referral bias and delayed diagnosis and may be responsible for the high number of patients with hyperleukocytosis. Early mortality remains high, despite despite almost complete coverage of patients receiving ATRA within the first 24 hours of admission in recent years, underscoring the need for improved pre-admission management. NRM during consolidation phases appears to have been influenced by the high incidence of cases related to prior cancer therapy in our cohort and deserves special attention Despite high curability, APL management in the public health system faces structural barriers. Ensuring early diagnosis, rapid referral to experienced centers, as well as intensive supportive care, are critical to reduce mortality and improve outcomes.

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ADVANCES IN CHEMOTHERAPY PROTOCOLS FOR CHILDHOOD LEUKEMIAS: EFFICACY, NEW THERAPIES AND CHALLENGES

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Introduction: Acute Lymphoblastic Leukemia (ALL) represents approximately 75% of childhood leukemia cases, with survival rates now exceeding 90% in high-income countries due to therapeutic advances. This review evaluates recent improvements in chemotherapy protocols, focusing on comparative efficacy between traditional regimens and novel approaches incorporating targeted therapies and immunotherapies. **Objectives:** To analyze survival outcomes, treatment efficacy, and cost-effectiveness of contemporary chemotherapy protocols for pediatric ALL, with emphasis on emerging therapeutic strategies. **Material and methods:** An integrative literature review was performed following the PICCO framework. Searches in PubMed and Cochrane databases employed Boolean operators, limited to studies published within the last five years. Selection criteria included clinical trials and systematic reviews addressing pediatric ALL treatment in hospital settings, while excluding diagnostic or prophylactic studies. After PRISMA-guided screening and duplicate removal, 13 studies met inclusion criteria. **Results:** The analysis revealed significant progress in treatment protocols. The ALL-B12 regimen demonstrated superior survival rates (≥90%) through intensified chemotherapy combining pulsed vincristine/dexamethasone with high-dose methotrexate and PEG-asparaginase, while showing reduced toxicity compared to conventional asparaginase. Immunotherapies exhibited remarkable outcomes, particularly in high-risk and relapsed cases. Blinatumomab improved survival rates while proving more cost-effective than standard chemotherapy. CAR-T cell therapy (tisagenlecleucel) achieved durable remission in refractory cases, and inotuzumab ozogamicin showed high response rates in relapsed B-cell ALL. The combination of venetoclax with chemotherapy enhanced survival in relapsed AML. Despite these advances, higher costs and infrastructure requirements for novel therapies pose challenges for implementation in resource-limited settings, highlighting disparities in global accessibility. **Discussion and conclusion:** Contemporary treatment protocols integrating chemotherapy with immunotherapy and targeted agents have transformed pediatric ALL management, particularly for high-risk cases. While therapeutic innovations show promising efficacy and safety profiles, equitable access remains a critical challenge. Future research should address cost barriers and optimize implementation strategies to ensure global benefit.

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ALBUMIN SERUM LEVEL AND INTENSITY OF PRE-PHASE CYTOREDUCTIVE THERAPY ARE MODULATORS OF EARLY MORTALITY IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute lymphoblastic leukemia (ALL) in adults has a substantial mortality within 30 days of diagnosis, defined as early mortality (EM). EM in ALL demonstrates relevant disparities between low-middle income countries (LMICs) and high-income, with reported rates of 10-25% versus <5%, respectively. This mortality gap persists due to multiple factors, exemplified by intensity of induction protocol, social disparities and others, but the precise contributors to elevated EM in LMICs remain poorly defined. **Objetivos:** Identify independent risk factors for EM in adult ALL patients in a high-complexity cancer treatment center in São Paulo, with focus on pre-therapeutic biomarkers and treatment intensity. **Material and methods:** Retrospective cohort study (2009 −2023) including adult patients (≥ 15 years) with newly diagnosed ALL or ambiguous lineage leukemia. Pre-phase regimens varied between corticosteroid alone and corticosteroid plus cyclophosphamide. Data were analyzed using Kaplan-Meier survival estimates and competing-risk methods for 60-day outcomes. Univariate and multivariable logistic regression identified EM risk factors; variables with $p < 0.2$ in univariate analysis or clinical relevance were included in the multivariable model, selected by lowest Akaike Information Criterion. A two-sided $p < 0.05$ denoted significance. **Results:** Of 203 patients (median age 36 years; 54.2% male; 76% B-cell phenotype; 34% Philadelphia chromosome−positive), 89.8% underwent corticosteroid-only pre-phase (prednisone 49.7%, dexamethasone 16.4%, methylprednisolone 1.6%), and 32.2% received cyclophosphamide + dexamethasone. The overall EM rate was 9.8% (95%CI:6.3-15.0). In univariate analysis, low

