Introdução: A anemia falciforme (AF) é um distúrbio hereditário homozigótico que leva à formação de hemoglobina S (HbS), alterando a estrutura das hemácias para o formato de foice através da polimerização da hemoglobina (Hb) anormal, resultando em hemólise e vaso-oclusão 1. A Leucemia Aguda (LA) de fenótipo misto ou bifenotípica compreende leucemias com características fenotípicas mieloides e linfoides em uma única população de blastos 11. O objetivo do trabalho é relatar um caso de leucemia de fenótipo misto em paciente com AF. **Caso clínico:** Paciente do sexo masculino, 42 anos, com AF realizava acompanhamento e uso contínuo de hidroxiureia, mantendo controle sintomático e Hb basal de 12 g/dL. Em janeiro/2023, apresentou crise vaso-oclusiva com dores difusas e queda da Hb para 7,2 g/dL e elevação das provas de hemólise, com necessidade de tratamento hospitalar em inúmeras ocasiões nos 2 meses seguintes. Em março/2023, paciente apresentou hemograma com presença de blastos, sendo encaminhado para serviço de onco-hematologia para atendimento, com Hb 8,9 g/dL, plaquetas 118.000/mm^3 e leucócitos 6235/mm^3, com 56% de blastos de tamanho médio, com relação núcleo-citoplasmática intermediária e presença eventual de bastões de Auer. A análise de medula óssea (MO) por citometria de fluxo, apresentou 21,2% de células blásticas com coexpressão de antígenos mieloides (CD13, CD33, CD117, MPO) e antígenos linfoides T (CD3 citoplasmático, CD7), sendo compatível com Leucemia Aguda de fenótipo misto T/Mieloide, com cariótipo com t(5;12) (q31;p13), del(7)(q21), -18, -19. Paciente realizou tratamento de indução, havendo refratariedade, com hemograma recuperado com 65% de blastos com fenótipo idêntico ao inicial. Submetido a 2ª linha de tratamento, evoluiu com neutropenia febril e evasão hospitalar, retornando em choque séptico e evoluindo a óbito. **Discussão:** Estima-se que o risco de neoplasias hematológicas na população com doença falciforme é de 2 a 11 vezes maior do que na população geral, apesar de mecanismo não bem estabelecido, a o alto turnover medular óssea pode gerar acúmulo de mutações somáticas e acelerar o processo de envelhecimento das células progenitoras hematopoéticas. O uso contínuo de HU interfere no processo de reparo do DNA, podendo gerar mutações adquiridas e, possivelmente, alteração leucêmica 6,7,12. A ausência de condições predisponentes à LA, como exposição a substâncias radioativas, doença mieloproliferativa ou propensão genética conhecida3, reforça a hipótese da AF e seu tratamento como principal fator na gênese da LA. Na revisão de literatura não foi encontrado relato de caso de leucemia de fenótipo misto em pacientes com anemia falciforme. A presença de cariótipo complexo e deleção do 7q, classificando a doença como de alto risco citogenético, possivelmente relacionan-se à refratariedade da doença ao tratamento quimioterápico. **Conclusão:** O caso apresentado demonstra rara evolução de um paciente com AF com quadro de leucemia aguda de fenótipo misto, evidenciando como a AF e seu tratamento com hidroxiureia, pode gerar mutações adquiridas que favorecem a transformação leucêmica. Há a necessidade de um monitoramento rigoroso e contínuo dos pacientes com AF, particularmente aqueles em uso prolongado de HU, para a detecção precoce e manejo adequado de complicações hematológicas graves como a LA.

https://doi.org/10.1016/j.htct.2024.09.659

CHARACTERISTICS OF THE ACTION OF OXYSTEROLS 7-KETOCHOLESTEROL AND CHOLESTANE-3β,5α,6β-TRIOL ON ABCS AND LRP TRANSPORT PROTEINS OF MESENCHYMAL STEM CELLS DERIVED FROM BONE MARROW OF PATIENTS WITH ACUTE MYELOID LEUKEMIA

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ABCs and LRP transport proteins are involved in several metabolic processes, among which the transport of lipids and xenobiotics can be highlighted. Thus, the overexpression of some of these proteins, such as ABC-G2 and the LRP protein, are associated with the phenotype of resistance to multiple drugs, one of the main causes of relapses and relapses in patients with acute myeloid leukemia. Mesenchymal stem cells (MSC) are multipotent cells present in the bone marrow and are part of the hematopoietic niche. Phenotypic changes in MSCs are related to AML progression. The oxysterols, 7-KC and Triol, are derived from the auto-oxidation of the cholesterol molecule; and have functions in cell signaling, survival and death. Therefore, the objective of this work was to evaluate the action of oxysterols, in subtoxic concentrations, of 7-KC (30 μM, 50 μM and 70 μM) and Triol (20 μM, 30 μM and 40 μM) on the ABCs and LRP transport proteins of MSCs derived from bone marrow from patients with AML (MSC-D), being used as a comparator MSC of bone marrow from healthy individuals (MSC-S). Using the indirect immunofluorescence technique, it was observed that the amount of ABC-A1 protein was higher in MSC-S strains and that treatment with 30 μM of 7-KC increased ABC-A1 only in MSC-S strains. On the other hand, treatment with Triol decreased the concentration of ABC-A1 in MSC-S strains, and this decrease in ABC-A1 was associated with a decrease in the amount of the LXR-β receptor. Furthermore, treatment with 70 μM of 7-KC decreased LRP protein expression in MSC-S strains, while in MSC-D strains there was no difference. Treatment with Triol showed no significant effect on LRP protein expression in MSC-S, only in MSC-D strains, where there was an increase in the concentration of 20 μM, followed by a decrease in the concentrations of 30 μM and 40 μM of Triol. Both 7-KC and Triol treatment increased the concentration of SMO protein in the cytoplasm and its translocation to the nucleus in MSC-S cell lines. This effect was not observed in MSC-D strains. Treatment with Triol increased the concentration of ABC-D4 protein in the cytoplasm. Furthermore, the presence of ABC-D4 protein was observed in the nucleus of MSC-S and MSC-D strains. Our results demonstrated that in the MSCs lineages the effect of 7-KC and Triol is mainly metabolic, in which an increase in the oxidized glutathione content, alteration in the processes of mitochondrial dynamics with induction of genes related to the fission and fusion process in both 7-KC and Triol-treated

