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THIAMINE FOR SEPTIC SHOCK: CLINICAL OUTCOMES AND UPDATES

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Abstract: Objective: To examine the effectiveness of thiamine in improving clinical outcomes of patients with septic shock, including mortality, length of hospital stays, and need for organ support, and to update clinical guidelines based on the latest evidence. **Methods**: Literature review developed according to the criteria of the PVO strategy through its guiding question: "How does thiamine supplementation influence the clinical outcomes of patients with septic shock?". The searches were carried out using the PubMed database using the search strategy: (septic shock) OR (sepsis) AND (thiamine). Immediately after applying the inclusion and exclusion criteria, 16 articles were selected to form the collection of this study. **Review**: The use of thiamine for septic shock is discussed, analyzing the effectiveness of this treatment in improving clinical outcomes in critically ill patients. Although initial studies suggest benefits, such as maintaining adequate blood pH and preserving cardiac and neurological function, studies in humans have shown inconsistent results, especially in relation to reduced mortality. Thiamine showed potential in eliminating lactate and controlling oxidative stress, suggesting a therapeutic role in specific cases. More rigorous studies are still needed to confirm these benefits, given the variability of the results observed. **Final considerations**: The results indicate that thiamine can improve some metabolic parameters and reduce mortality in certain cases, but the evidence is inconsistent, requiring further studies. The safety profile of thiamine is good and has therapeutic potential, but its effectiveness varies depending on the patient's metabolic status and the presence of thiamine deficiency. Future research must focus on identifying which patients benefit most from its use and optimizing dosages and administration methods.
Keywords: Thiamine; Septic shock; Sepsis.

INTRODUCTION

Annually, sepsis affects approximately 30 million people globally, with current estimates indicating approximately 6 million deaths per year. Septic shock represents a significant challenge in modern clinical practice, being one of the main causes of morbidity and mortality in critically ill patients (Counts et al., 2019). The diagnosis of this condition is established when there is a suspected or confirmed infection, combined with the Sequential Organ Failure Assessment. It is crucial to highlight that the primary causal factors of sepsis, as well as changes in the internal environment and hemodynamics during disease progression, can induce massive cytokine release, oxidative stress imbalance, and mitochondrial dysfunction. Mitochondria, central to both the production and targeting of reactive oxygen species, play a crucial role in the pathogenesis of sepsis. Restoration of mitochondrial function, or metabolic reanimation, may be key to mitigating organ dysfunction in septic patients and improving their prognosis (Zhang et al., 2023).

Despite advances in treatment, sepsis and its complications continue to be a global concern due to the high incidence and devastating consequences (Costa et al., 2021). The metabolic response to septic shock is vital to the clinical outcome of these patients. Changes in intermediary metabolism, including increased glycogenolysis, inhibition of glycogenesis, and increased glucose production through gluconeogenesis, are common and can lead to various clinical complications, such as metabolic acidosis, hypotension, and organ dysfunction (Zhang et al., 2023).

Among the essential nutrients involved in energy metabolism, thiamine emerges as a promising candidate for therapeutic intervention. Estimates indicate that between 10% and 70% of patients with sepsis have thiamine deficiency (Moskowitz; Donnino, 2020; Heming et al., 2020). Thiamine, or vitamin B1, is water-soluble and essential for mitochondrial energy metabolism, being involved in several cellular metabolic processes in mitochondria and peroxisomes. In its active form, thiamine pyrophosphate, it plays crucial roles in carbohydrate metabolism and energy production, particularly in the critical step of converting pyruvate to acetyl-CoA (Counts et al., 2019). This study aims to examine the effectiveness of thiamine in improving clinical outcomes of patients with septic shock, including mortality, length of hospital stays, and need for organ support, and to update clinical guidelines based on the latest evidence.

METHODOLOGY

Bibliographic review developed according to the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome. Used to prepare the research through its guiding question: "How does thiamine supplementation influence the clinical outcomes of patients with septic shock?". The searches were carried out using the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) database. The search terms were used in combination with the Boolean terms "AND" and "OR" through the search strategy: (Septic Shock) OR (Sepsis) AND (thiamine). From this search, 198 articles were found, subsequently submitted to the selection criteria. The inclusion criteria were: articles in English; published over a period of 5 years and which addressed the themes proposed for this research, review-type studies, observational studies, experimental studies, meta-analysis and clinical trials made available in full. The exclusion criteria were: duplicate articles, available in abstract form,

which did not directly address the proposal studied and which did not meet the other inclusion criteria. After initial screening, 63 articles were selected. Immediately after applying the inclusion and exclusion criteria, 16 articles were selected to form the collection of this study.

DISCUSSION

Each year, countless people around the world are impacted by sepsis, resulting in thousands of deaths. Faced with this scenario, health professionals continually seek new therapeutic approaches. Recently, the role of vitamins and nutrients in the response to sepsis has gained attention. In particular, thiamine deficiency has been associated with lactic acidosis in patients without significant liver damage, and thiamine administration has demonstrated a rapid reduction in lactate levels in patients with septic shock, suggesting its potential as an intervention in cases of sepsis and delirium. (Sedhai et al., 2021).

