leucemia mieloide aguda, crônica, linfocítica aguda e crônica. Os sintomas incluem febre, fadiga, palidez e propensão a infecções. No Brasil, a doença tem impacto significativo na saúde pública, dessa forma destaca-se a importância da análise epidemiológica da patologia, bem como o diagnóstico precoce para melhorar seu prognóstico. **Objetivo:** Descrever o perfil epidemiológico das internações e dos óbitos por leucemia no estado do Piauí no período de 2019 a 2023. **Metodologia:** Trata-se de um estudo epidemiológico descritivo de base populacional, realizado através dos dados obtidos no Sistema de Informações Hospitalares do SUS (SIH/SUS), disponíveis no DATASUS. Os casos de leucemia foram analisados no estado do Piauí entre os anos de 2019 e 2023. As variáveis analisadas foram registros de internação e óbito por diferentes tipos de leucemia, categorizados por ano, sexo e faixa etária. **Resultados e discussão:** Entre 2019 e 2023, foram registradas 3.431 internações por leucemia no estado do Piauí. A análise dos dados revela uma constância no número de internações, com 2019 apresentando o maior número de casos, totalizando 794 internações, e 2021 apresentando o menor número com 589 internações, enquanto os demais anos apresentaram variações entre 580 e 800 internações. As faixas etárias mais afetadas situam-se entre 1 e 14 anos, concentrando mais de 20% dos casos anuais, enquanto o restante dos casos distribui-se desigualmente nas outras faixas etárias, com a maior concentração abaixo dos 30 anos. O sexo masculino predominou entre os internados, representando 56% dos casos, superado apenas nas faixas etárias de 20 a 50 anos. Em relação aos óbitos, foram registrados 231 casos no mesmo período, com 2019 novamente apresentando o maior número, totalizando 62 mortes. A quantidade de óbitos variou entre 40 e 50 por ano, com exceção de 2022, que registrou 31 óbitos, menor número registrado no período analisado. Diferentemente das internações, os óbitos concentraram-se em faixas etárias mais elevadas, com quase 40% dos casos situados entre 20 e 29 anos e entre 50 e 69 anos. O sexo masculino foi novamente o mais afetado, correspondendo a 54% dos óbitos. **Conclusão:** Os resultados mostraram uma constância nas internações por leucemia no estado do Piauí entre 2019 e 2023, com maior prevalência entre homens jovens. Os óbitos foram mais frequentes em faixas etárias mais elevadas. Compreender esses padrões é essencial para desenvolver estratégias de saúde pública mais eficazes, focadas no diagnóstico precoce e tratamento adequado, com o objetivo de reduzir a mortalidade e melhorar a qualidade de vida dos pacientes com leucemia no estado.

https://doi.org/10.1016/j.htct.2024.09.609

TOWARD OPTIMIZED TREATMENT: INCIDENCE OF HYPERSENSITIVITY REACTIONS AND INACTIVATIONS IN BRAZILIAN CHILDREN RECEIVING PEG-ASPARAGINASE FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: PEG asparaginase (PEG-ASNase) is an essential drug in the treatment of acute lymphoblastic leukemia (ALL). However, asparaginase-related hypersensitivity and silent inactivation continue to represent clinical challenges. **Objective:** Describe the incidence of hypersensitivity reactions and inactivations associated with PEG-ASNase in Brazilian children undergoing first-line treatment for ALL. **Material and methods:** Prospective, multicenter and randomized trial. Patients younger than 18 years with ALL who received PEG-ASNase between February 2021 and February 2024 in eigth differents hospitals were included. ASNase activity was monitored in all patients 7 days and 14 days after each PEG-ASNase. **Results:** 305 patients were included. 33 (10.8%) patients had clinical allergic reactions and 43 (14.1%) patients had inactivation (asparaginase activity < 0.1 IU/mL). Among those who had allergic reactions, 45.5% also inactivated the drug. There was a significant association between clinical allergic reaction and inactivation ($p < 0.001$). However, among those who inactivated, 65% did not have an allergic reaction. The silent inactivation rate was 9.2% (n = 28). **Conclusions:** Our findings are consistent with the literature, underscoring the importance of therapeutic monitoring of asparaginase for all patients. We aim to further contribute to the treatment of children with ALL by investigating the influence of pre-medication on inactivation and hypersensitivity reactions.

