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ORIGINAL ARTICLE

CAN NEURON-SPECIFIC ENOLASE AND S100 MARKERS EVALUATE NEURO-DAMAGE FROM SEVOFLURANE IN CHILDREN?

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Abstract

Sevoflurane, a commonly used inhalation anesthetic agent in pediatric surgery, has revolutionized the field of anesthesia by providing a safe and effective means of rendering unconscious children during surgical procedures. However, amid the benefits it offers, concerns have emerged regarding its potential neurotoxicity, particularly in developing brains. This has prompted the exploration of novel methods to evaluate neuro-damage in pediatric patients exposed to sevoflurane.

In this article, we delve into the intriguing possibility of employing Neuron-Specific Enolase (NSE) and S100 markers as diagnostic tools for assessing neuro-damage resulting from sevoflurane exposure in children. These biomarkers, found in blood and cerebrospinal fluid, hold promise in shedding light on the intricate relationship between sevoflurane anesthesia and potential neurological effects. To comprehend this subject fully, it is imperative to explore the background of sevoflurane in pediatric anesthesia, understand the significance of NSE and S100 markers, review pertinent research findings, and consider the practical implications in clinical settings.

Key Words: *neuro-damage, neuron-specific enolase, pediatric anesthesia, S100, sevoflurane*

Introduction

Sevoflurane in Pediatric Anesthesia

Sevoflurane, a halogenated inhalation anesthetic, has gained widespread popularity in the field of pediatric anesthesia due to its desirable properties. It offers rapid induction and emergence from anesthesia, making it well-suited for pediatric patients who require anesthesia for surgical procedures (1). Furthermore, its relatively low pungency and pleasant odor make mask induction more tolerable for children.

Sevoflurane is generally considered safe and effective, providing the desired depth of anesthesia with minimal cardiovascular and respiratory side effects. Its use has been associated with shorter

recovery times and reduced post-operative agitation, contributing to its preference in pediatric anesthesia.

However, the growing concern among clinicians and researchers revolves around its potential neurotoxicity, especially when administered to developing brains (2). Several studies in animal models have suggested a link between sevoflurane exposure and neurocognitive deficits. This concern has sparked interest in identifying reliable markers to assess neuro-damage and, ultimately, improve the safety of pediatric anesthesia.
In the subsequent sections of this article, we will explore the role of NSE and S100 markers in evaluating neuro-damage associated with sevoflurane exposure in children, shedding light on the crucial aspects of this ongoing debate (3).

Discussion:
NSE and S100 Markers:
Neuron-Specific Enolase (NSE) and S100 proteins have emerged as potential biomarkers for assessing neuro-damage in various clinical settings, including pediatric anesthesia with sevoflurane. Understanding these markers is essential to appreciate their relevance in evaluating the impact of sevoflurane on the developing nervous system.
1. Neuron-Specific Enolase (NSE):
- NSE is an enzyme found predominantly in neurons and neuroendocrine cells. It plays a crucial role in glycolysis within neurons, making it a neuron-specific marker (4).
- Elevated levels of NSE in the blood or cerebrospinal fluid can indicate neuronal damage, as it is released into the bloodstream following neural injury.
- NSE has been studied extensively in various neurological conditions, such as traumatic brain injury and ischemic stroke, as a marker of neuronal damage (5).
2. S100 Proteins:
- The S100 protein family comprises a group of calcium-binding proteins primarily found in glial cells (such as astrocytes and Schwann cells) and some neurons (6).
- S100 proteins are involved in various cellular processes, including regulation of calcium homeostasis and inflammatory responses.
- Elevated levels of certain S100 proteins, particularly S100B in blood or cerebrospinal fluid, have been associated with glial cell damage and neuroinflammation.
These biomarkers have garnered attention for their potential to provide insights into the extent of neuro-damage induced by sevoflurane anesthesia in pediatric patients. By measuring the levels of NSE and S100 markers before and after anesthesia exposure, researchers aim to establish correlations between marker levels and potential neurological effects (7).
Many research studies and findings have examined the utility of NSE and S100 markers in assessing neuro-damage in children undergoing sevoflurane anesthesia, shedding light on their diagnostic potential and limitations.
Studies and Findings:
Research into the use of NSE and S100 markers to evaluate neuro-damage from sevoflurane anesthesia in children has generated considerable interest in recent years. While the field is still evolving, several key studies have provided valuable insights:

1. Animal Studies:
- Numerous animal studies have been conducted to investigate the effects of sevoflurane on the developing brain. These studies often measure NSE and S100 markers to assess neuro-damage.
- Findings from some animal studies have suggested that sevoflurane exposure can lead to increased levels of NSE and S100 markers in the bloodstream, indicating neuronal and glial cell damage.
2. Human Studies:
- Human studies have also explored the relationship between sevoflurane anesthesia and NSE/S100 marker levels in pediatric patients (8).
- Some studies have reported associations between elevated marker levels and prolonged exposure to sevoflurane, raising concerns about potential neurotoxicity.
- However, it's important to note that findings from human studies have been mixed, and not all studies have shown consistent results.
3. Limitations and Confounding Factors:
- Interpreting NSE and S100 marker levels can be challenging due to various factors, including individual variability, age-related differences and comorbidities.
- Anesthesia techniques, duration and patient's characteristics can also influence marker levels, making it difficult to establish a direct causal link between sevoflurane exposure and neuro-damage.

