High-intensity transient signals during laparoscopic surgery in children

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Background. Laparoscopic interventions in children gain increasing popularity. Pneumoperitoneum as applied during laparoscopic surgery can induce gas emboli formation, but it is unclear whether this is associated with cerebral embolic events. To investigate the hypothesis that pneumoperitoneum causes cerebral emboli in children, the number and intensity of high-intensity transient signals (HITS) detected using transcranial Doppler ultrasonography were assessed before and after induction of pneumoperitoneum.

Methods. Twenty children were monitored during laparoscopic surgery. General anaesthesia was performed using sevoflurane and sufentanil or alfentanil. Pressure-controlled ventilation was adapted to maintain end-tidal $P_{\text{CO}_2}$ ($P_{\text{ET}_0\text{CO}_2}$) between 4.7 and 6.0 kPa. Baseline measurement of HITS rate, cerebral blood flow velocity, and mean arterial pressure (MAP) were recorded during steady-state anaesthesia before skin incision and during pneumoperitoneum with intra-abdominal pressure of 1.6–2.0 kPa applied using CO2.

Results. In 14 children (70%), HITS were detected during baseline and pneumoperitoneum. Three additional children (15%) developed HITS during pneumoperitoneum only and another three children (15%) presented no HITS during the investigation period. MAP and cerebral blood flow velocity increased with pneumoperitoneum.

Conclusions. HITS are present in 70% of paediatric surgical patients under balanced anaesthesia before surgical interventions. Pneumoperitoneum further increased the occurrence of HITS.

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The use of laparoscopic surgery for paediatric operations is increasingly utilized in children. In order to optimize visualization, pneumoperitoneum is created by insufflation of CO2 into the abdomen.1 This results in absorption of intra-abdominal CO2 with hypercapnic cerebral vasodilatation and increases in cerebral blood volume and regional cerebral oxygen saturation.2 Additionally, adult patients with pneumoperitoneum are prone to gas emboli as monitored using transoesophageal echocardiography.3 In children, however, it is unclear whether pneumoperitoneum is also associated with emboli. In the present study, transcranial Doppler ultrasound (TCD) was used as a non-invasive tool for the detection of cerebral emboli. Emboli in basal cerebral arteries are detected as high-intensity transient signals (HITS) within the Doppler waveform of TCD. The present study investigated cerebral HITS using TCD before and during pneumoperitoneum in children.

Methods

Patients

After approval from the local ethics committee and acceptance of consent by parents, 20 children undergoing laparoscopic surgery were included in the present study. Exclusion criteria were known persistent cardiologic, pulmonary or cerebral diseases, or disapproval by the parents.
Anaesthesia

Thirty minutes before induction of general anaesthesia, all children received oral midazolam 0.4 mg kg$^{-1}$ for premedication. General anaesthesia was induced with i.v. sufentanil 0.3 μg kg$^{-1}$ or alfentanil 20 μg kg$^{-1}$ followed by propofol 2–4 mg kg$^{-1}$ and mivacurium 0.2 mg kg$^{-1}$ and was maintained with 0.8–1.5 age-adjusted minimum alveolar anaesthetic concentration of sevoflurane calculated by the monitor software (Primus, Dräger, Lübeck, Germany). Pressure-controlled mechanical ventilation with PEEP 5 mm Hg was adjusted to maintain an end-expiratory CO$_2$ partial pressure ($P_{b_{CO_2}}$) between 4.7 and 6.0 kPa throughout the study. During steady-state anaesthesia, the rate of i.v. infusion was constant. Postoperative analgesia was initiated with piritramid 0.1 mg kg$^{-1}$ and acetaminophen 15 mg kg$^{-1}$ 20 min before the end of anaesthesia. Peripheral oxygen saturation, body temperature, and fraction of inspired and expired oxygen and sevoflurane were continuously monitored and constant throughout the study (Primus and Infinity Delta, Dräger). Mean arterial pressure (MAP) was measured at 3 min intervals. Children lay in a horizontal position during the whole investigation.

