Brazilian Journal of Anesthesiology 2021;71(1) 1–3

Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

EDITORIAL

A call for more pediatric anesthesia research

Pediatric anesthesia research is less expressive than in other anesthesiology fields. Children are considered a vulnerable population, increasing the challenges of recruitment for clinical trials.[1] The main challenge is ethical, mostly due to a child's incapability to consent to be submitted to a clinical trial. Also, physiological development makes the child more susceptible and with a higher risk for long-term harm and changes.

Additionally, the ethics committee assessment process for pediatric anesthesia trials can be stressful. A few Institutional Review Boards (IRB) have specific guidelines or dedicated groups for clinical trials involving children.[2] These challenges are even more remarkable when the control group is not feasible.

In Brazil, the *Conselho Nacional de Saúde*, a collegiate board from the Ministry of Health, states that an assent term should be written in accessible language and applied to children who can understand, read, and sign.[3] Besides the assent term, an Informed Consent form must be freely signed by parents or guardians. Although these policies may vary among countries, it is essential to point out that IRB evaluations and approval of clinical studies involving children are different and can be more complicated than studies with adults.

Although the findings of many adult therapeutic and diagnostic trials could be translated to the pediatric population, clinical research in children is also essential, considering all differences in outcomes, particularly in pediatric anesthesia. It is not unusual for pediatric anesthesiologists to face that most of their anesthetic arsenal is classified as ''off-label''. More than 75% of the drugs used in pediatric anesthesia have not been approved in children under 10 years of age.[2] Should it also be unethical?

Besides the ethical issues, to define priorities in pediatric anesthesia is another challenge. The joint National Institute of Academic Anaesthesia/James Lind Alliance, with the participation of the Association of Paediatric Anaesthetists of Great Britain and Ireland, listed the 10 top questions related to anesthesia.[4] Only one was explicitly associated with the care of children: what are the effects of anesthesia on the developing brain?[5] Even though other questions may be extended to the pediatric population, it is essential to recognize that this specific question should not be the only one to be answered. To address the problem listed by the James Lind Alliance, an extensive research project would be required, preferably a multicenter and collaborative approach. But there are ''little questions'' more related to clinical practice. In 2012, the members of the board of the Pediatric Anesthesia journal and of pediatric anesthesia societies also listed ten priority questions.[6] Many came from clinical practice, such as optimizing fluid management, reducing emergence delirium, providing regional blockade to decrease postoperative pain, and others. The pediatric anesthesiologist has a critical role to define these fundamental questions. Although not all pediatric anesthesiologists are involved in research, they must be aware of specific problems, which are addressed by pediatric anesthesiologist-researchers.[5]

The Canadian Society of Anesthesia also listed its top 10 priorities for anesthesia and perioperative care research.[7] One of the top 10 included elderly patients, but, unfortunately, there were none specifically related to pediatric patient care. Some priorities may also be extended to children, but it is another example that a call for more pediatric anesthesia research is critical.

One of the questions derived from the James Lind Alliance was the outcomes used to measure anesthesia and perioperative care success. The definition of the most relevant perioperative outcomes to be measured in research is a priority for adult perioperative care. The Core Outcomes Measures in Effectiveness Trials (COMET) initiative has been developed to define clinical trials' core outcomes. Core outcomes are a standardized set of results that should be minimally measured and reported in all clinical trials in specific areas of healthcare.[8] In parallel with the Core Outcomes Measures in Perioperative and Anesthesia Care, specifically

https://doi.org/10.1016/j.bjane.2020.12.001

for adults, the Pediatric Perioperative Outcomes Group has also been developing core outcomes for children submitted to anesthesia and surgery.[9] The initiative of the Pediatric Perioperative Outcomes Group included a definition of core outcomes for clinical research and clinical practice. In a systematic review of pediatric anesthesia-controlled trials, the group reported different outcomes according to age groups. Outcomes related to patient comfort, such as pain, analgesic requirements, postoperative nausea and vomiting, emergence delirium, and postoperative behavior changes were most frequent for infants, children, and adolescents, followed by cardiovascular and respiratory adverse events.[10]

In contrast, medication-related and cardiovascular and respiratory events were the most frequent adverse outcomes in neonates. The initiative of these pediatric anesthesia researchers is crucial to guide future clinical research and quality improvement research in pediatric anesthesia.[10]

More complex and rigorous IRB evaluation, differences in obtaining informed consent and assent, lack of pediatric anesthesia research priorities, and lack of core outcomes definition, all together, may partially explain the low number of pediatric anesthesia studies. A quick search in the highest impact factor anesthesia jour-nals shows a few clinical pediatric studies, and only a few journals with specific pediatric anesthesia sections.

The first 2021 issue of the Brazilian Journal of Anesthesiology (BJAN) is dedicated to pediatric anesthesia. The BJAN is committed to publishing well-designed pediatric anesthesia studies, especially those investigating core outcomes or answering priority research questions.

Following the priorities listed by the board of the Pediatric Anesthesia journal and the pediatric anesthesia societies, Souza-Júnior F A et al. conducted a clinical trial to compare whether intraoperative intravenous clonidine prevents emergence delirium in children submitted to inhalation anesthesia with sevoflurane for adenotonsillectomy.[11] They randomized 62 children between 2–12 years to receive either clonidine 1 mcg. kg^{-1} IV or placebo. Children who received clonidine had significantly less emergence delirium compared to placebo. Emergence delirium is a challenge to the pediatric anesthesiologist, especially in children submitted to adenotonsillectomy under sevoflurane anesthesia, given the incidence could be greater than 80%. The authors also reported similar adverse events in both groups. The study endorses well-known IV clonidine, an adjuvant in pediatric anesthesia, as a pharmacological prevention measure for emergence delirium.

In line with the core outcomes in pediatric anesthesia and perioperative care, Yilmaz et al., in a randomized and double-blinded clinical trial, investigated whether a rigid neck collar could improve airway patency during MRI examination under propofol-based sedation in children.[12] The authors randomized 125 children to either a rigid neck collar in a supine position or only standard approach. All children were submitted to MRI examination, and measurements of airway dimensions were taken. Children with rigid neck collars presented improved retropalatal, retroglossal airway dimensions and higher oxygenation than children without neck collars. Procedural sedation is not always feasible for many pediatric anesthesiologists, and this study gives a straightforward and viable alternative to avoid airway obstruction and desaturation during MRI examinations in children.

Fortunately, there has been an increase in multicenter studies in pediatric anesthesia in the past few years. Examples from Europe, the USA, Canada, and Australia/New Zealand, such as the APRICOT,[13] the NECTARINE,[14] and the GAS trial,[15] show that collaboration among countries is essential to answer ''big and little'' questions regarding anesthesia and perioperative care in children. It is necessary to encourage global contribution to address important research questions, define core outcomes, and make pediatric anesthesia research a priority. Currently, Brazilian pediatric anesthesiologists have little participation in multicenter studies. Besides being part of global collaborations, Brazil and other Latin-American countries could contribute with each other and develop a network to improve clinical practice and clinical research in pediatric anesthesia.

Conflicts of interest

The authors declare no conflicts of interest.

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