Use of Non-Cryopreserved Hematopoietic Progenitor Cells in Autologous Transplantation for Lymphoma and Multiple Myeloma: A Systematic Review

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Abstract

Objective: To compare the effectiveness and safety of using non-cryopreservation techniques for hematopoietic progenitor precursors versus traditional cryopreservation techniques in the transplantation of autologous derivatives in patients with Lymphoma and Multiple Myeloma.

Methods: The studies that were included for this systematic review were identified by searching databases such as Scopus, Medline/Pubmed and Clinical trials, with no time limit on publication.

Results: A total of 200 published articles were obtained, of which 16 studies met the inclusion criteria.

Conclusions: Autologous transplantation of hematopoietic progenitor precursors without cryopreservation is a feasible and safe alternative to consider especially in institutions with limited resources.

Keywords: Cryopreservation, non-cryopreserved, Lymphoma, Multiple Myeloma.

Resumen

Objetivo: Comparar la efectividad y seguridad del uso de técnicas de no criopreservación de precursores hematopoyéticos frente a las técnicas tradicionales de criopreservación en el trasplante de derivados autólogos en pacientes con linfoma y mieloma múltiple.

Métodos: Los estudios incluidos en esta revisión sistemática se identificaron mediante búsquedas en bases de datos como Scopus, MEDLINE/PubMed y ClinicalTrials, sin límite temporal en la publicación.

Resultados: Se identificaron un total de 200 artículos publicados, de los cuales 16 estudios cumplieron con los criterios de inclusión.

Conclusiones: El trasplante autólogo de precursores hematopoyéticos sin criopreservación es una alternativa factible y segura, especialmente en instituciones con recursos limitados.

Palabras clave: criopreservación, no criopreservación, linfoma, mieloma múltiple

Introduction

One of the most widely used strategies in the treatment of various hematologic diseases is hematopoietic progenitor cell transplantation (1,2). Among the modalities, based on the type of progenitor cell donor, there is autologous transplantation, in which the infused cells come from the patient, and allogeneic transplantation, in which the infused cells come from a compatible donor (3).

The goal of this treatment modality is to eradicate the underlying disease through high-dose chemotherapy ± radiotherapy, followed by the infusion of previously collected hematopoietic progenitor cells (4).

Multiple myeloma is the most common indication for autologous transplantation, being the treatment of choice in newly diagnosed patients without significant comorbidities. In patients with Hodgkin and non-Hodgkin lymphomas, as well as those with germ cell tumors, it is considered a preferred option as salvage therapy in cases of relapse or refractory disease after first-line treatment, or even as consolidation therapy following initial chemotherapy in patients with mantle cell lymphoma and high-grade lymphomas (5,6).

After progenitor cell collection, the cells must be stored while the patient undergoes conditioning therapy (high-dose chemotherapy and/or radio-

therapy). Traditionally, this storage is performed by adding dimethyl sulfoxide to the collected cells and then freezing them at temperatures between –190°C and –80°C (7,8).

Currently, the possibility of storing hematopoietic progenitors without cryopreservation by refrigerating them at a temperature of 4 °C has been studied and evaluated, with the goal of reducing costs, eliminating access barriers, avoiding complex techniques, and minimizing adverse reactions.

The objective of this research is to deepen the understanding of autologous transplantation techniques without cryopreservation, including their history, procedural methods, advantages, and disadvantages compared to standard cryopreservation.

Outcomes have been evaluated in terms of safety, efficacy, cell viability, hematologic recovery, failure rate, adverse effects, and mortality. It has been found that refrigeration of hematopoietic cells at 4 °C for up to six days preserves a sufficient and adequate number of progenitor cells to achieve complete and rapid hematopoietic reconstitution following the administration of myeloablative doses of chemotherapy.

Therefore, autologous transplantation without cryopreservation may serve as a standard alternative in patients with lymphomas and multiple myeloma, provided it is carried out in appropriate centers with the infrastructure and expert medical personnel trained in the management of benign and malignant hemato-oncological disorders, but lacking cryopreservation capabilities. Current studies support its efficacy and safety.

Methodology

A systematic review of the literature was conducted using the following databases: Scopus, MEDLINE/PubMed, and ClinicalTrials. Randomized clinical trials, systematic reviews, prospective and retrospective studies were included, with no publication time limit. Studies involving patients with non-hemato-oncological diseases or those not meeting the predefined inclusion criteria were excluded.