MSC lines. Increased expression of the BCL2 gene and cytoplasmic survivin was also observed in MSCs treated with 7-KC. In conclusion, it is possible to observe differences in the expression of ABC transporters and LRP between CTM-S and CTM-D strains. Furthermore, at the same concentrations of 7-KC and Triol used, the observed effect was different between MSC-S and MSC-D, which demonstrates that there are different mechanisms between mesenchymal stem cell lines. In summary, our results are characteristic of the metabolic action of the oxysterols 7-KC and Triol on MSCs.

https://doi.org/10.1016/j.htct.2024.09.660

MOLECULAR CHARACTERIZATION OF DIFFERENT GENE FUSIONS ASSOCIATED WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN FROM THE BRAZILIAN AMAZON

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Objective: Acute Lymphoblastic Leukemia (ALL) is classified according to its genetic abnormalities, which are associated with the clinical and biological characteristics of the disease. The detection of gene fusions assists in diagnosis, risk stratification, and targeted therapy. This study aims to evaluate the status of gene fusions in pediatric ALL patients from the Brazilian Amazon and their association with known hematological parameters. **Materials and methods:** The research was approved by the ethics committee under number 4.040.805 and included a total of 160 patients diagnosed with ALL at the Octávio Lobo Children's Oncology Hospital during the period from 2017 to 2023. Clinical data (leukometry, platelets, and hemoglobin) and epidemiological data (gender and age) were collected from the hospital's database system. For the analysis of gene fusions, c-DNA was obtained for the detection of molecular biomarkers by PCR using specific primers. Agarose gel electrophoresis was performed to visualize the PCR products. Finally, Sanger Sequencing was carried out to confirm the PCR results. For qualitative variables, descriptive statistics were used, determining absolute and percentage frequencies. For quantitative variables, median and standard deviation values were calculated according to the variables under study. The Kruskal-Wallis test was performed to test the association of the presence of one of the gene fusions (BCR::ABL, TCF3::PBX1, KMT2A::AFF1, ETV6::RUNX1 and SIL::TAL) with the clinical data, adopting a p-value ≤ 0.05 as significant. Statistical analyses were performed using RStudio 12.1 software. **Results:** Regarding gene fusions, 21% of patients had the TCF3::PBX1 fusion, 19% ETV6::RUNX1, 11% BCR::ABL, 3% KMT2A::AFF1, 2% SIL::TAL, and 44% had none of the studied fusions. 61% of the patients were male and 39% female, with a median age of 6 years. Regarding clinical data, the patients had a median white blood cell (WBC) count of 13,150/mm^3; a median platelet count of 36,000/mm^3; and a median hemoglobin level of 8 g/dL. The Kruskal-Wallis test revealed a significant statistical difference between gene fusions and white blood cell count (p-value = 0.0024), and Dunn's post-test showed that in TCF3::PBX1, the WBC count is significantly higher mainly compared to ETV6::RUNX1 (p-value = 0.007). **Discussion:** Studies have reported ETV6::RUNX1 as the most frequent fusion, but this work found TCF3::PBX1 as the most frequent find, which may be explained by the highly mixed population of the Amazon, supporting the existence of ethnic differences. Other studies found significant statistical differences in white blood cell count between the TCF3::PBX1 fusion and others, which corroborates the findings of this study, indicating that this molecular biomarker has a poor prognosis and is characterized by a white blood cell count above 50,000/mm^3, which was found in about 35% of the patients in this study. **Conclusion:** In the study, the frequency of the TCF3::PBX1 fusion was observed to be relatively higher than what is reported in the literature. The TCF3::PBX1 fusion leads to the activation of genes encoding proteins with malignant potential, and that the fusion showed a statistical difference between groups regarding white blood cell count, which is used as a risk classification according to the National Cancer Institute.

https://doi.org/10.1016/j.htct.2024.09.661

RESGATE À BASE DE VENETOCLAX INDUZ MAIS RESPOSTA QUE 7+3 EM LMA NO SUS

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Objetivos: O objetivo primário é reportar a taxa de mortalidade global aos 30 dias. Os objetivos secundários são avaliar a taxa de mortalidade aos 30 dias por tratamento e as taxas de mortalidade aos 60 dias, sobrevida global (SG), tempo para resposta completa (TRC) e duração da resposta RC (DRC), taxa de remissão completa à indução (RC), globais e por tratamento; bem como a taxa de RC ao resgate com esquema à base de venetoclax (VEN) e tempo para resposta com esquema à base de VEN no resgate. **Métodos:** Estudo retrospectivo, a partir da revisão de prontuário eletrônico, de 53 pacientes que foram sequencialmente diagnosticados com leucemia mieloide aguda (LMA) no Hospital Universitário de Brasília (HUB), entre novembro de 2018 e janeiro de 2024. Destes 10 foram excluídos devido ao diagnóstico de leucemia promielocítica aguda e 4 por terem linhagem ambígua. **Resultados:** Incluídos 39 pacientes, mediana de idade de 56,7 anos