sedation Scale (RASS) greater than 0. Secondary outcomes were fentanyl dosages, length of stay, propofol consumption, events during anaesthesia (adjustments of sevoflurane, additional fentanyl doses, regional anaesthesia, extensive surgical stimuli, airway responses, or other reactions from patient), pain scores, postoperative nausea and vomiting (PONV) and the use of analgesics within the first 24 h after surgery.

Methods

Ethics

This study was approved by the Ethics committee in the Region of Southern Denmark (Damhaven 12 7100, Vejle, Denmark, registration number s2018-0119, chairperson Kirsten Ohm Kyvik), and The Danish Data Protection Agency (case numbers 18/48/390 and 20/5326).

The study was registered in RedCAP online trial database on 1 November 2018 at *https://open.rsyd.dk/OpenProjects/openProject.jsp?openNo=720&lang=da*.

Data collection was commenced on 29 March 2019 and ceased on 12 June 2020. Written informed consent was obtained from all participants' parents or legal surrogates.

Inclusion and exclusion criteria

Inclusion criteria

Children aged 1 to 6 years, ASA 1-2, scheduled to undergo minor general surgical procedures, mostly hernias and orchidopexy repair, including reoperations and bilateral procedures. The airways were managed with either laryngeal mask airways or facemasks. Induction and rescue dosages of propofol were permitted.

Exclusion criteria

Children younger than 1 year and older than 6 years; ASA greater than 2, lack of consent; endotracheal intubation; medications that interfered with autonomic nervous system reactivity, for example, inhaled beta-agonists for bronchial asthma, total intravenous anaesthesia (TIVA).

The CONSORT diagram: see Appendix 1, http://links.lww.com/EJA/A671.

Study protocol

Information about this study was sent out to potential participants by mail 2 days before surgery. On arrival at the hospital, the project was orally presented to the child and parents, and written informed consent was obtained. Randomisation was then made by 6-6-9 clusters using the RedCap Randomisation module. All children received paracetamol and diclofenac premedication according to body weight. Both parents were allowed to come to the operation room and the child was then anaesthetised using sevoflurane 8% in an oxygen/air mixture via a facemask while sitting on the lap of one of the parents. Conventional multiparameter monitoring was employed; noninvasive arterial blood pressure (BP), heart rate (HR), ECG, peripheral capillary oxygen saturation (SpO_2), and an intravenous catheter was sited. Fentanyl (2 to 4 $\mu g\,kg^{-1}$ i.v.) was then administered in doses clinically

appropriate to the type of surgery, and a laryngeal mask airway was then inserted. The aim was to achieve and maintain a well anaesthetised, spontaneously breathing patient during the entire procedure. The peri-operative sevoflurane concentration was maintained at a Minimum Alveolar Concentration (MAC) of 0.9 to 1.1. All children received wound infiltration by the surgeon at the end of the procedure using 0.25% bupivacaine (0.3 to 0.5 ml kg^{-1}). Children below 3 years of age who had bilateral procedures (hernia and orchidopexy repairs) received a caudal block. In the intervention groups, the study monitors (Mdoloris ANI monitor for HRV or Narcotrend EEG monitor) were then sited. For all 3 groups, any peri-anaesthetic events were noted. Placement of airway devices, skin incisions, skin suturing and removal of airway devices were obligatory events in all participants. Additional potential events were surgical stimulation, additional fentanyl dosages, adjustments of sevoflurane levels, caudal blocks, coughing or moving. Index values in the Narcotrend (NCT) and Anaesthesia Nociception Index (ANI) groups were evaluated every 5 min and adjusted according to protocol. In the ANI group, a supplementary fentanyl dose of 1 μg kg^{-1} was given when reaching an ANI threshold of 50 and sevoflurane levels adjusted according to the clinician's usual practice. In the NCT group, the Narcotrend index was maintained in the 40 to 60 range. The anaesthetist in charge was allowed to overrule the protocol if this was deemed to be in the best interests of the child. The derived effects of adjusted sevoflurane and fentanyl levels were monitored and reported in the usual manner. After the procedure, the parents were asked to join their child in the PACU. The children were RASS-scored every 15 min until discharge. Very low RASS scoring (−5, −4) were not expected and clinically irrelevant to this study, and the PACU nurses were instructed not to stimulate or disturb sleeping children, which is a requirement in exact RASS scoring.[10] Furthermore, in addition to the routine Face Legs Activity Cry Consolability (FLACC)[11] score, the PACU nurses were asked to quantify the worst pain they believed the child had in the PACU on a 0 to 10 numerical Visual Analogue Scale (VAS). If pain was detected, morphine 25 μg kg^{-1} body weight was administered intravenously (FLACC >2). PONV was rated 0 to 3, with '0' representing no PONV and '3' representing severe PONV. If nonpharmacological interventions were not effective, ondansetron 0.1 mg kg^{-1} i.v. was administered as first-line medical treatment.