Thiamine, also known as vitamin B1, is an essential micronutrient that functions as a coenzyme in glucose metabolism. This compound plays a critical role in the Krebs Cycle, transforming pyruvic acid into acetyl coenzyme A, a fundamental step in the production of adenosine triphosphate (ATP) (Prasad et al., 2021; Sun et al., 2023). Due to its vital role in energy metabolism and the comorbidities associated with its deficiency, several studies have explored the possible benefits of thiamine supplementation in critically ill patients, particularly those with septic shock and severe sepsis.

Initial research in animal models suggested that thiamine may contribute to maintaining a higher blood pH, adequate blood pressure levels, and the preservation of cardiac and neurological activity, resulting from an improvement in mitochondrial function (Moskowitz; Donnino, 2020). However, human studies have not consistently demonstrated these benefits, indicating a lack of robust evidence of its impact on reducing morbidity and mortality. Even so, it has been observed that the use of thiamine in critically ill patients can help eliminate lactate, suggesting therapeutic potential in specific contexts (Moskowitz; Donnino, 2020; Vine et al., 2024). Furthermore, thiamine plays a significant antioxidant role, helping to neutralize reactive oxygen species (ROS). This antioxidant effect contributes to redox balance and may help modulate the inflammatory response by controlling pro-inflammatory metabolites that stimulate cytokine activity (Sun et al., 2023). Given its excellent safety, biological plausibility, and favorable clinical evidence, thiamine is considered a promising, low-risk adjuvant therapy in critically ill patients, especially those with septic shock and severe thiamine deficiency. Nandhini et al. (2022) conducted the only double-blind randomized clinical trial that demonstrated a statistically significant reduction in the Intensive Care Unit (ICU) mortality rate in the thiamine-treated group compared to placebo, particularly in patients with pre-existing thiamine deficiency.

On the other hand, Prasad et al. (2021) found no statistically significant relationship between a patient's initial thiamine level and survival or the development of shock in their cohort study. Furthermore, Sangla et al. (2023) performed a meta-analysis to evaluate the effects of thiamine when used alone in septic patients in the ICU. At the time of the study, there were only five randomized controlled trials evaluating the effect of thiamine supplementation alone in patients with septic shock. Of these ones, only one showed a significant benefit in reducing the mortality rate.

The limitation in the number of studies available, together with relevant intrinsic

weaknesses and the small number of patients evaluated in each study, means that it is not yet possible to validate definitive conclusions, as existing studies have limited clinical significance. Therefore, more randomized clinical trials are needed to evaluate the true benefit of thiamine supplementation in patients with septic shock, especially those who are deficient in this vitamin.

It is crucial to highlight that approximately one third of septic patients have thiamine deficiency, with an even higher prevalence among high-risk patients, such as alcoholics, users of high doses of diuretics and malnourished patients (Nandhini et al., 2022). As there is no rapid test to determine a patient's thiamine levels and there is no scientific evidence to support its routine administration to patients in septic shock, supplementation must be considered on a case-by-case basis. It is not necessarily beneficial for everyone, but it can be crucial for those with disabilities (Moskowitz; Donnino, 2020).

Currently, there is no consensus on the ideal dosage of thiamine or the frequency of its administration. Dosages employed in recent studies range from 100 to 1500 mg per day, administered intravenously due to limited oral absorption in healthy individuals. The lack of robust pharmacokinetic data makes it difficult to formulate universal recommendations for all patients. However, based on the available evidence, it is reasonable to consider regimens ranging from 200 mg intravenously twice daily to 500 mg intravenously every 8 hours (Counts et al., 2019).

Shen, Li and Qu (2021) observed that the combined administration of hydrocortisone, ascorbic acid and thiamine was effective in reducing the Sequential Organ Failure Assessment (SOFA) score over 72 hours, reducing the need for vasopressors and increasing procalcitonin clearance. However, this combination did not demonstrate significant benefits in terms of mortality, duration of mechanical ventilation, length of hospital stay or ICU stay. In contrast, Reddy et al. (2020) and Moskowitz et al. (2020) report that, in resuscitation protocols for patients with septic shock using hydrocortisone alone or in conjunction with ascorbic acid, thiamine did not significantly impact the time needed to reverse the shock, nor did it influence the change in the SOFA score over 72 hours. or the incidence of renal failure and 30-day mortality.

On the other hand, Iglesias et al. (2020) found that thiamine demonstrated a significant improvement in shock reversal, an effect that remained even after adjusting for corticosteroid administration, suggesting a possible synergistic effect with ascorbic acid in potentiating the hemodynamic effects of corticosteroids.

Finally, Moskowitz et al. (2017) noted a higher incidence of kidney injury and need for renal replacement therapy in patients with septic shock who did not receive thiamine compared to those who were treated, indicating a potential benefit of treatment in preventing kidney deterioration.

FINAL CONSIDERATIONS

The results indicate that although thiamine may improve certain metabolic parameters and reduce mortality in specific cases, the evidence is still inconsistent and suggests the need for more rigorous research. Research suggests that while thiamine has a favorable safety profile and therapeutic potential, its effectiveness can vary significantly depending on the patient's metabolic status and the presence of thiamine deficiency. It is essential that future studies focus on clearly delineating which patients may benefit most from its administration, as well as determining the most effective dosages and administration methods. The implications of these findings

are vast, offering avenues for more targeted and personalized interventions in the treatment of septic shock, a condition that continues to challenge healthcare professionals around the world. The need for multidisciplinary and evidence-based approaches in emergency medicine is highlighted, promoting a better prognosis and quality of life for patients in critical conditions.

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