tratamento com a equipe multiprofissional. Estas ações conjuntas e centradas no paciente buscam aumentar a expectativa e a qualidade de vida.

https://doi.org/10.1016/j.htct.2025.104174

ID - 1762

PLASMA LIPIDOMICS REVEALS MARKERS OF LEG ULCER IN SICKLE CELL DISEASE – PRELIMINARY RESULTS

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Introduction: Leg ulcers represent a severe complication of sickle cell disease (SCD), driven by multifactorial pathophysiological mechanisms. The identification of metabolic biomarkers may support clinical risk stratification and therapeutic decision-making. **Objectives:** To investigate the plasma metabolic profile, particularly lipid alterations, associated with the development of leg ulcers in patients with SCD. **Material and methods:** Plasma samples from 129 individuals with SCD were analyzed, including 72 with a history of leg ulcers and 57 controls without lesions. Participants were clinically matched, including for hydroxyurea use. An untargeted lipidomic approach using high-resolution LC-MS was applied. Statistical analyses included t-test, PCA, and SVM to construct and validate a predictive model. **Results:** A total of 57 metabolites were significantly altered, including 51 lipids (glycerophospholipids, fatty acids, and sphingolipids). Patients with leg ulcers showed elevated plasma levels of lysophospholipids (LysoPCs, LysoPEs), fatty acid esters of hydroxy fatty acids (FAHFAs), and oxidized derivatives of polyunsaturated fatty acids. The predictive model achieved an AUC of 0.973, with 94.4% accuracy in the ulcer group and 96.5% in controls. The lipidomic signature suggests persistent oxidative stress, chronic inflammation, and membrane remodeling as key mechanisms in ulcer pathogenesis. **Discussion and conclusion:** This study identified a distinct plasma lipid signature associated with leg ulcer development in SCD. Key biomarkers included lysophospholipids (LysoPC 16:0, 18:2, 22:6; LysoPE 16:0, 18:0), which function as pro-inflammatory mediators and indicate enhanced membrane turnover and phospholipase A2 activation. The elevation of FAHFAs and oxylipins derived from polyunsaturated fatty acids supports a pathophysiological model involving unresolved oxidative stress and chronic inflammation. These alterations likely reflect an imbalance between vascular injury and compensatory mechanisms, contributing to lesion persistence and recurrence. Additionally, reduced levels of structural phospholipids (e.g., PC, PE, and PS) and sphingolipids (e.g., SM 36:2 and ceramides) suggest membrane instability and endothelial dysfunction. These lipid pathways are closely related to vascular permeability, inflammation, and apoptosis — central components of SCD pathophysiology. The predictive model based on these metabolites demonstrated excellent performance (AUC 0.973), underscoring the potential of plasma lipidomics as a promising tool for risk stratification and clinical decision support in SCD-related cutaneous complications. Our preliminary findings demonstrate that untargeted plasma lipidomics enables the identification of a robust metabolic signature associated with leg ulcer development in SCD. The elevation of lysophospholipids, FAHFAs, and oxylipins, along with the reduction of structural phospholipids and sphingolipids, reflects a systemic environment characterized by chronic inflammation, oxidative stress, and membrane dysfunction. The high predictive accuracy of the identified metabolite panel highlights the translational potential of metabolomics for personalized prognostics and therapeutic strategies in SCD. These findings lay the foundation for future clinical validation and integration of biomarkers into routine care to prevent and manage leg ulcers more effectively. Funding: This work was supported by FINEP (grant number 01.22.0589.00).

https://doi.org/10.1016/j.htct.2025.104175

ID – 2707

PORTADORES DE ANEMIA FALCIFORME COM ACIDENTE VASCULAR CEREBRAL PRÉVIO EM SEGUIMENTO SEM TRANSFUSÃO

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Introdução: Relato de 12 pacientes com anemia falciforme e história de Acidente Vascular Cerebral isquêmico (AVC) prévio que, por diversas razões tiveram seu esquema transfusional suspenso. **Descrição do caso:** Foi realizado um estudo descritivo, retrospectivo e longitudinal com dados de prontuários médicos de 12 pacientes portadores de doença falciforme, acompanhados em um centro de referência na cidade de São Paulo entre 1994 e 2025. A mediana (AIQ) de idade do primeiro AVC foi de 7,5 (5-11) anos. Cinquenta por cento dos pacientes tiveram mais de 1 episódio de AVC, sendo que o número de episódios variou de 2 a 7, e todos os episódios ocorreram durante o período de profilaxia secundária. A mediana (AIQ) de tempo de tratamento transfusional foi de 10,5 (3,5-13,0) anos. Dois pacientes nunca realizaram transfusão profilática e apenas um destes teve um segundo episódio de AVC 24 anos após o primeiro. Quando foram

