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CHALLENGES AND ADVANCES IN ANESTHESIA OF PEDIATRIC CANCER PATIENTS: EFFICACY, SAFETY AND LONG-TERM IMPLICATIONS

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ABSTRACT

Objective: The present study aims to analyze the available scientific evidence on the relationship between anesthetic techniques and the prognosis of cancer patients, focusing on tumor progression and long-term survival. Methodology: A narrative review of the literature was conducted, covering studies investigating the impacts of regional and general anesthesia in oncological surgeries, as well as the use of ketamine in the management of chronic pain in cancer patients. The research used the PubMed and Scopus databases, using terms such as "Pediatric Anesthesia", "Pediatric Oncology", "Chronic Pain," and "Neurological Development". Results: The literature indicates that regional anesthesia can moderate the immune response of patients, potentially reducing the risk of tumor recurrence. However, the available data are controversial and do not provide a definitive conclusion. The use of ketamine, especially in combination with opioids, shows promise in pain management but requires caution due to the possible adverse effects on neurological development, especially in pediatric patients. Conclusion: The choice of anesthetic technique in cancer patients should be made with attention to the long-term implications, considering both the immediate efficacy in pain control and the possible impacts on disease progression and quality of life of patients.

Keywords: Pediatric Anesthesia. Pediatric Oncology. Chronic Pain and Neurological Development.

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INTRODUCTION

Anesthesiology in oncology is a field full of challenges, given the intrinsic setbacks of this cohort of patients, who often have multiple comorbidities and undergo adjuvant treatments before surgical procedures. These are the conditions under which it becomes very difficult to deal with anesthesia. The anesthesiologist not only has to ensure the safety of the surgery but also be confronted by issues such as severe chronic pain, which is often difficult to control, even in the postoperative period. Therefore, the relationship between chronic pain and anesthesia in neoplastic patients is a critical aspect that deserves special attention to improve the quality of health care provided (Cuomo et al., 2020).

Furthermore, the impact of anesthesia on the evolution of oncological disease – including the potential to influence tumor recurrence – is an increasingly important issue in clinical practice. Pain, standing out as one of the most important symptoms of pediatric patients with neoplasia, also represents a difficult issue for the anesthesiologist. Especially today, when he must administer a pharmacological arsenal carefully amid the physiological changes caused by both the treatment and the disease itself (Collins et al.; 2002).

The picture becomes even more complicated when it comes to anesthesia in children with neoplasia. In addition to the challenges common to adults, these children are in a critical period of central nervous system (CNS) development. Exposure to anesthetics, sedatives, and analgesics in children raises concerns similar to those raised by the safety of these drugs in the growing nerve centers of children, and there is a growing need for studies examining the effects of such substances (Lancaster et al.; 2003).

In Brazil, the number of cancer cases in children and adolescents is significant. This fact reflects the need to continue with research in Oncology. Only in this way can both extended survival per treatment and maintaining the post-treatment quality of life be guaranteed. For many pediatric cancer patients, anesthesia requires a special focus that goes beyond pain control during surgical procedures, also considering the long-term impact of treatments on the patient's health and overall development (INCA.; 2024).

Anesthesia is not only indispensable during surgical procedures but also in all phases of cancer treatment. It is necessary to ensure patient safety and comfort. Regarding the choice of anesthetic line, the type of intervention to be performed, the general condition of the patient, and the specific characteristics of the neoplasm should be considered very carefully. This process becomes even more complicated when it comes to pediatric oncology patients, where the sensitivity of the central nervous system that is still in the growth phase requires careful analysis of the possible anesthetic options available to minimize the risks of long-term adverse impact (Kress et al.; 2019).

Pain management is a critical aspect of all cancer care, especially in children: not only within the disease itself but also in diagnostic procedures. Pain is perhaps the biggest concern. Pain related to neoplasia can result both from direct invasion by the tumor and treatments and diagnostic procedures, such as bone marrow aspiration (Suiza, 1999). Specialized care for children with cancer, therefore, should be continuous and comprehensive, not limited to solving the disease. It also needs to treat its complications and side effects. This holistic approach is essential to provide a better quality of life during and after treatment, highlighting the importance of anesthetic and therapeutic strategies that are safe and effective in this vulnerable population (Brunner & Sudarth, 2005).

Therefore, this review aims to consolidate and analyze the current and available knowledge about anesthesiology in pediatric cancer patients. In this way, it investigates the challenges for pain control, implications in interventions, as well as the influences of these practices on their clinical evolution and quality of life, providing a solid basis for the future improvement of anesthetic use in these patients.

METHODOLOGY

The methodology for this narrative review involved a systematic search of major academic databases to identify and analyze recent publications on anesthesia in pediatric cancer patients. The searches were carried out in the following databases: PubMed, SciELO, and VHL.

A combination of descriptors and operators was used to refine the results. The descriptors in Portuguese used were: "Pediatric Anesthesia", "Pediatric Oncology", "Chronic Pain," and "Neurological Development". The search strategy was configured as follows: "Pediatric Anesthesia and Chronic Pain"; "Pediatric Oncology and Neurological Development"; "Anesthesia and Pediatric Oncology"; and "Chronic Pain and Neurological Development".