https://doi.org/10.1016/j.htct.2024.09.610

CLINICAL VALIDATION OF FLOW CYTOMETRY 10 COLOR PANEL FOR ASSESSMENT OF MEASURABLE RESIDUAL DISEASE IN ACUTE MYELOID LEUKEMIA

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Given the usefulness of measurable residual disease (MRD) in evaluating treatment efficacy and to predict relapse, MRD monitoring is becoming more frequent for the management of patients with acute myeloid leukemia (AML). Therefore, the accuracy of the methods is essential to obtain reliable results in order to incorporate MRD into therapeutic protocols. MRD AML by multiparametric flow cytometry (MFC)

requires complete standardization of processes to ensure optimal results. In addition, clinical validation of the MRD assessment strategy is essential. This study aimed to retrospectively evaluate the clinical effectiveness of a previously analytically validated 10-color MFC protocol to detect AML MRD. **Material, patients and methods:** Databases from the flow cytometry laboratory and from the bone marrow transplantation service as well as information from the electronic medical records of AML patients were accessed. Inclusion criteria: patients with MRD evaluated by the validated 10-color MFC protocol, with at least four months of follow-up after the last MRD assessment or who died due to leukemia relapse before the end of this 4-months follow-up. The samples included should have at least 500,000 evaluable CD45+ cells. All levels of MRD positivity were considered for survival analysis. Eighty-two patients with non-promyelocytic AML with a median age of 38 (10-69) years were included in the cohort; 43 were female. Seventy-six patients underwent allogeneic hematopoietic stem cell transplantation (alloHSCT) and six were treated with intensive chemotherapy. The strategy to validate the effectiveness of the 10-color MFC protocol in detecting AML MRD was the concordance of MRD results with patients' expected outcomes. Clinical sensitivity and specificity, positive and negative predictive values, and diagnostic concordance were calculated even for patients with MRD evaluations post-alloHSCT and after the second cycle of induction chemotherapy. Overall survival (OS) and relapse free survival (RFS) were estimated using the Kaplan-Meyer method and the cumulative incidence method was used to calculate the incidence of relapse (CIR). p-values ≤ 0.05 were considered statistically significant. The results showed high sensitivity (87%), specificity (97%), positive predictive value (78%), negative predictive value (98%) and diagnostic concordance (95%) of the 10-color MFC protocol. The two-year OS, RFS, and CIR of pre-HSCT patients (N = 68) according to MRD < or > 0.1% were 76.4% vs 51.5% (p = 0.117), 79.8% vs 5.3% (p = 0.006), and 53% vs 2% (p < 0.001), respectively. Regarding post-HSCT and after 2nd cycle of intensive chemotherapy patients (N = 74), OS and RFS were higher in patients with MRD < 0.1% vs > 0.1% (75.5% vs 50% p = 0.008%) and (78.4% vs 14.3% p < 0.006) respectively, with smaller CIR (3% vs 6% p < 0.001). In conclusion, objective parameters were used in this study to calculate the clinical sensitivity and specificity of the MRD method. However, the aspects such as the clonal evolution, the MRD kinetics and the therapeutic interventions have impact on sensitivity of MRD results and should be considered for the interpretation of AML relapse. Despite the small cohort and short follow-up time, the 10-color MFC protocol for AML MRD showed high correlation of levels of MRD with clinical outcome and proved to be useful for clinical decision-making.

https://doi.org/10.1016/j.htct.2024.09.611

IMMUNOPHENOTYPIC SIGNATURE OF LEUKEMIA ARREST STAGE IS ASSOCIATED WITH NPM1/FLT3 MUTATIONAL PROFILE AND PROGNOSIS IN ACUTE MYELOID LEUKEMIA