referenciados ao Serviço de Hematologia de adultos, por diferentes razões, o tratamento transfusional foi suspenso e iniciado hidroxiureia. A mediana (AIQ) de sobrevida após esta mudança de conduta é de 19,5 (15,8-23,3) anos. Vale ressaltar, que dois pacientes perderam o acompanhamento neste período e nestes casos foi considerado apenas o tempo de seguimento. O AVC é manifestação frequente em crianças com doença falciforme, mais especificamente na anemia falciforme. Por vezes, trata-se de uma manifestação catastrófica resultando em sequelas motoras e/ ou neurológicas e impedindo que este indivíduo tenha uma vida normal. Sabe-se que a transfusão de hemácias é tratamento importante para evitar o primeiro episódio (profilaxia primária) e para evitar recidivas (profilaxia secundária). Em nosso relato, as causas de suspensão do esquema transfusional teve várias razões, sendo as mais frequentes: recusa do paciente, dificuldade de comparecer com frequência ao serviço e irregularidade do acompanhamento. Nos casos apresentados, estes pacientes encontram-se há cerca de 20 anos em acompanhamento sem transfusão. O estudo STOP 2 (Optimizing Primary Stroke Prevention in Sickle Cell Anemia Trial) não foi capaz de determinar se a suspensão de transfusão regular pode ser indicada nestes pacientes, e não existe até o momento, nenhum estudo que comprove que a suspensão do regime transfusional e o início de hidroxiureia tenha a mesma resposta na profilaxia. **Conclusão:** Este relato chama a atenção para o fato de haver necessidade de mais estudos controlados para determinar o período mínimo de tratamento transfusional destes pacientes, levando-se em conta as complicações associadas a transfusões frequentes por muitos anos.

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https://doi.org/10.1016/j.htct.2025.104176

ID – 1922

POTENTIAL IMMUNOMODULATORY FUNCTIONS OF THE ACKR1 GENE IN THE CONTEXT OF AUTOIMMUNE ANEMIAS

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Introduction: The Atypical Chemokine Receptor 1 (ACKR1) gene encodes a transmembrane protein found on red blood cells and endothelial cells. This protein functions as a receptor for inflammatory chemokines; however, it is signaling mechanism differs from that of a conventional receptor. Associated with the Duffy blood group system, it also plays a role in inflammation regulation. The FY*BES allele, prevalent among individuals of African descent, results in the cessation of Duffy antigen production, leading to the Fy(a−b−) phenotype, which has been associated with immune system alterations. In autoimmune hemolytic anemia, the presence or absence of the Duffy antigen influences the severity of red blood cell destruction and the subsequent immune response. **Objectives:** The objective of this study is to ascertain the potential role of the ACKR1 gene in the regulation of the immune system and its association with the process of hemolysis, defined as the breakdown of red blood cells in patients diagnosed with autoimmune anemias. **Material and methods:** A comprehensive review of studies from 2019 to 2025 was conducted using the databases PubMed, SciELO and LILACS. The following words were used to describe the project: The keywords “ACKR1”, “chemokines” and “autoimmune hemolytic anemia”, were entered into the search engine. A total of 17 articles were identified using the specified descriptors, however, only five of these were ultimately selected for further analysis. **Discussion and conclusion: Results:** Research demonstrated a correlation between a specific trait, designated as the Fy(a−b−) and phenotype, and the absence of a particular protein on red blood cells, known as Duffy. This absence has significant consequences for the immune system. The manner in which certain cells within the body adhere to one another may undergo alterations, potentially impeding the body’s ability to regulate inflammation and compromising the functionality of the immune system. A substantial body of research has indicated that an insufficient intake of a specific protein, known as Duffy antigen, may result in elevated levels of chemical mediators that trigger inflammatory responses within the body. These elevated levels have the potential to render the immune system more susceptible to self-attack. When combined with genetic susceptibility, this condition can contribute to the breakdown of immune tolerance and the onset of red blood cell destruction caused by autoantibodies. Discussion: This phenomenon can result in an immune system that is more active, which can increase the likelihood of sensitivity to certain substances, particularly in individuals who are genetically predisposed to such reactions. Conclusion: The absence of Duffy antigen expression on red blood cells may play a significant role in the process of inflammation and the autoimmune causes of certain types of anemia. Genetic testing for the Duffy gene in patients with AIHA enhances medical professionals’