Follow-up

Follow-up was performed with a telephone call a minimum of 24 h after the procedure. VAS scores and the amount and type of analgesics administered during the first 24 h postoperatively (paracetamol and NSAIDS) were obtained from the parents.

The monitors

The Mdoloris Anaesthesia Nociception Index (ANI) monitor (Mdoloris Medical Systems, Lille, France) is a computer-based ECG monitor that does beat-to-beat analysis of HRV. It evaluates HRV via signals from two separate monitor electrodes placed on the patient's chest. The HRV is then estimated via the R-R intervals from the QRS waves. It outputs an 'ANIi' and 'ANIm' value on a numerical unit-free scale ranging from 0 to 100 on the monitor screen and displays a graphic trend. The ANIi represents the the 120 seconds moving average of the instantaneous ANI values and the ANIm represents the 240 seconds moving average. According to information provided by the manufacturer, the threshold for intervention was an ANI value of 50. ANIi values below this limit prompted immediate supplementary fentanyl administration. In paediatrics, ANI has previously been shown to be effective in detecting surgical stimuli,[12] predicting inadequate peri-operative antinocieption,[13,14] and measuring acute postoperative pain.[15]

The Narcotrend (NCT) EEG monitor (MonitorTechnik, Bad Bramstedt, Germany) measures brain wave activity. With increasing depth of anaesthesia, the brain wave activity follows a similar brain wave pattern as during normal sleep. These patterns are divided into six stages from the awake 'A' state to the burst suppression and electrical silence 'F' stage. The NCT monitor collects EEG signals from three electrodes placed on the patient's forehead. A raw EEG is displayed on the monitor alongside a stage letter A to F and a unitless index number (NI) from deeply comatose at '0' to fully awake at '100'. From the raw EEG to a numerical NCT value, a delay of approximately 20 s is expected. The manufacturer's guidelines recommend titrating the NI from 20 to 60; however, we chose to narrow the intervention interval to 40 to 60 to ensure acute anaesthetic depth titration and preventing burst suppression. The NCT monitor is the only monitor on the market that has an age-related algorithm,[16] taking into consideration the different brain wave patterns for different ages, with promising results even with smaller children below 1 year of age.[6] Reduced propofol consumption[13] and tight correlation with end-tidal sevoflurane have been demonstrated.[17] The treatment protocol is summarised in Appendix 2, http://links.lww.com/EJA/A672.