While the research on NSE and S100 markers in the context of sevoflurane anesthesia is promising, it is important to approach these findings with caution. More studies are needed to confirm their reliability and to establish clear guidelines for their use in clinical practice.

Limitations and Challenges:

It is noted in the literature that even the benefits of the use of NSE and S100 as markers in assessing neuro-damage associated with sevoflurane exposure in pediatric patients, several limitations and challenges must be acknowledged:

1. Variability in Marker Levels:
- Individual variability in baseline marker levels can complicate the interpretation of results. What constitutes an elevated level, may differ from one patient to another.
2. Age-Related Differences:
- The levels of NSE and S100 markers may vary with age, making it challenging to establish age-specific reference ranges for pediatric patients.
3. Comorbidities and Coexisting Conditions:
- Preexisting medical conditions or coexisting neuroinflammatory processes can influence marker levels, potentially leading to false-positive results.
4. Anesthesia Factors:
- The choice of anesthetic agents, duration of anesthesia, and surgical procedures can affect marker levels, making it difficult to attribute changes solely to sevoflurane exposure.
5. Lack of Established Thresholds:

- Currently, there are no universally accepted threshold levels of NSE and S100 markers that definitively indicate neuro-damage. Researchers are working to establish clinically relevant cutoffs.

6. Ethical Considerations:
   - Research involving pediatric patients raises ethical questions, particularly in cases where potential neurotoxicity is a concern. Balancing the need for scientific investigation with patients' safety is crucial.
7. Need for Longitudinal Studies:
   - Long-term follow-up studies are essential to determine whether elevated marker levels correlate with lasting neurological deficits in pediatric patients exposed to sevoflurane.
8. Ongoing Research:
   - The field of anesthesia-induced neurotoxicity is evolving rapidly. New research may uncover additional biomarkers or refine the use of NSE and S100 markers in this context.

Considering these limitations and challenges, it is imperative to exercise caution when interpreting NSE and S100 marker results. These biomarkers should be considered as part of a comprehensive evaluation of the potential neuro-damage associated with sevoflurane anesthesia in children.

Clinical Implications:

The potential use of NSE and S100 markers in assessing neuro-damage from sevoflurane anesthesia in children holds significant clinical implications:

1. Early Detection and Monitoring:
   - NSE and S100 markers offer the possibility of early detection and monitoring of neuro-damage, enabling healthcare providers to identify at-risk patients and implement interventions when necessary.
2. Tailored Anesthesia Strategies:
   - The availability of reliable biomarkers could lead to development of personalized anesthesia strategies, allowing for adjustments in anesthesia dose and duration for vulnerable pediatric patients.
3. Improved Patient Safety:
   - Utilizing these markers may contribute to enhanced patients' safety by minimizing the potential risks associated with sevoflurane anesthesia, particularly in sensitive populations.
4. Research and Development:
   - Continued research in this area may lead to the discovery of additional biomarkers or refinement of existing ones, improving our ability to assess neuro-damage accurately.
5. Ethical Considerations:
   - Ethical considerations regarding the use of sevoflurane in pediatric patients may evolve with advancements in biomarker-based assessments, prompting discussions on anesthesia protocols and informed consent.

It is important to note that while NSE and S100 markers hold promise, they should be considered as part of a broader clinical evaluation. The interpretation of marker levels should be done in conjunction with other clinical assessments to make informed decisions about patients' care.

As the field of pediatric anesthesia and neurotoxicity continues to evolve, ongoing research and collaboration among clinicians and researchers are vital to refine our understanding of sevoflurane's effects on the developing brain and the role of biomarkers in this context.

Conclusion:

The evaluation of neuro-damage resulting from sevoflurane anesthesia in pediatric patients is a complex and evolving field of study. Neuron-Specific Enolase (NSE) and S100 markers have emerged as potential tools in this pursuit, offering a glimpse into the intricate relationship between anesthesia exposure and potential neurological effects.

While promising, the use of NSE and S100 markers comes with limitations and challenges. Variability in marker levels, age-related differences, comorbidities, and the lack of established thresholds underscore the need for caution in their interpretation. Ethical considerations and the ongoing evolution of research in pediatric anesthesia further complicate the landscape.

However, the clinical implications of utilizing these biomarkers cannot be understated. Early detection, tailored anesthesia strategies, and improved patients' safety are promising outcomes that could result from their use. As research in this field continues to advance, healthcare providers, researchers and ethicists must collaborate to refine our understanding of sevoflurane's effects on the developing brain and the role of biomarkers in assessing neuro-damage.

In the journey to unravel the mysteries of sevoflurane anesthesia and its potential impact on pediatric patients, NSE and S100 markers stand as beacons of hope, guiding us towards safer and more informed practices in pediatric anesthesia.

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