MATCHED-SIBLING, MATCHED-UNRELATED, OR HAPLOIDENTICAL TRANSPLANTATION FOR ACUTE LEUKEMIAS AND MYELODYSPLASIA IN BRAZIL: A PROSPECTIVE MULTICENTER STUDY IN COLLABORATION WITH THE CIBMTR

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Introduction: Matched-Sibling Donor (MSD) is considered the gold standard in Hematopoietic Cell Transplantation (HCT). However, for patients lacking an MSD, alternative options include a Matched-Unrelated (MUD) or Haploidentical (HAPLO) donor. Although MUD is an established procedure in Brazil, with the third-largest unrelated donor registry (REDOME), HAPLO with Posttransplant Cyclophosphamide (PTCy) is a novel procedure that has become extremely popular worldwide since the original report in 2008. **Objectives:** To compare outcomes of HCT using MSD, MUD, and HAPLO in Brazil. **Methods:** This is a registry-based multicenter prospective study including patients who underwent HCT with MSD, MUD, or HAPLO (with PTCy) donor for Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), or Myelodysplasia (MDS) between 2018 and 2021. The data were reported to the Center for International Blood and Marrow Transplant Research (CIBMTR), which curated the database before providing it to us. Studied outcomes were Overall Survival (OS) and Graft-versus-host disease-, Relapse-Free Survival (GRFS). Survival curves were estimated with the Kaplan-Meier method and compared with the logrank test. Multivariable analysis was performed with Cox models. Multivariable models were selected based on the lowest AIC. This study was approved by the CIBMTR and by local Ethics Committees. Disclaimer: The CIBMTR has not yet reviewed or endorsed the results. **Results:** We included 513, 262, and 480 patients in the MSD, MUD, and HAPLO groups, respectively, with median follow-up times of 25-, 33-, and 24-months. MSD patients were generally older, and MUD patients had a longer time to transplant. Almost all MUD patients received ATG. Other variables were roughly balanced. Two-year OS was 58% for MSD, 61% for MUD, and HAPLO 54% ($p = 0.03$). In OS multivariable analysis, HAPLO was associated with inferior OS (HR = 1.30, $p = 0.009$) compared with MSD, while MUD was not significantly different (HR = 0.93, $p = 0.58$). Additionally, HAPLO was associated with lower OS compared with MUD (HR = 1.39, $p = 0.007$). Of note, results were poorer in older patients, those receiving peripheral blood (PBSC, HR = 1.21, $p = 0.05$), and higher DRI groups. Two-year GRFS was 27% for MSD, 37% for MUD, and 28% HAPLO ($p = 0.05$). In GRFS multivariable analysis, HAPLO led to inferior GRFS (HR = 1.19, $p = 0.03$) compared with MSD, with MUD showing no significant difference (HR = 0.95, $p = 0.59$). HAPLO also had a lower GRFS compared to MUD (HR = 1.26, $p = 0.02$). **Discussion:** Our results show that HAPLO's outcomes are slightly poorer compared to MSD or MUD. Some international reports have reached the same result, especially when MUD receives PTCy. Many factors may have influenced the results, two of the most obvious being the high prevalence of CMV in our population and the high genetic miscegenation in Brazil. Moreover, time-to-transplant was longer in MUD, indicating that there could be some kind of survival bias. Our series represents one of the largest in the world in a study conducted with the support of the CIBMTR. **Conclusion:** MUD transplants should not be systematically replaced by HAPLO in Brazil. However, in situations where the expected time to transplant with MUD donors is long, HAPLO can offer acceptable results, given the small magnitude of the effect and the possibility of survival bias in the MUD group.

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SOBREVIDA APÓS UM SEGUNDO TRANSPLANTE DE CÉLULAS TRONCO HEMATOPOIÉTICAS (TCTH) EM PACIENTES PEDIÁTRICOS COM LEUCEMIAS AGUDAS: PODEMOS FAZER MELHOR?