Scales and scoring systems used in this study

Reliability and Validity of the Richmond Agitation-Sedation Scale

The RASS scale was originally designed for adult intensive care patients. It consists of a 10-step scale from the unarousable patient who does not respond to any stimuli at −5 to the highly agitated, combative patient at +4. As our focus was agitation, regardless of cause, we chose to use this scale. Although it is not considered standard practice in the setting of paediatric emergence agitation,

Table 1 Richmond Agitation-Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has an aggressive behaviour to staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert but has sustained (more than 10 s) eye contact to voice
−2	Light sedated	Briefly awakens (less than 10 s) with eye contact to voice
−3	Moderate sedation	Any movement (but not eye contact) to voice
−4	Deep sedation	No response to voice but any reaction to physical stimulation
−5	Unarousable	No response to voice or any physical stimulation

it has been used in several emergence agitation studies in both adults and children.[2,18,19] It has the advantage of simplicity, and excellent inter-rater reproducibility,[10,20] even in critically ill postoperative children.[21] The RASS scale is presented in Table 1.

Visual Analogue Scale

The 0 to 10 Visual Analogue Scale[21] is widely used for pain scores in adults and older children; '0' represents no pain, and '10' represents the worst pain imaginable. It is simple to use and suitable as we wanted to compare the nurses' perception of the child's pain with parents' perception of their child's pain in the follow-up phone interview.

Statistical analyses

All statistical analyses were performed using STATA 16.1/17 (StataCorp LLC, 4905, Lakeway Drive, College Station, Texas 77845-4512, USA).

Power calculation

The sample size calculation was based on a two-group study and with an estimated and clinically relevant reduction in the incidence of emergence agitation from 40 to 9%. With a power of 80% and a type 1 error of 5% each group would require 30 patients. With a three-group study, the robustness of the results obtained was increased and we were able to examine two separate interventions with one control group only.[22]

Statistical methods for the primary outcome

For the primary outcome evaluation, a Kaplan–Meier survival analysis was conducted as follows. Patients were marked out as soon as they had a RASS score greater than 0, and hence excluded from further analysis from that point onwards. Intergroup comparison was performed with the log-rank test for equality of survivor functions.

Statistical methods for descriptive statistics and the secondary outcomes

Data are shown as a mean (range) for continuous variables and median [range] for discrete variables. Discrete and categorical variables were compared using the χ^2 test, or Fisher's exact test if the numbers of observations were less than five. All continuous variables were tested for skewness and kurtosis. If this revealed a non-normal distribution, the Kruskal–Wallis test was applied. For normally distributed data, a one-way ANOVA was applied.

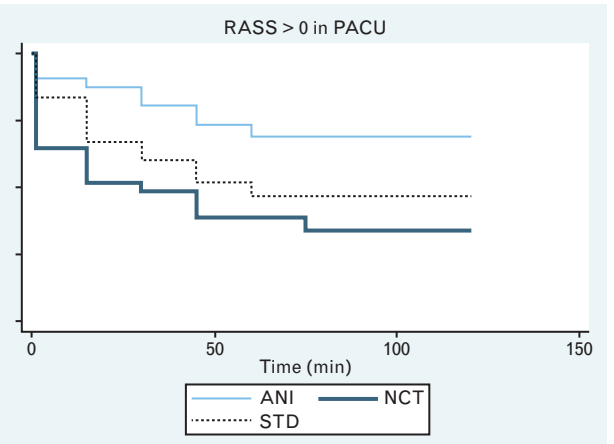
Results

Ninety-eight children were enrolled. Five children were excluded after randomisation; three children because of unplanned intubation, one child because of equipment failure and, finally, one child because of missing data. In this patient, the primary outcome data was not collected but the child received the intervention and was thus included in all the other analyses. No parents or patients withdrew consent. A total of 93 patients were included for analysis, 31 to the control group, 31(30) children to the ANI group and 31 to the NCT group.

Despite several telephone calls to the families in the immediate days after surgery, 23 patients (STD n=12, ANI n=6, NCT n=5) were lost to follow-up regarding postanaesthetic pain scores and analgesic usage.

During the entire PACU stay, a total of 49% (44/92) of patients developed agitation, constituting 48% (15/31) in the STD group, 30% (9/30) in the ANI group and 65%

Fig. 1 Kaplan–Meier graph



ANI, Anaesthesia Nociception Index group; NCT, Narcotrend group; STD, standard (control) group.