baseline serum albumin (OR 0.31; 95%CI:0.14-0.68; p = 0.004), cyclophosphamide use (OR 5.45; 95%CI:1.88-18.09; p = 0.003), positive CSF cytomorphology (OR2.82; 95%CI:0.97-7.86; p = 0.049) and year of diagnosis ≥ 2016 (protective, OR 0.24; 95%CI:0.09-0.63; p = 0.004) were associated with EM. In the best multivariable model, albumin (OR 0.27; 95%CI:0.06-0.94; p = 0.048) and cyclophosphamide pre-phase (OR8.41; 95%CI:1.42-72.28; p = 0.028). Obesity also emerged as a significant predictor (OR 7.24; 95%CI:1.07-54.72; p = 0.041). At 60 days, non-failure mortality was 11.5% (95%CI:7.5-17.0) and cumulative failure (relapse/refractory) 32%. Complete response after induction was achieved in 51.2% of patients. **Discussion and conclusion:** Low serum albumin and cyclophosphamide use during pre-phase were strong independent predictors of EM in adult ALL patients from a Brazilian cohort. Low albumin likely reflects malnutrition and higher toxicity risk, while cyclophosphamide may worsen immunosuppression, contributing to infections - observed in 72.9% of patients. These results support the use of simple markers like albumin to guide risk-adapted pre-phase intensity. Adjusting cytoreductive therapy and antimicrobial prophylaxis could reduce EM in resource-limited settings.

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ALTA EXPRESSÃO DE ΔNP73 COMO POTENCIAL MECANISMO DE RESISTÊNCIA À FAGOCITOSE NA LEUCEMIA MIELOIDE AGUDA

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Introdução: A leucemia mieloide aguda (LMA) é uma neoplasia hematológica caracterizada pela proliferação clonal de células mieloides imaturas na medula óssea. Apesar dos avanços terapêuticos, a resistência ao tratamento e as recaídas permanecem desafios clínicos importantes, frequentemente associados à capacidade das células leucêmicas de evadir respostas imunes efetoras. A isoforma dominante negativa ΔNp73, pertencente à família p73/p53, está relacionada à progressão tumoral, mau prognóstico e resistência terapêutica, embora seu papel na modulação da fagocitose na LMA ainda seja pouco explorado. **Objetivos:** Neste estudo de prova de conceito, investigamos se a alta expressão de ΔNp73 contribui para a resistência à fagocitose em células de LMA, visando elucidar um possível mecanismo de evasão imunológica e identificar novas oportunidades terapêuticas. **Material e métodos:** Três linhagens celulares de LMA com TP53 selvagem (MOLM13, MV411 e OCI-AML3) foram transduzidas com partículas lentivirais para induzir a hiperexpressão de ΔNp73 ou, como controle, com o vetor vazio pMEG. A eficiência da transdução foi confirmada pela detecção do sinal de GFP em microscópio de fluorescência EVOS. Macrófagos M1-*like* foram gerados a partir da diferenciação de monócitos isolados de sangue periférico de doadores saudáveis (n = 2) e polarizados com IFN-γ (20 ng/mL) por 24 horas. Para o ensaio de fagocitose, as células leucêmicas foram cocultivadas com macrófagos na proporção de 3:1 por 3 horas. Ao término da incubação, os macrófagos foram marcados com anticorpo anti-CD11b conjugado a APC, e a fagocitose foi quantificada por citometria de fluxo como a porcentagem de macrófagos $CD11b^+$ que apresentavam fluorescência GFP, indicando a internalização das células leucêmicas. **Resultados:** Nas linhagens MV411 e OCI-AML3 não houve diferença significativa na porcentagem de fagocitose entre as células ΔNp73 e as células controle. Em contrapartida, na linhagem MOLM13, observou-se uma redução expressiva da fagocitose nas células ΔNp73 em comparação ao controle, sugerindo que a alta expressão de ΔNp73 pode conferir resistência à fagocitose específica para esse modelo. Essa discrepância entre as linhagens pode estar associada a diferenças genéticas ou moleculares intrínsecas, como variações em vias de sinalização, na expressão de moléculas de superfície envolvidas na interação com macrófagos ou no microambiente celular. **Discussão e conclusão:** Nossos achados preliminares corroboram o papel do ΔNp73 como modulador da evasão imunológica em contextos celulares específicos, abrindo caminho para novas estratégias terapêuticas na LMA. Ensaios complementares são necessários para identificar as vias moleculares que sustentam esse mecanismo.

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ALTERNATIVAS PARA O TRATAMENTO DE LEUCEMIA LINFOBLÁSTICA AGUDA COM CROMOSSOMO FILADÉLFIA POSITIVO

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Introdução: A leucemia linfoblástica aguda com cromossomo Filadélfia (LLA Ph+) representa 25–30% dos casos de LLA em adultos, com prognóstico historicamente desfavorável. A introdução dos inibidores de tirosina quinase (TKIs) melhorou os desfechos, embora a melhor estratégia combinatória de fármacos ainda esteja em investigação. Diretrizes da National Comprehensive Cancer Network (NCCN) incluem protocolos com TKIs de intensidades variadas, enquanto o papel do transplante alogênico de células-tronco hematopoéticas (alo-TCTH) na primeira remissão completa (RC1) vem sendo reavaliado devido ao advento das terapias-alvo, imunoterapias e esquemas quimio-light/free. **Objetivos:** Buscar regimes que maximizem remissão com menor toxicidade e uso do alo-TCTH. **Material e métodos:** Foi conduzida uma revisão de