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Acute Myeloid Leukemia (AML) is a severe hematopoietic disorder marked by uncontrolled proliferation of immature myeloid progenitors due to differentiation arrest, with significant immunophenotypic diversity. *FLT3-ITD* mutations' prognostic impact varies with *NPM1* mutation presence and the *FLT3* allelic ratio. While cytogenetic and molecular features are well-established for risk stratification by European LeukemiaNet (2017 ELN), the role of leukemia arrest stages in prognosis remains unclear. This study classified the maturation arrest stages of leukemic blasts in a Brazilian AML cohort, analyzing its association with genetic risk and clinical data. Bone marrow from 148 *de novo* AML patients (Sep-2015-Jul-2024) was evaluated for *FLT3* and *NPM1* mutations, *FLT3* allelic ratio, and immunophenotyping. MPO cytochemistry stains and phenotypic markers by flow cytometry defined six stages of leukemia arrest (SLA): Hematopoietic Stem Cells-like (HSC-L:CD34^{+} CD117$^{\pm}$CD13^{-}CD33^{-}HLA-DR^{+}MPO^{-}); Multipotent Progenitors-like (MPP-L:CD34^{+}CD117^{+}CD13$^{\pm}$CD33$^{\pm}$HLA-DR^{+}MPO^{-}); Common Myeloid Progenitors-like (CMP-L:CD34$^{\pm}$CD117^{+}CD13^{+}CD33$^{\pm}$ HLA-DR^{+}MPO^{+}); Granulocyte-Monocyte Progenitors-like (GMP-L:CD34$^{\pm}$CD117$^{\pm}$CD13$^{\pm}$CD33^{+}HLA-DR^{+}MPO^{+}); Monocyte Progenitors-like (MP-L:CD34^{-}CD117$^{\pm}$CD13^{+}CD33^{+}HLA-DR^{+}MPO^{+}); and Granulocyte Progenitors-like (GP-L:CD34^{-}CD117$^{\pm}$CD13^{+} CD33^{+}HLA-DR^{-}MPO^{+}). SLA showed highest frequency in MP-L (n = 57, 38.5%) and GP-L (n = 53, 35.8%), followed by GMP-L (n = 23, 15.5%), CMP-L (n = 7, 4.7%), MPP-L (n = 6, 4.1%), and HSC-L (n = 2, 1.4%). Predominance of *FLT3*^{wt}/*NPM1*^{mut} patients (n = 80, 54.1%) was observed, with similar distribution among *FLT3*^{mut} patients (*FLT3*^{mut} /*NPM1*^{mut}:n = 32, 21.6%; *FLT3*^{mut}/*NPM1*^{wt}:n = 36, 24.3%). CMP-L and GMP-L frequencies were increased in *FLT3low/NPM1*^{wt} and *FLT3*^{high}/*NPM1*^{wt} vs. *FLT3*^{wt}/*NPM1*^{mut} (CMP-L:13.33%, 14.28% vs 1.25%, p < 0.05; GMP-L:40%, 42.85% vs 7.5%, p < 0.05). GP-L frequency was decreased in *FLT3*^{low}/*NPM1*^{wt} and *FLT3* ^{high}/*NPM1*^{wt} vs. *FLT3*^{wt}/*NPM1*^{mut} (0%, 9.52% vs 43.75%, p < 0.05). Response to treatment (CR/CRi, CR/CRiMRD^{+} and PD–Persistence disease) was evaluated after 1st and 2nd cycles of Induction of Remission (1IR, 2IR). GMP-L was increased in PD after 1IR (OR:6.09, 95% CI:1.22–30.19, p < 0.05). Immature (HSC+MPP +CMP) SLA was higher in MRD+ patients compared to MRD- (OR:6.81, 95% CI:0.86–47.05, p < 0.05). Overall survival (p = 0.81) and relapse-free survival (p = 0.27) analyses showed that GMP-L patients relapsed sooner. In 2017 ELN risk assessment, *FLT3-ITD* stratification was based on allelic ratio and *NPM1* mutation status. A high *FLT3-ITD* allelic ratio with *NPM1* mutation