Table 2 Patient characteristics

	Total	STD	ANI	NCT	*P*
Age (years)	3.1 (1.0 to 6.9)	3.1 (1.0 to 6.9)	3.1 (1.0 to 6.5)	3.1 (1.0 to 6.5)	0.938[a]
Weight (kg)	15.4 (7 to 31)	14.9 (9 to 31)	16.0 (7 to 28)	15.2 (9 to 22)	0.798
Male sex	76 (82)	25 (81)	26 (84)	25 (81)	0.931
Female sex	17 (18)	6 (19)	4 (16)	6 (19)	1.000
Procedure types					
Hernia repair, unilateral	21	6	9	6	0.685
Hernia repair, umbilical/midline	17	5	4	8	
Orchidopexy repair, unilateral	20	7	7	6	
Orchidopexy repair, bilateral	5	4	1	0	
Re-operations, all kinds	8	3	3	2	
Minor procedures	22	6	7	9	
Total	93	31	31	31	

Data are mean (range), number (%), and number. ANI, Anaesthesia Nociception Index group; *n*, number of observations; NCT, Narcotrend group; STD, standard (control) group. [a]Bimodal normally distributed around 2 and 4 years.

(20/31) in the NCT group. Very low RASS (−5) was not detected. Three different Kaplan–Meier curves were constructed (Fig. 1). The RASS trends in the intervention groups were situated on either side of the control group (STD) on the Kaplan–Meier graph, demonstrating significant differences in the primary outcome between the groups ($P = 0.016$) with the highest RASS in the NCT group, and the lowest RASS scores in the ANI group. Pairwise intergroup comparison, however, did not show a significant difference between ANI and STD ($P = 0.070$) or NCT vs. STD ($P = 0.265$) but it did show a significant difference between the ANI and the NCT groups ($P = 0.043$). For patient characteristics, see Table 2.

The secondary endpoints, apart from fentanyl dosage, were all nonnormally distributed (Table 3).

Four children accepted intravenous induction and did not receive high-dose sevoflurane for induction. Some children received minor rescue propofol boluses to diminish immediate reflexes concerning short lived stimuli. The total propofol doses in the three groups were comparable (Table 4).

The ANI group received significantly higher fentanyl doses; ANOVA: ANI 3.07 $\mu g\,kg^{-1}$ [95% confidence interval (CI), 2.76 to 3.36], NCT 2.68 $\mu g\,kg^{-1}$ (95% CI, 2.42 to 2.94), STD 2.56 $\mu g\,kg^{-1}$ (95% CI, 2.27 to 2.83), $P = 0.0267$ (Table 4). Six patients were still agitated despite regional anaesthesia ($P = 0.160$). Significantly higher VAS scores in the PACU were found in the STD group ($P = 0.015$), even though more patients ($P = 0.026$) received a caudal block. However, Cox regression analysis, adjusting for this, did not show any difference between the groups. The NCT group had the highest number of patients with sevoflurane adjustments ($P = 0.010$). One child received intravenous morphine in the PACU and no children were treated for PONV. Other baseline characteristics and secondary outcomes were comparable; procedure type and duration, age, sex, weight, propofol consumption, PONV, use of other analgesics and VAS scores 24 h after the procedure. All study procedures were noninvasive, and no harmful effects were noted in these patients.

Discussion

This study demonstrated that the use of ANI reduced postoperative agitation without affecting other outcomes. Despite higher doses of fentanyl in the ANI group, the procedure duration did not differ from the other groups, they did not experience more PONV and, importantly, the incidence of agitation was less. The timing of the fentanyl administration might be a factor here, as the duration of the surgical stress response is minimised. This supports findings from previous studies using ANI, which have demonstrated that ANI can detect surgical stimuli and support immediate antinociceptive therapy.[12,23] Our study supports the common belief that pain is an important part of emergence agitation.