Transcranial Doppler ultrasound

For detection of HITS, the Mulidop T with Software MF (DWL Medizintechnik, Sipplingen, Germany) was used. This device includes an automatic artifact detection system by using two depths of insonation. Only signals with a short delay between both depths, like an object flowing in the blood stream, were counted as HITS. The validity of signals was controlled offline and further artifacts were ruled out. Intensity threshold for HITS was set above 9 dB, the time resolution below 300 ms, and the typical high-pitch chirping or clicking sounds were additionally used to verify the signal.$^4$

After induction of general anaesthesia, cerebral blood flow velocity (CBFV) was detected in both middle cerebral arteries (MCA) using two 2 MHz Doppler probes. The TCD probes were placed over the temporal bone window and fixed with a special frame to ensure that the angle of insonation and the individual depth of insonation remained constant during the entire investigation. Baseline measurements were started after probe fixation during anaesthesia in the absence of surgical stimuli for 10 min. Then, abdominal insufflation of CO$_2$ was started to an initial intra-abdominal pressure of 2.0 kPa. After insertion of surgical instruments, intra-abdominal pressure was reduced to 1.6 kPa. To make total number of HITS comparable with different times of observation, they were normalized to HITS per hour. Mean CBFV was continuously monitored.

Statistical analysis

Data are summarized as mean and standard deviation (SD) for parametric data and median and inter-quartile range (IQR) for non-parametric data. Statistical analyses were performed as parametric paired $t$-test (SPSS, version 15.0.1, SPSS Inc., Chicago, IL, USA). A probability value of $<0.05$ was regarded as statistically significant. The 95% confidence interval (CI) is shown in parentheses.

Results

Seven girls and 13 boys aged between 13 months and 10 yr were included with 15 children undergoing herniorrhaphy, two children undergoing appendectomy, one child undergoing gastrostomy, and one child undergoing orchiopexy. The median age was 59 months (IQR 41–90, total range 13–131). All children were ASA status I or II. No child had manifest haemodynamic or pulmonary diseases or received medication. One of the children suffered from developmental delay. The baseline measurement was maintained for 11 (1) min, pneumoperitoneum was maintained for 25 (12) min, and the duration of surgery maintained for 43 (34) min.

Fourteen of the children (70%) had HITS during anaesthesia before pneumoperitoneum, 17 (85%) had HITS during pneumoperitoneum, while three children (15%) had no HITS during the investigation. The HITS were not clustered and there were no i.v. injections during measurement except the constant infusion of saline solution. The intensity of the observed HITS was between 9 and 15 dB. The rate of HITS increased insignificantly from 28 (36) HITS h$^{-1}$ during baseline to 62 (141) HITS h$^{-1}$ during pneumoperitoneum with a mean difference of 44 HITS h$^{-1}$ ($P=0.189$, CI $-85$ to 18) (Fig. 1). There were no differences in HITS count between an intra-abdominal pressure of 2.0 kPa at the beginning of surgery and a pressure of...
1.6 kPa during the rest of surgery. There were also no differences between boys, girls, and the kind of surgery. MAP increased from 59 (8) to 69 (15) mm Hg (P < 0.0001, CI 7–14) and CBFV increased from 65 (19) to 74 (21) cm s⁻¹ during pneumoperitoneum (P < 0.0001, CI 6–13) (Fig. 2). These changes in MAP and CBFV were similar in all children independent of the presence of HITS. The $P_{\text{aCO}_2}$ during baseline was 4.7 (0.4) kPa, whereas during pneumoperitoneum, it was 5.0 (0.4) kPa.

**Discussion**

HITS were detected in 70% of subjects in the absence of surgery or pneumoperitoneum. With pneumoperitoneum, HITS occurred in 85% of subjects. These results suggest the presence of ultrasound sensitive aggregates during steady-state balanced anaesthesia which shunt into the cerebral circulation.

