

Autologous Stem Cell Transplant with Non-Cryopreserved Grafts

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Autologous stem cell transplantation (ASCT) after a high dose conditioning is an established treatment modality with definitive indications for many haematological disorders.

However, this line of treatment requires many expensive resources, such as freezing of the harvest product in order to maintain cell viability until stem-cell reinfusion. The storage of harvested stem cells, in standard refrigerators at +4°C, is an alternative to cryopreservation.

In 2007, Wannesson et al. published a systematic review in which they demonstrated the feasibility and the safety of ASCT without cryopreservation of the graft [1].

They reviewed the methodologies and results of sixteen papers published from 1984 to 2006, on the subject of ASCT with non-cryopreserved stem cells. 661 auto transplanted patients were reported in this reviewed literature, and two of them (0.32%) failed to engraftment.

Wannesson et al. concluded that ASCT with stem cell stored in the refrigerator at +4°C is a safe procedure as long as we use short regiment schedules [1].

In 2009 we started to perform ASCT without freezing of the harvested bags, and the high dose chemotherapy regiments were inspired from Wannesson et al. publication.

Until now we performed 150 ASCT without cryopreservation of the graft. At the beginning we thought that it would be more prudent to use only short conditioning regiments. Mobilization, with G-CSF alone, was started 4 days before leukapheresis at the dose of 15 µg/kg/d at 07:00 pm. one or two cytapheresis were performed twelve hours after the fourth injection (07:00 am), the number of CD34+ cells is assessed immediately after the end of the cytapheresis and if a minimum number of 2×10⁶ CD34+ cells/Kg is not reached another cytapheresis is performed the next morning. Viability of the harvested cells is assessed every day, by flow cytometry using 7AAD (7 Amino-Actinomycine D) until the reinjection of the harvests [2]. The chemotherapy conditioning regiment is started once a minimum of 2×10⁶ CD34+ cell/kg is obtained. In case of a myeloma patient the MEL200 (Melphalan 200mg/m², a 30 minutes injection) is used and in case of a Hodgkin lymphoma CBV (a 3 days schedule: Cyclophosphamide 60 mg/kg D-3 and D-2, BCNU: 400 mg/m² D-3 and VP16 700 mg/m² D-3, D-2 and D-1), the stem cells are reinfused 24 hours after the end of the chemotherapy regiment at D0 in order to insure drug clearance. The aplastic phase is managed only by using transfusions and antibiotics and there is no use of growth factors. In case of myeloma patients the majority of the harvested bags were stored in a standard refrigerator at +4°C for 24 to 48 hours, and in Hodgkin lymphomas the grafts were stored for a minimum of four to five days without being freeze [3,4].

112 patients with myeloma were autotransplanted using this procedure. The median duration of neutropenia was 10 days (6 to 17) and of thrombopenia was 13 days (9 to 24) [3]. We deplored only one graft failure (0.8%) and it was a patient transplanted during hepatic failure.

17 patients received CBV conditioning chemotherapy before

autologous transplant, the median duration of neutropenia 13 days (9 to 24) and thrombopenia 12 days (9 to 37). There was one transplant related mortality (TRM) due to a staphylococcus sepsis of the catheter, 7 days after transplant [4].

Since the viability results of the harvested cells were satisfactory (50% to 60% of viable cells after 8 days of liquid storage), we decided to use more intensive and longer conditioning schedules. From Jan 2011 until now, we auto-transplanted 6 patients after standard BEAM regiment (BCNU: 300 mg/m² at D-2, VP16: 200 mg/m² at D-5 to D-2, Arac: 400 mg/m² at D-5 to D-2, Melphalan: 140 mg/m² at D-1), in case of unavailability of BCNU we used -EAM protocol which is an even more intensive schedule in 15 patients (VP16: 200 mg/m² at D-5 to D-2, Arac: 2000 mg/m² at D-5 to D-2, Melphalan: 140 mg/m² at D-1) [5,6]. In these cases the harvested grafts were stored in the refrigerator at +4°C for a minimum of 5 to 7 days.

The median duration of neutropenia was 13 days (10 to 32) and of thrombopenia was 13 days (9 to 24), there was no mortality in these cases.

We can conclude that ASCT with non-cryopreserved grafts is feasible and safe even with long time regiments such as BEAM. The harvested cells can be kept in the refrigerator for until their reinfusion.

However the lake of freezing possibilities requires an efficient coordination of stem-cell mobilization, apheresis, administration of the high-dose therapy and the stem-cell reinfusion that may be more flexible in centers that use cryopreservation.

References

1. Wannesson L, Panzarella T, Mikhael J, Keating A (2007) Feasibility and safety of autotransplants with noncryopreserved marrow or peripheral blood stem cells: a systematic review. *Ann Oncol* 8: 623-632.
2. Brahimi M, Osmani S, Yafour N, Bekadja S (2011) Viabilité et fonctionnalité des greffons de cellules souches périphériques non cryopreservées à une température de + 4°C. *Revue Algerienne d'Hematologie* 5 :46-48.
3. Bekadja MA, Brahimi M, Osmani S, Arabi A, Bouhass R, et al. (2012) A simplified method for autologous stem cell transplantation in multiple myeloma. *Hematol Oncol Stem Cell Ther* 5: 49-53.
4. Bekadja MA, Brahimi M, Osmani S, Arabi A, Tedj F, et al. (2011) Intensification thérapeutique selon le protocole CBV suivie d'autogreffe de cellules souches hématopoïétiques (CSH) non cryopréservées au cours des lymphomes hodgkiniens : résultats préliminaires. *Revue Algerienne d'Hematologie* 5: 50-53.

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5. Bekadja MA, Osmani S, Brahimi M, Talhi S, Bekadja S, et al. (2012) High-dose etoposide, cytarabine and melphalan as conditioning regimen for autologous stem cell transplantation in patients with refractory or relapsed Hodgkin's lymphoma. EBMT 38th meeting: Geneva, Switzerland.
6. Talhi S, Osmani S, Brahimi M, B Entasoltan, Arabi A, et al. (2012) Intensification par étoposide, cytarabine et melphalan (EAM) suivie d'autogreffe de cellules souches périphériques au cours des formes réfractaires ou en rechute de la maladie de Hodgkin de l'adulte. Hématologie.