The study population is comparable with other paediatric emergence agitation studies regarding age, anaesthesia, surgical procedures, outcomes[24–27] and the overall rate of agitation (30 to 65%). All children were anaesthetised similarly with sevoflurane and fentanyl. Occasionally

Table 3 Primary outcome. Kaplan–Meier table and Ramsay Agitation and Sedation Score max

	Total events observed during entire PACU stay	Events expected	Median RASSmax (mean)
STD	15	14.9	1 (1.3)
ANI	9	16.7	0 (0.6)
NCT	20	14.1	1 (1.0)
Total	44	44.0	1
P		0.016	(0.155)

ANI, Anaesthesia Nociception Index group; NCT, Narcotrend group; RASS, Ramsay Agitation and Sedation Score; STD, standard (control) group.

Table 4 Secondary outcomes

	STD	ANI	NCT	Total	*P*
Fentanyl ($\mu g\,kg^{-1}$) (95% CI)	2.56 (2.27 to 2.83)	3.07 (2.76 to 3.36)	2.68 (2.42 to 2.94)	2.78 (2.60 to 2.93)	0.027
Time (min), anaesthesia	53 (17 to 110)	51 (8 to 120)	45 (11 to 75)	49 (8 to 120)	0.021
Time (min), PACU	98 (15 to 230)	97 (45 to 180)	95 (40 to 140)	96 (15 to 230)	0.863
Time (min), total	152 (48 to 306)	148 (68 to 280)	140 (80 to 190)	147 (48 to 306)	0.0672
Propofol ($mg\,kg^{-1}$) accumulated	0.67 (0 to 4.55)	0.37 (0 to 5.55)	0.40 (0 to 3.18)	0.48 (0 to 5.55)	0.294
PCM ($mg\,kg^{-1}$)[a]	43 (0 to 161)	34 (0 to 71)	35 (0 to 120)	37 (0 to 161)	0.576
Diclofenac [$mg\,kg^{-1}$][b]	1.9 (0 to 6)	0.9 (0 to 4)	1.7 (0 to 16)	1.47 (0 to 16)	0.187
Misc. analgesics (*n*) (total obs.)	4 (21)	5 (25)	0 (23)	9 (69)	0.053
Pain, PACU	**STD**	**ANI**	**NCT**	**Total**	***P***
Mild (VAS 0 to 3)	21	30	29	80	0.015
Moderate (VAS 4 to 6)	5	0	1	6	
Severe (VAS 7 to 10)	4	1	1	6	
Pain, 24 h	**STD**	**ANI**	**NCT**	**Total**	***P***
Mild (VAS 0 to 3)	13	13	17	43	0.288
Moderate (VAS 4 to 6)	5	6	1	12	
Severe (VAS 7 to 10)	2	4	4	10	
PONV, PACU	**STD**	**ANI**	**NCT**	**Total**	***P***
None (0)	26	23	25	74	0.540
Mild (1)	0	3	2	5	
Moderate to severe (2 to 3)	2	1	2	5	
Events	**STD**	**ANI**	**NCT**	**Total**	***P***
Total additional fentanyl events	6	17	7	30	0.106
Total adjusting sevoflurane events	28	24	35	87	0.583
Individuals w. additional fentanyl	6	14	7	27	0.051
Individuals w. sevoflurane events	16	9	21	46	0.009
Extensive surgical stimuli	16	35	17	68	0.063
Caudal block	6	3	0	9	0.023
Caudal block with RASS >0	4	2	0	6	0.160
Coughing	1	0	1	2	1.000
Moving	1	0	0	1	1.000

The data are mean (95%, CI), mean (range), and n. STD, standard (control) group. ANI, Anaesthesia Nociception Index group; NCT, Narcotrend group; 24 h, 24 hours after surgery; n, number of observations; PACU, Post Anaesthesia Care Unit; PCM, paracetamol; PONV, postoperative nausea and vomiting; Misc analgesics, other analgesics given at home by the parents. [a]Mixture of oral and rectal administration. [b]Rectal suppository.

