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TIROFIBAN IN ACUTE STROKE AND ITS CLINICAL IMPLICATIONS

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Abstract: Objective: To investigate the efficacy and safety of using tirefiban in patients with acute stroke, comparing it with other frequently used medications and discussing its implications for clinical practice. Methodology: Narrative Bibliographic Review through the PubMed - Medline database, with a search strategy:(acute ischemic stroke) AND (tirofiban) AND ((efficacy) OR (prognosis), which resulted in 104 articles initially. After screening, 16 articles were selected for detailed analysis. Review: Tirofiban shows promising results, especially in specific subgroups of patients, such as elderly people with large infarcts. Studies have indicated a reduction in hospital mortality and functional improvements with the use of girofiban, without significantly increasing the risk of intracranial hemorrhage. However, there are still issues to be clarified, such as defining ideal patient selection criteria and precise dosing protocols to optimize clinical results. Final considerations: Tirofiban's potential as a valuable therapeutic option in the treatment of acute stroke is highlighted, although its integration into clinical practice requires careful considerations to maximize benefits and minimize risks.
Keywords: Tirofiban; Selective and reversible antagonists of platelet glycoprotein receptors; Stroke.

INTRODUCTION

The endovascular treatment of acute ischemic stroke (IS) has evolved significantly, driven by the continuous search for more effective and safe therapies. Within this context, girofiban, a selective and reversible antagonist of platelet glycoprotein receptors, emerges as a promising therapeutic option. Ischemic stroke, resulting from the interruption of cerebral blood flow, represents a serious threat to health, requiring rapid and effective interventions to reestablish blood perfusion.

The use of tirefiban in the intravenous context appears to be a promising strategy, although it still requires a more comprehensive evaluation regarding its efficacy and safety. Historically, the therapeutic window for endovascular treatment has included mechanical thrombectomy, angioplasty, and stent implantation, with intravenous thrombolysis with alteplase being the therapy of choice. However, its limitations have fueled the search for effective alternatives. Mechanical thrombectomy, although useful, can cause endothelial injury and platelet activation, increasing the risk of early reocclusion and worsening the prognosis, as highlighted by Cai et al. (2021). This reality drives the investigation of new pharmacological approaches with recent studies demonstrating promising results with the use of tirefiban, but there are still significant gaps in the literature. According to Cait et al. (2021), the relationship between independent variables and favorable outcomes associated with the use of girofiban is still unclear, highlighting the absence of significant differences in critical clinical outcomes, such as intracerebral hemorrhage (ICH) and symptomatic intracerebral hemorrhage (sICH). Furthermore, differences in outcomes between anterior and posterior circulation strokes suggest the need for more detailed studies in specific subgroups.

Zi et al. (2023) advanced this area with the RESCUE BT 2 study, testing the efficacy and safety of girofiban compared to aspirin in patients within the first 24 hours after the onset of symptoms. Using the Modified Rankin Scale (mRS) to assess functional outcomes, the study defined success as an mRS score of 0 to 1 at 90 days after randomization. The results indicated a higher incidence of favorable functional outcomes, a higher rate of recanalization and a reduction in mortality with the use of girofiban, without significant differences in the occurrence of intracranial hemorrhages between the treatment groups.

This study aims to investigate the efficacy and safety of using tirefiban in patients with acute stroke, comparing it with other frequently used medications and discussing its implications for clinical practice. The need to further explore the potential advantages of girofiban is highlighted by the gaps highlighted by Cait et al. (2021) and the promising results of the clinical trial by Zi et al. (2023).

METHODOLOGY

The structured narrative bibliographic review through the criteria of the PVO strategy, which focuses on three main axes: population or research problem, variables of interest and expected outcomes. This framework was used as a facilitating tool to formulate the central research question: "How does the use of girofiban in patients with acute stroke, who do not have proximal occlusion and have not responded to thrombolysis, affect clinical outcomes?"

For the bibliographic survey, the PubMed - Medline (Medical Literature Analysis and Retrieval System Online) database was used. The search strategy involved combining the terms "acute ischemic stroke", "tirofiban", "efficacy" and "prognosis", using the Boolean operators "AND" and "OR". The search initially resulted in 104 articles. After an initial screening, 35 references were considered relevant and, subsequently, 16 articles were selected for detailed analysis after a second screening. The inclusion criteria adopted were: articles in English published between April 2019 and April 2024, which addressed topics relevant to this research, including meta-analyses, observational studies, statistical analyses, clinical trials, multicenter trials and retrospective studies available in full. The exclusion criteria were: duplicate articles, studies that did not directly address the research question, studies with a low level of

scientific evidence and articles only available in abstract form.

DISCUSSION

Tirofiban, as a reversible antagonist of platelet glycoprotein IIb/IIIa receptors, has stood out for its effectiveness in blocking platelet aggregation, particularly in the context of ischemic stroke, either as monotherapy or in combination with intravenous thrombolysis and therapies. endovascular. The main function of glycoprotein IIb/IIIa, an integrin widely expressed on platelets and megakaryocytes, is to mediate the binding of fibrinogen and other agents to the surface of activated platelets, triggering platelet aggregation essential in thrombus formation.