Initially, 60 relevant articles were found. After applying the selection criteria, 20 relevant articles were identified in the PubMed, SciELO, and VHL databases. Of these, 12 articles were selected to compose the final collection of this review, providing a comprehensive and up-to-date view of anesthetic challenges and strategies in the context of pediatric oncology.

DISCUSSION

The choice of anesthetic technique for an oncological surgical procedure is not limited to pain control during the procedure itself. In addition, it can also indirectly affect a

patient's long-term survival through suspected tumor disease progression. Prospective studies have shown that regional anesthesia, by moderating the need for opioid agents and thereby moderating patients' response to surgical stress, improves the immune response, which could reduce the risk of tumor recurrence (Biki et al.; 2008 and Koumpan et al.; 2018). However, the studies do not provide conclusive evidence. As a result, the research does not provide a clear understanding of this relationship. Therefore, the issue remains controversial, and the association between some aspects of anesthesia and the duration of relapse-free illness is not definitive. Although they report a reduction in the risk of biochemical recurrence as measured by the PSA level of rats after radical prostatectomy among patients in the control group who were anesthetized under general and combined anesthesia (Biki et al.; 2008), it showed lower tumor recurrence rate, measuring invasion in non-invasive pathogenesis in patients anesthetized under spinal anesthesia (Koumpan et al.; 2018).

In this scenario, it is interesting to think about the administration of ketamine for chronic pain in cancer patients. According to Singh et al., while several studies have suggested the efficacy of ketamine, especially in combination with opioids, the need for more research is evident to create a robust safety and efficacy profile. For example, intranasal administration is particularly promising given its excellent availability and bioavailability, which is especially noteworthy given the potential breakthrough in enabling the management of chronic outpatient pain in oncology. In addition, the authors explicitly mention that, given the risk of anesthesia, the use of ketamine should be cautious, especially in the pediatric population, since exposure to anesthetics can have long-term consequences for the neurological development of the patient. The long-term administration of opioids for chronic pain in cancer patients without surgery has even more complex implications. There are varying implications for the immunological parameters important for antitumor outcome, with conflicting results regarding survival in terminally ill patients. Heavy-duty systemic opioids are associated with lower survival in patients with a longer prognosis, although methodological limitations emphasize the need to treat the results with caution. The response to opioid treatment is affected by pharmacogenetic factors, such as the μ receptor A118g polymorphism. This polymorphism is also associated with varied survival outcomes in cancer patients, the approach is further complicated by variations in global geographic polymorphisms (Bolan & Pockley; 2018).

The fundamental importance of the benefits offered by medications in the management of chronic pain in cancer patients. In particular, oral dosages of opioids play a vital role in achieving effective pain relief. While methadone is prescribed when other

opioids prove ineffective, serving as an effective alternative within the scope of the protocol, they also include ketamine therapy as a promising option in cases of refractory neuropathic, bone, and mucositis pain (Bradley & Boland, 2023). In addition, neuroellitic interventions and intrathecal drug delivery therapies are integrated, providing complementary pain management approaches. The study further highlights the complexity of the effects of opioids on the course of the immune response. Thus, when using anesthetic approaches, it is essential to consider not only the immediate effectiveness of analgesia but also the future effect on cancer progression. Therefore, when necessary, it is critical to adopt an appropriate anesthetic approach. As noted, the pain associated with cancer is a complex challenge that requires careful action. In addition, pain not only puts patients at risk of centro-autonomic failure but also causes psychological problems resulting from frequent painful procedures. Sedation and analgesia should reassure the child, helping to reduce anxiety and fear resulting from pain. The common approach of lumbar punctures and bone marrow aspiration is traumatizing for children and must be adequately managed (Bradley & Boland, 2023).

In addition, the potential neurotoxicity of anesthetics in pediatric patients exposed during critical phases of brain development is a rapidly expanding concern. Evidence from studies in animal models supports the possibility of long-term neurobehavioral changes due to early exposure to anesthesia (Lin et al.; 2014).

This review highlights the importance of balancing anaesthesia to provide immediate benefits and potential lifelong risks, especially in developing patients exposed to a disease as devastating as cancer. Therefore, it is essential to respect informed and personalized decisions for each patient.

CONCLUSION

In conclusion, anesthesia in oncology patients, especially pediatric ones, is a complex field that requires a careful and integrated approach for analgesia to balance immediate efficacy with its long-term implications. The review showed approaches such as the use of regional anaesthesia that can decrease the individual's opioid requirement and improve the immune response; However, the direct influence of cancer progression and tumor recurrence still lacks conclusive evidence. The promising efficacy of ketamine and several other therapeutic approaches for chronic pain still requires considerable investigations to ensure safety and efficacy, especially in susceptible populations such as children. Most crucially, the neurotoxicity associated with developmental anesthetic exposure associated with excessive anesthetic exposure illustrates the essentiality of

discrete administration to minimize neurodevelopmental risks. Therefore, anesthetic practice must be customized to meet unique requirements while considering immediate benefits as opposed to possible future implications. The continuity of research and improvement of anesthetic practice is essential to achieve optimal results and ensure a satisfactory quality of life for pediatric cancer patients.

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