additional propofol doses were used. The complex pathways involved in nociception involve both cortical and subcortical signalling, thus, an EEG that only measures signals from the surface of the cortex may be inadequate in assessing nociception in its entirety.[28]

In the NCT group, the number of patients who required sevoflurane adjustments to remain within the thresholds was higher ($P = 0.009$). Surprisingly, they had a significantly higher incidence of emergence agitation than the ANI group ($P = 0.043$). A possible explanation for this could be the presence of unnoticed epileptiform EEG patterns during anaesthesia. This study focused on agitation regardless of cause and not on delirium. Still, sevoflurane is known to cause epileptiform discharges,[29] and this has recently been correlated to emergence delirium in paediatric practice.[25] Adjusting the anaesthetic plane up and down several times during the course of an anaesthetic might induce more epileptiform phases, as compared with maintaining a steady-state plane regardless of its depth, and thus might provoke more emergence agitation/emergence delirium. This aspect is supported by recent similar studies suggesting that deep levels of anaesthesia do not affect the incidence of emergence delirium. Thus, the underlying causes for emergence agitation/emergence delirium must be sought elsewhere.[30,31]

Traditionally, the psychometrically tested Paediatric Emergence Delirium (PAED) scale has been used to evaluate postoperative delirium in children. It has several limitations as assessments are subjective, resulting in inter-rater variability and false positive ratings. Furthermore, there is a lack of consensus regarding which threshold value to apply to categorise the rating symptoms as actual delirium. Many signs and symptoms in the PAED scale overlap with the FLACC scale (consolability, restlessness), thus symptoms that one scale defines as delirium, would be defined as pain with the other. Several other scales used to evaluate agitation, pain and delirium in children exist, adding to the heterogenicity in this field, and making comparison rather difficult.[2,4]

In our opinion, focusing on agitation regardless of cause eliminates the dilemma of the difficult differentiation between delirium and pain. A disadvantage of this might be that we miss some cases with 'quiet' emergence

delirium, a specific population for whom very little data is available.

Crying and agitation are completely innate responses in young children who experience anything against their needs and perceptions. Thus the challenges in evaluating emergence agitation in preschool children will probably never fully disappear. During the preschool ages, these behaviours develop, albeit at varying degrees and speed. Objective monitoring seems particularly relevant in smaller and nonverbal children where the clinician's ability to apply optimal treatment could be so enhanced. Noninvasive, simple monitoring, such as ANI providing instant feedback to support an optimal antinociceptive treatment may be helpful here.

Study limitations

The duration of similar procedures varied among different surgeons, although there were no significant differences in durations overall. The administration of additional fentanyl doses according to the study protocol (ANI <50) was in some instances withheld by the anaesthetist in charge because of clinical judgements made regarding patient comfort and both operation theatre and day ward flow imperatives.

A higher incidence of epileptiform EEG patterns in the NCT group can not be excluded. Unfortunately, evaluation of the raw EEG pattern was not a part of our study and are not revealed by the numerical NCT value. Moreover, the risk of type II statistical error should always be born in mind in studies like these.

Conclusion

In this study of an unselected population of preschool daycare children, the use of ANI monitor-guided anaesthesia reduced the incidence of emergence agitation, albeit with a slightly higher fentanyl dosing but without affecting other outcomes (length of stay in PACU or hospital, PONV and other analgesics), compared with Narcortend guided or standard anaesthesia. ANI monitor-guided anesthesia might be a promising tool to minimise emergence agitation.

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Presentations: none.

Author contributions: LGL, idea, background, study protocol, inclusion, randomisation, data collection and handling, statistical analyses and primary authorship.

MW, inclusion, randomisation, data collection, handling and article review; SLG, inclusion, randomisation, data collection, handling and article review. LE, inclusion, randomisation, data collection, handling and article review; TGH, idea, supervision, article review.

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