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Adverse events related to PBPC collection and mobilization for autologous transplantation in 10 years' experience: procedures, efficiency, variables related to collection and safety profile

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Objectives: We tried to evaluate the efficiency, safety and risk factors of aphaeresis procedures used for autologous PBPC collections in a 10-year period in our transplant center. Thrombocytopenia, hypotension and citrate related adverse effects were evaluated as different biological variables.
Material and methods: A total of 155 patients with hematological malignancies were analyzed (57 AML in first remission, 33 HD, 37 MM, 20 NHL, 4ALL) that underwent mobilization of PBPC. The patients were mobilized either with CTX 3gr/m² + G-CSF 10mcg/kg starting or VP-16 (2gr/m²)+G-CSF 10mcg/kg. Collections of PBSC were performed using Cobe spectra Baxter CS3000 aphaeresis system. Target of collection was >2, 0x10(6)/kg CD34+. The procedure was initiated when leukocyte count reached to 5x10(9)/L.
Results: Both regimens were effective in the progenitor cell mobilization and almost 84% of analyzed patients reached at least 2x10(6)/kg CD34+ cells with median 3 (ranges 1-6) aphaeresis procedures. In 6% of patients adequate cell dose was not reachable and overall failure rate of mobilization of 17, 5%. Furthermore 15.6% failed to harvest the optimal 4x10(6)/kgCD34+cells with >1 aphaeresis attempt. 48% patients in the CT/G-CSF group initiated aphaeresis on day 9, 34% on day 8 and 31% on day 10. Good mobilizers (GM) experienced at least one adverse event during aphaeresis compared with the no-GM. The percentage of absolute CD34+ before aphaeresis correlated with CD34+/cells/kg collected (R2=0, 62). The median of blood volume processed for body weight and the median time of aphaeresis was 7215ml (980ml-13450ml) in 202 min for GM and 8054ml (1450ml-14659ml) and 207min or no-GM. No correlation was found between CD34+/kg and volume processed. High correlation was found between the number of CD34+/kg and volume processed in the GM subject that reached the target of CD43+cells/kg only with one aphaeresis procedure (R2=0,87)
We can conclude that the mobilizing regimens were adequate to achieve PBSC harvest in 84% of pts in our center that underwent autologous transplantation. The optimal approach to remobilization strategy remains unclear. Also we did not observe any significant difference between GM and no-GM subjects in the adverse effect manifestation in reaching the CD34+cells/kg target, concerning the number of cells and volume processing. Maybe volume reducing of aphaeresis technique in future will shorten the time of achieving CD34+ target in GM subject.

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Severe neurotoxicity following peripheral blood stem cell transplantation

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Introduction: Dimethyl sulphoxide (DMSO) is used as a cryoprotectant for long-term storage of hematopoietic stem cells (HSC). Various complications during infusion of cryopreserved HSC have been described. Until recently, there has been little information on the neurological toxicity of DMSO. DMSO-related neurotoxicity even coma, has been described, mostly as anecdotic events.
Case reports: We are reporting 3 cases of transient neurotoxicity out of 286 autologous peripheral blood stem cell transplantation (PBSCT) performed in our center between 2000.-2010. All patients (pts) - 2 males, 1 female, 51, 59 and 39 years old, have stage III of multiple myeloma. Each one has received Dexamethasone–based induction. A PBSC collection was performed with Cyclophosphamide (4g/m²) and rhG-CSF (5 µg/kg/day) and optimal numbers of mononuclear cells (MNC- median $8x10^8$/kgBW) were harvested. The cells were cryopreserved on 10% DMSO using a controlled–rate freezer and stored at -900C. The conditioning regimen in autologous setting was consisted of Melphalan at a dose 200 mg/m². The bags were thawed in a 37ºC water bath and infused at a rate of 10ml/min. Despite standard premedication on day "0", during infusion all pts were developed a complete loss of consciousness accompanied by incontinence, without clonic convulsions or focal neurological sings. Pulse rate and blood pressure were normal. The pts were transferred to intensive care unit (ICU) for ventilation. No laboratory abnormalities, including electrolytes, osmolarity, coagulation screen, serum glucose and enzymes, were evidenced upon repeated testing. The urgent CT scans were unremarkable. Pts were treated with steroids and forced hydration. All pts recovered consciousness in 3-5h after assistance ventilation was started. Finally, they were extubated within 24h and discharged from ICU on day +1. All pts have optimal engraftment.
Discussion: Because of the strict temporal relationship between the infusion and development of neurological sings and their resolution upon forced hydration, we circumstantially attribute the encephalopathy to the infusion of DMSO-contained in the PBSC suspension. The risk-factors for development of DMSO–neurotoxicity are still unclear. The preconditioning exposure to central nervous system (CNS)-penetrating agents and M protein in multiple myeloma pts might contribute to the occurrence of DMSO –associated neurological toxicity , but a large analyzes are needed.

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In vivo plus ex vivo purging during autologous peripheral blood stem cell transplantation in high-grade B cell non-Hodgkin's lymphoma

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Background: The importance of the residual disease and the tumour contamination of the graft on relapse in lymphoma patients who underwent autologous peripheral blood stem cell transplantation (auto PBSCT) has been shown.
In this study we evaluated two commonly used B-cell purging methods, in vivo purging with rituximab and ex vivo purging with CD 34 (+) selection (CliniMacs) during auto PBSCT in high-grade relapsed B-cell non-Hodgkin's lymphoma (NHL).
Patients: Nine patients were enrolled in this study. Patients 37-78 years of age with a chemosensitive relapsed high-grade B-cell NHL (6 diffuse large cell, 3 mantle cell). Six of them had bone marrow involvement before R-DHAP regimen. The conditioning regimens were TBI+Cy (n=6) or BEAM (n=3). Five patients received rituximab after transplantation. The median CD34 (+) cells/kg infused was 1.17 x 106.
Results: No patient experienced primary or secondary graft failure. We observed no CMV and other serious infections during six months after transplantation. Median follow up was 18.1 months. Five patients are still alive and disease free. Three patient relapsed and two patients died due to progressive disease and chronic C type hepatitis. The disease free and overall survival at two years were 76% and 62.5%, respectively.
Conclusion: In conclusion, in vivo plus ex vivo purging during auto PBSCT in high-grade relapsed B-cell NHL is feasible and safe. It may play an effective role on residual disease and tumor contamination of the graft and improve outcome.