portadores de deficiência hereditária de FVII dificulta a abordagem terapêutica adequada com reposição de rFVIIa. Este caso corrobora o conceito de ausência de correlação direta entre níveis plasmáticos do FVII e gravidade das manifestações clínicas, mas também levanta a discussão sobre o papel da plaquetopenia como potencial cofator hemorrágico em coagulopatias subjacentes. Convém salientar que a paciente, embora submetida a diversos desafios hemostáticos ao longo da vida, apresentou sangramento grave apenas na vigência de plaquetopenia. Por ser condição rara, a descrição de casos semelhantes pode ser útil para a melhor compreensão de potenciais preditores de risco de sangramento, auxiliando na condução individualizada desses pacientes.

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ID – 1960

SPLEEN TYROSINE KINASE INHIBITORS FOR IMMUNE THROMBOCYTOPENIA: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: Immune thrombocytopenia (ITP) is an autoimmune disorder, characterized by decrease of the platelet count and increased risk of bleeding. Although spleen tyrosine kinase (SYK) inhibitors have shown promise in treating ITP, no meta-analysis has yet synthesized the evidence from randomized controlled trials (RCTs) across the entire class. Therefore, there is no consolidated evaluation of the efficacy and safety of SYK inhibitors as a group, nor comparisons among different agents, limiting guidance for clinical practice and research. **Objectives:** This paper aims to synthesize the evidence from RCTs for SYK inhibitors in adults with chronic ITP and to compare the effects of different agents, conditional on the availability of data. **Material and methods:** Eligible studies were phase III RCTs comparing SYK inhibitors to placebo in ITP patients and reporting at least one relevant clinical outcome. Studies with overlapping populations, duplicate reports, or secondary ITP were excluded. Data were extracted from published reports on PubMed, Embase, and Cochrane. Risk Ratios (RR) with 95% Confidence Interval (95% CI) were pooled across trials. The primary efficacy outcome was the stable response rate (defined as ≥ 4 platelet count ≥ 50×10^9/L in 14-24 weeks). Secondary efficacy endpoints included other platelet count improvements and the need for rescue therapy. Safety outcomes comprised any Adverse Events (AEs) and other AEs. **Results:** Four trials (n = 372) were included. Syk inhibitors were given to 249 patients (66.9%): 123 (49.3%) received Fostamatinib and 126 (50.6%) Sovlepenib. SYK inhibitors significantly increased stable and overall platelet responses compared to placebo (RR = 17.77; 95% CI 5.13–61.61; $p < 0.00001$ and RR 4.17; 95% CI 2.63–6.61; $p < 0000.1$). Among individuals presenting with more pronounced thrombocytopenia at baseline (< 15×10^9/L), SYK inhibitors were favored in the increase of platelet count of ≥ 30×10^9/L and ≥ 20×10^9/L from baseline at weeks 12 and 24 (RR = 3.53; 95% CI 1.96– 6.37; $p < 0.0001$, and RR = 3.67; 95% CI 2.00–6.71; $p < 0.001$). SYK inhibitor use reduced rescue treatment need but increased AEs, particularly hypertension, while severe AEs were not significantly different. Subgroup analyses comparing different SYK inhibitors were exploratory, due to the low number of studies involved, and none of the outcomes demonstrated a statistically significant difference between subgroups. **Discussion and Conclusion:** The present study is the first systematic review with meta-analysis to specifically evaluate the class of SYK inhibitors for the treatment of chronic ITP based solely on data from RCTs. Compared to the previous meta-analysis restricted to fostamatinib, in their subgroup analysis of RCTs, our findings suggest a stronger treatment effect for SYK inhibitors overall, particularly for stable response (RR 17.77 vs. 6.43) and overall response (RR 4.17 vs. 3.04), while the direction of benefit remained consistent across studies. In conclusion, this study provides evidence supporting SYK inhibitors as viable options in the treatment of chronic ITP. Given the small number of contributing studies, these results should be interpreted cautiously. Large-scale multicenter RCTs are needed to assess the safety and effectiveness of different SYK inhibitors in order to guide clinical decisions and optimize ITP management.

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TERAPIAS EM HEMOFILIA B: PADRÃO vs. INOVADORAS – REVISÃO DE LITERATURA SOBRE SEGURANÇA, EFICÁCIA E DESFECHOS

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Introdução: A Hemofilia B (HB) é uma coagulopatia rara, ligada ao X, que levam à produção deficiente do Fator IX (FIX). Pacientes com HB grave apresentam sangramentos espontâneos frequentes, com risco de artropatia crônica e hemorragias fatais. O tratamento padrão é a profilaxia com concentrados de FIX de meia-vida padrão (SHL). Apesar de eficazes, infusões Intravenosas (IV) frequentes comprometem adesão e controle ideal. Novas abordagens incluem FIX de meia-vida estendida (EHL), terapias gênicas (scAAV2/8-LP1-hFIXco, etranacogene dezaparvovec e fidanacogene elaparvovec) e agentes não-fatoriais (concizumab, marstacimab, fitusiran). Apesar de promissoras em reduzir a carga terapêutica