The occurrence of HITS during balanced anaesthesia without surgical stimuli in children has never been described. In healthy adults, spontaneous, speckle-like intensity fluctuations of the Doppler flow signal with a decibel threshold between 3 and 9 dB exist. These signals are likely related to transient erythrocyte aggregates. The intensity of the detected HITS in the present study ranged between 9 and 15 dB during baseline and pneumoperitoneum, thus minimizing the probability of measuring artifacts (e.g. erythrocyte or platelet aggregates). However, the origin of these particles detected by ultrasound, which get access to the cerebral circulation, is unknown. In contrast, HITS detected solely during pneumoperitoneum in 15% of the children are likely to be CO₂ gas emboli due to CO₂ entering open peritoneal veins during moderate pressure pneumoperitoneum. After pulmonary passage, these emboli will be detected in cerebral vessels. Previous investigations in children have demonstrated that HITS during the use of extracorporeal circulation and scoliosis surgery and the quantity of HITS were comparable with the present study (range 2–200 HITS h⁻¹ during extracorporeal circulation). However, no baseline measurement was established in either study.

Several potential sources for artifacts during HITS measurement are possible. Turbulence in the blood could be an origin of HITS, but the HITS in the present study were detected without any regularity and the Doppler spectrum was measured in the middle of the M1 segment of the MCA with adequate distance to the bifurcation. As the i.v. infusion rate was low (2–4 ml kg⁻¹ h⁻¹) and kept constant, it is unlikely that the observed HITS are caused by i.v. infusion. It is not known if there are HITS in unanaesthetized children, because the measurement in small awake or sleeping children is not easy and many artifacts such as movement can lead to insufficient data quality. To differentiate between the surgical effect and the effect of the pneumoperitoneum, a direct comparison of the HITS rate between open and laparoscopic operations would be interesting. However, open abdominal surgery in children is not performed for these indications in our hospital, so no comparison of laparoscopy and laparotomy could be performed. Despite comparable anaesthesia and similar surgical procedures, no HITS could be detected in three children. As all parameters of these patients were comparable with the patients with HITS, no obvious explanation could be found.

Neurological deterioration, like postoperative cognitive dysfunction (POCD), after coronary artery bypass grafting correlates with the intraoperative occurrence of HITS. After non-cardiac surgery, the incidence of POCD was higher in elderly patients in comparison with younger (18–39 yr), where 3 months after surgery POCD persisted in only 5.7% of the younger patients. The incidence of POCD in young children has never been studied, in part because the instruments for its detection have not been validated in this age group. However, POCD is assumed to be very uncommon on the basis of a low incidence in young adults. This study was therefore not powered to detect POCD. Surrogate markers such as magnetic resonance imaging do not correlate well with HITS and POCD.

The MAP and CBFV increased during pneumoperitoneum in the present study. The MAP-elevation might be triggered during pneumoperitoneum, due to (i) pain, induced by peritoneal distension, or (ii) release of endogenous catecholamines with consecutive systemic vasoconstriction. However, increased MAP and elevated endogenous norepinephrine concentrations per se do not lead to an increase in CBFV as long as cerebrovascular autoregulation is intact. Therefore, it seems to be more probable that the increase in CBFV can be explained by the elevation of $P_{\text{aCO}_2}$ from 4.7 (0.4) kPa during baseline to 5.0 (0.4) kPa during pneumoperitoneum. Although $P_{\text{aCO}_2}$ was measured in the present study, it may not adequately reflect dynamic changes in $P_{\text{aCO}_2}$. In
adult patients without pulmonary disorders undergoing laparoscopic cholecystectomy, $P_{aCO_2}$ and $P_{aCO_2}$ were comparable throughout anaesthesia.\textsuperscript{18} However, there are anatomical and functional differences between children and the adult. Pneumoperitoneum in children can easily induce basal atelectasis with a secondary increase in transpulmonary shunt and dissociation between $P_{aCO_2}$ and $P_{aCO_2}$.\textsuperscript{19} Because of the invasive nature of blood gas analyses, $P_{aCO_2}$ was not controlled in the present study. However, the duration of pneumoperitoneum was relatively short, and therefore, the effect of atelectasis should have been minor.

In conclusion, HITS occur in 70\% of paediatric surgical patients under balanced anaesthesia before surgical interventions. Pneumoperitoneum was associated with HITS in 85\% of the patients. This suggests the presence of ultrasound sensitive aggregates during steady-state balanced anaesthesia which shunt into the cerebral circulation.

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