Blocking this pathway, promoted by Tirofiban, directly interferes with the pro-thrombogenic mechanism, representing a significant therapeutic approach in patients with ischemic cerebrovascular disease, especially those with progressive stroke (Yang et al., 2019).

Due to its short half-life, approximately 2 hours, and rapid elimination mainly via the kidneys, Tirofiban has a lower incidence of bleeding complications, making it suitable for use in combination with thrombolytics or during endovascular procedures. It is necessary to adjust the dosage in patients with severe renal impairment due to the reduction in the drug clearance rate by more than 50% in these individuals (Yang et al., 2019).

Although endovascular treatment, such as thrombectomy and intravenous thrombolysis, are the established standards for acute stroke, its limitations and the risk of reocclusion highlight the need for effective alternatives, such as Tirofiban. This drug offers a valuable therapeutic strategy and is increasingly being considered due to its ability to improve neurological outcomes and reduce in-hospital mortality in specific cases, such as elderly patients with large infarcts (Gong et al., 2020).

In recent studies, such as the one carried out by Zi et al. (2023), Tirofiban showed promise when compared with aspirin in patients with recent-onset stroke, resulting in better functional outcomes and reduced mortality. However, although the incidence of cerebral hemorrhage was low, it occurred more frequently in the Tirofiban-treated group, requiring careful assessment of patient selection and dosing to minimize risks (Zi et al., 2023).

According to Hu et al. (2022), discussion about the safety and risks associated with the use of tirefiban, as well as considerations about patient selection and the integration of this medication into clinical practice, become essential as its applicability expands. Originally used in patients with acute coronary syndrome without ST segment elevation, girofiban has been progressively used in cases of ischemic cerebrovascular disease, especially in patients with progressive cerebrovascular accident (CVA). Currently, multiple guidelines recommend it as a crucial short-term antithrombotic therapy in situations of progressive arteriolar occlusion and in perioperative patients undergoing endovascular interventions. Its mechanism of action, selective blockade of the GPIIb/IIIa receptor, positions it as an extremely potent platelet inhibitor.

Subgroup studies indicate a significant reduction in in-hospital mortality in elderly patients over 80 years of age who have suffered large hemispheric infarcts, suggesting the safety and efficacy of girofiban even in high-risk populations and in severe conditions. Furthermore, it has been observed that low and prolonged doses of the drug can significantly improve early neurological function in patients with large hemorrhagic infarctions, further reducing in-hospital mortality without increasing the risks of intracranial

hemorrhage or other systemic bleeding events. These findings reinforce the potential of tirefiban to improve outcomes in patients with acute strokes, especially in specific subgroups, although further investigation is needed to confirm these findings and clarify its optimal role in clinical practice (Hu et al., 2022).

On the other hand, a meta-analysis conducted by Fu et al. (2020) explored the effects of girofiban in the context of endovascular treatment of acute ischemic events. The results did not indicate an increase in the risk of intracranial hemorrhage, which is a significant safety advantage for this therapeutic protocol. Furthermore, a reduction in the mortality rate was observed in patients treated with girofiban compared to controls, particularly in the three-month post-intervention outcomes. Although no improvements in the rate of vascular recanalization or functional outcomes were identified, the data suggest that preoperative use of girofiban may be crucial to optimizing functional outcomes, possibly by improving microvascular reperfusion status.

However, this analysis highlights the importance of future research to define optimal patient selection criteria, establish accurate dosing protocols, and determine the most effective administration methods (Fu et al., 2020). This information not only underscores the promise of tirefiban as an integral component of endovascular treatment, but also indicates the need for more detailed and comprehensive approaches to determining best clinical practices with the goal of optimizing outcomes in patients with acute ischemic events.

Finally, a meta-analysis by Gong et al. (2020) concluded that Tirofiban does not increase the risk of intracranial or systemic hemorrhage or mortality, although it did show a potential increase in fatal intracranial hemorrhages. This reinforces the need for careful protocols in the administration of Tirofiban, particularly regarding the route of administration and the management of patients with specific characteristics of stroke (Gong et al., 2020). Consequently, current clinical practices must consider the integration of Tirofiban as a safe and effective therapeutic option, respecting the particularities of each case to maximize benefits and minimize risks.

FINAL CONSIDERATIONS

The endovascular treatment of acute ischemic stroke has progressed, with the emphasis on tirefiban, a platelet glycoprotein receptor antagonist, which has shown improvements in clinical outcomes, such as reduced mortality and improved vascular recanalization. Despite these advances, the relationship between the use of girofiban and outcomes such as intracerebral hemorrhage still needs clarification, with additional studies needed to understand its effect in specific subgroups and in combination with other therapies. Continued research is essential to refine the dosing and administration of girofiban, maximizing its benefits and minimizing risks in diverse clinical settings, which can significantly improve outcomes and quality of life for patients with acute stroke.

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