e melhorar a hemostasia, há escassez de comparações diretas entre seus desfechos e os da terapia padrão. **Objetivos:** Comparar terapias avançadas (gênica, não-fatorial, FIX EHL) com convencionais (FIX SHL), reunindo dados sobre segurança, eficácia e desfechos clínicos. **Material e métodos:** Revisão sistemática em bases de dados, com artigos publicados nos últimos 5 anos. A extração de dados focou nas intervenções, comparadores, segurança, eficácia e desfechos. **Resultados e discussão:** As novas terapias melhoram o controle hemostático e a qualidade de vida (QoL), com maior conveniência, eficácia e potencial "cura". Terapias gênicas reduziram a Taxa Anualizada de Sangramento (ABR): scAAV2/8-LP1-hFIXco de 14,0 para 1,51; etranacogene de 4,19 para 1,516; fidanacogene de 4,4 para 1,34. A scAAV2/8-LP1- hFIXco manteve FIX estável e controle hemostático por 13 anos com dose única. Com etranacogene, 96% suspenderam profilaxia após 18 meses, mesmo com anticorpos pré-existentes. Há relatos de remissão sem inibidores, trombose ou hepatotoxicidade, embora com elevação transitória de aminotransferases. Agentes não-fator são úteis em pacientes com inibidores ou que evitam administração IV, por aplicação subcutânea, que melhora adesão e QoL. Todos reduziram ABR: concizumab de 14,9 para 1,68; marstacimab de 38 para 3,18 sob demanda e de 7,9 para 5,1 em profilaxia; fitusiran com mediana de 0,877. Houve relatos de risco trombótico com concizumab e fitusiran, manejados com ajustes de dose e monitoramento. FIX EHL mostrou redução na ABR (1,29 *vs.* 3,12 com FIX SHL) e maior proporção sem sangramentos (0,53 *vs.* 0,24). Menor frequência de infusão aumentou adesão e QoL. Os desfechos clínicos são profundos: QoL aprimorada, ABR reduzida, saúde articular e funcionalidade melhoradas. Terapias não-fator se mostraram cruciais para pacientes com inibidores. Entretanto, os estudos ainda têm limitações: fases iniciais, amostras pequenas, tempo de seguimento curto, viés em não-randomizados. A ausência de ensaios comparativos diretos e sub-representação feminina limitam a generalização. **Conclusão:** As terapias inovadoras em HB mostram avanços relevantes em segurança, eficácia e desfechos, superando a abordagem padrão. Apesar do potencial de conveniência, superior eficácia e até remissão, faltam estudos comparativos amplos e de longo prazo.

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ID – 383

THE ROLE OF INTERLEUKIN-10 GENE VARIANTS IN INHIBITOR DEVELOPMENT IN HEMOPHILIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: A major therapeutic challenge in hemophilia is the development of inhibitors that neutralize replacement therapies. Interleukin-10 (IL-10), an anti-inflammatory cytokine, regulates immune responses and influences antibody production, suggesting a potential role in inhibitor formation. **Objectives:** This systematic review aimed to investigate the association of IL-10 polymorphism with inhibitor formation in patients with hemophilia. **Material and methods:** Following PRISMA guidelines, the study was registered in PROSPERO (CRD42024590045). Genetic studies on IL-10 polymorphisms and inhibitors were included, while case reports, reviews, and animal studies were excluded. A comprehensive search was conducted in PubMed and Scielo, covering records up to June 16, 2025. Methodological quality was assessed using Q-genie, and a meta-analysis was performed for polymorphisms with data from at least three studies, using the Mantel-Haenszel method. **Discussion and Conclusion:** Of 107 screened studies, 19 were included in the systematic review and 12 in the meta-analysis. Fifteen studies referred to hemophilia A patients only, with sample sizes ranging from 15 to 935, and inhibitor development rates varying from 6/50 (12%) to 130/260 (50%). High variability was observed among the studies, particularly regarding sampling locations, which included Europe (n = 6), Asia (n = 6), the Americas (n = 4), Africa (n = 1), and two multicentric studies spanning Europe and North America. All included studies investigated at least one IL-10 polymorphism potentially associated with the risk of inhibitor development. The most frequently studied variants were rs1800896 (n = 9 studies), rs1800871 (n = 7), and rs1800872 (n = 6), all located in the regulatory region of the IL-10 gene. No significant association was found between IL- 10 polymorphisms and inhibitor formation. To assess the impact of hemophilia type on the findings, studies involving hemophilia A and B were analyzed separately leading to the same results. In a subgroup analysis, the T-rs1800871 and A-rs1800872 recessive models were associated with protection against inhibitor development in subjects with severe hemophilia A. Although IL-10 polymorphisms do not appear to play a central role in inhibitor development across all hemophilia populations, protective associations identified in patients with severe hemophilia A suggest a potential immunomodulatory role in specific subgroups. These findings underscore the importance of further studies exploring IL-10-mediated mechanisms in immune tolerance and their implications for personalized treatment strategies in hemophilia.

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ID – 374

TRADUZINDO A HEMOFILIA PARA LEIGOS: EXTENSÃO UNIVERSITÁRIA PARA EDUCAÇÃO EM SAÚDE E COMBATE À DESINFORMAÇÃO

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