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Objetivos: Avaliar a Sobrevida Global (SG) após o segundo TCTH em pacientes (pts) pediátricos com leucemias agudas no período de 2010 e 2021 em 4 centros brasileiros. Descrever a incidência cumulativa de progressão e a Sobrevida Livre de Progressão (SLP), as principais causas de óbito após o TCTH. **Material e métodos:** Estudo retrospectivo observacional não randomizado por análise de prontuários. Análise estatística realizada com a plataforma R (versão 4.4.0) **Resultados:** No período do estudo, 376 pts foram submetidos ao TCTH por leucemias agudas (LLA = 263; LMA = 96; Bifenotípica = 14), sendo que 33 receberam um segundo TCTH (LLA = 21 e LMA = 12). A mediana de idade foi de 9 anos (1–18 anos), sendo 66% (n = 22) do sexo masculino. As indicações de re-transplante foram: recidiva (n = 21, 64%) e rejeição (n = 12, 36%). Quanto ao status da doença pré-transplante, 69% tinham Doença Residual Mínima (DRM) negativa por imunofenotipagem, 21% positiva e em 10% tinham o dado indisponível. A maioria dos pts re-transplantados por recaída (19/21, 90%), receberam um condicionamento mieloablativo (26% com TBI), enquanto os demais receberam de intensidade reduzida. A mediana de tempo entre o 1° e 2° TCTH foi de 299 dias (60–1819). A maioria (93%) dos pts recebeu o enxerto de um doador diferente do primeiro transplante, e destes, 57% foram haploidênticos. A fonte de células foi medula óssea em 57% dos casos. Dos 33 pts, 2 apresentaram rejeição primária. A sobrevida mediana após o 2° TCTH foi de 267 dias (95% IC, 90–1129 dias), e as principais causas de óbito foram infecção (52%) e recaída (36%). A mortalidade não relacionada à recaída nos primeiros 100 dias foi de 33% (95% IC, 18%–50%). Com uma mediana de seguimento de 4 anos, a SG e a SLP após o 2° TCTH em 2 e 5 anos foi de 36% e 22%, e de 27% e 20% respectivamente. A incidência cumulativa de progressão em 5 anos foi de 33% (95% IC, 18%–50%) e a mortalidade não relacionada à recaída foi de 46% (95% IC, 28%–62%). Na análise univariada, a DRM negativa pré-transplante (p = 0,038) e a utilização de um doador diferente do primeiro transplante (p = 0,037) foram associadas à maior probabilidade de sobrevida global, porém estes resultados não foram confirmados na análise multivariada. **Discussão:** A recidiva pós transplante é a principal causa de mortalidade em pts com leucemias agudas submetidos a TCTH. Embora um segundo TCTH seja uma opção curativa, os desfechos dependem da morbidade relacionada aos tratamentos prévios, performance do paciente, além do status da doença pré-transplante. A sobrevida global após o segundo transplante encontrada em nossa coorte foi semelhante àquela descrita em trabalhos exclusivamente pediátricos, foi impactada pela presença de DRM negativa pré-transplante e pela utilização de um doador diferente no segundo TCTH. **Conclusão:** Neste estudo, a baixa SG e elevada mortalidade não relacionada à recidiva podem refletir o longo período de análise em que poucos pts tiveram acesso a estratégias de resgate mais eficientes e menos tóxicas como imunoterapia, o que poderia ter aumentado a chance de re-transplantar com DRM negativa. Estes dados reforçam a necessidade de novas opções terapêuticas para evitar as recidivas pós-transplante, como desenvolvimento de programas de terapia celular, principalmente para pts do SUS.

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INFLUENCE OF INTERLEUKIN-12 (IL-12) ON MINIMAL RESIDUAL DISEASE (MRD) OF MULTIPLE MYELOMA PATIENTS TREATED WITH AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: EXPERIENCE FROM A SINGLE BONE MARROW TRANSPLANT SERVICE

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Introduction: Interleukin-12 (IL-12) appears to play an antitumor role through immunomodulatory and antiangiogenic mechanisms in human B-cell neoplasms. In a previous study we demonstrated an increase in serum IL-12 levels after bone marrow recovery in Multiple Myeloma (MM) patients who underwent Autologous hematopoietic Stem Cell Transplantation (ASCT). Based on these findings, we hypothesized a possible influence of IL-12 on the positivity of Minimal Residual Disease (MRD) in MM patients treated with ASCT. **Methods:** From March 2020 to April 2023, 62 patients with newly diagnosed MM, care provided by the National Health System (SUS) were enrolled. All patients were treated with protocols containing bortezomib, cyclophosphamide and dexamethasone (09 CR, 12 VGPR, 41 PR). Blood samples were taken after the characterization of bone marrow functional recovery. IL-12p70 quantification was performed using an ELISA kit (R&D Systems, MN, EUA). MRD testing was carried out by multiparametric flow cytometry 90-days after hospital discharge. Fisher's exact test was used to evaluate the categorical variables and p-values lower than 0.05 were considered significant. **Results:** Among the 62 patients, the median IL-12 concentration was 171 pg/mL, ranging from 28 to 971 pg/mL. Overall, MRD absent (MRD-) was found in 26 and present (MRD+) in 36 patients. A scatter plot showed that patients with higher levels of IL-12 had a lower proportion of MRD+; for this reason, patients were divided into groups with values above (A) and below (B) the median IL-12 concentrations, groups A (high IL-12 concentrations, n = 27) and B (low IL-12 concentrations, n = 35), respectively. In group A, 18 had MRD- against 8 MRD- in group B (Odds Ratio = 6.7, 95% CI 2.2–20.7, p = 0.0007). **Discussion:** Despite limitations such as the number of patients from a single center, the quality of remission before transplantation and the techniques used to detect MRD, we observed that 42% of patients showed MRD- and these results are comparable to previous studies that demonstrated absence of MRD in 42% to 58% of MM patients treated with ASCT. Based on the above arguments, the antitumor effect of IL-12 might explain, at least partly, the high concentration of IL-12 in patients without MRD. **Conclusion:** Our data suggest that IL-12 levels obtained in the bone marrow recovery phase seem to be inversely associated with the occurrence of MRD.

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