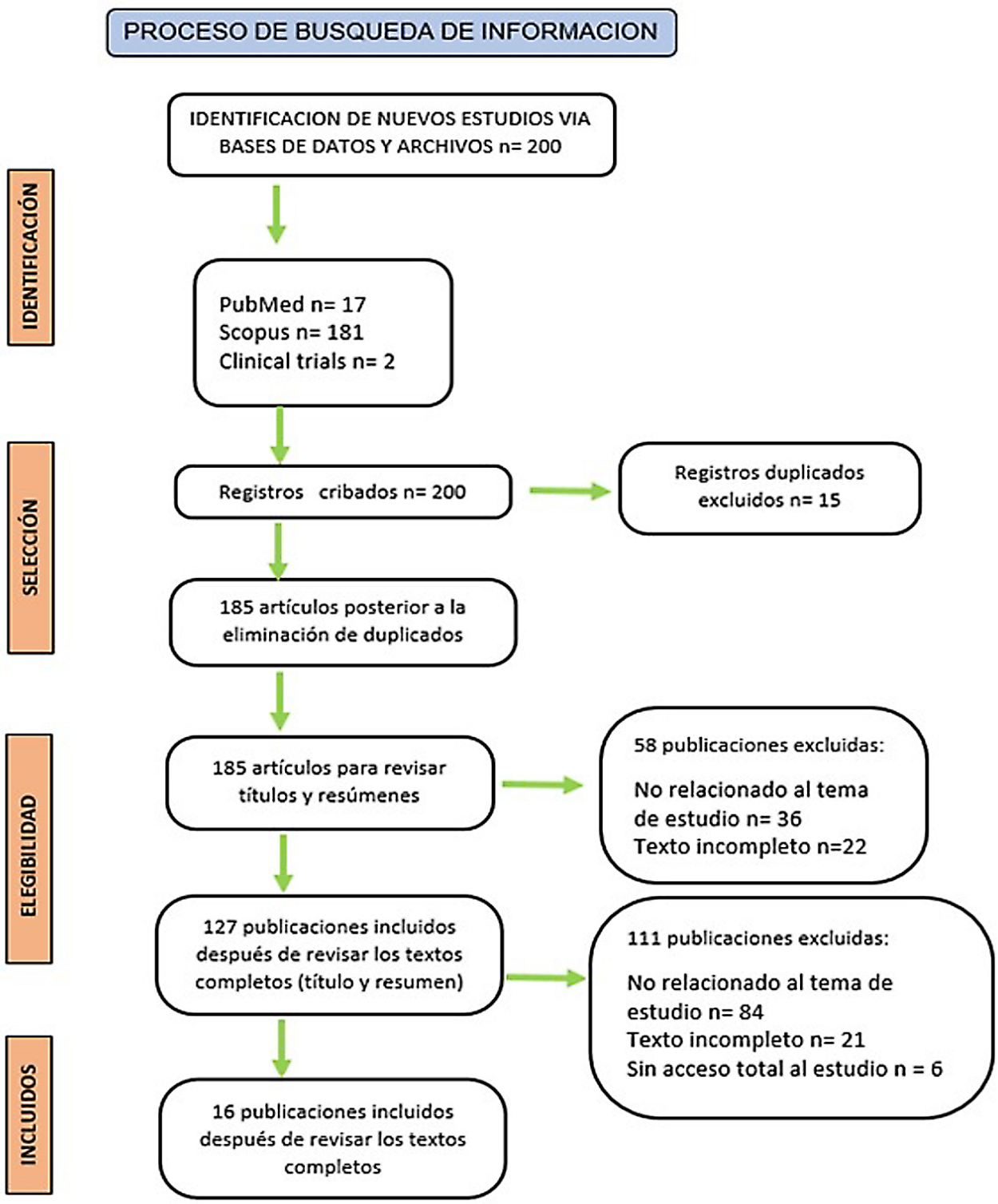
The search equations for PubMed were: exp Lymphoma AND Multiple Myeloma AND #1 OR #2 (for PubMed: #1 OR #2) AND exp Cryopreservation AND bone marrow AND peripheral blood #4 OR #6 AND non-cryopreserved AND noncryopreserved AND non-frozen AND Nonfrozen AND #8 OR #11 OR #3 AND #7 AND #12. For Scopus, the search equation was defined as: Lymphoma OR Multiple Myeloma AND Cryopreservation OR bone marrow OR peripheral blood AND non-cryopreserved OR non-

cryopreserved OR non-frozen OR nonfrozen. In ClinicalTrials, a total of two relevant articles were identified.

A total of 200 published articles were obtained, which were transferred to the Rayyan platform for duplicate evaluation. Fifteen publications were excluded due to duplication, leaving 185 articles to continue the filtering process. Subsequently, 58 articles were excluded for not meeting the inclusion criteria in the title and abstract. During full-text screening, of the 127 remaining articles, 111 publications were excluded. Finally, 16 articles were selected for the systematic literature review.

It is important to note that no randomized clinical trials were found. The selected publications primarily consist of retrospective studies, clinical experience reports, literature reviews, and only one systematic review, which significantly limits the scope of this review (Figure 1).

Figure 1. PRISMA Flow Diagram for Study Selection

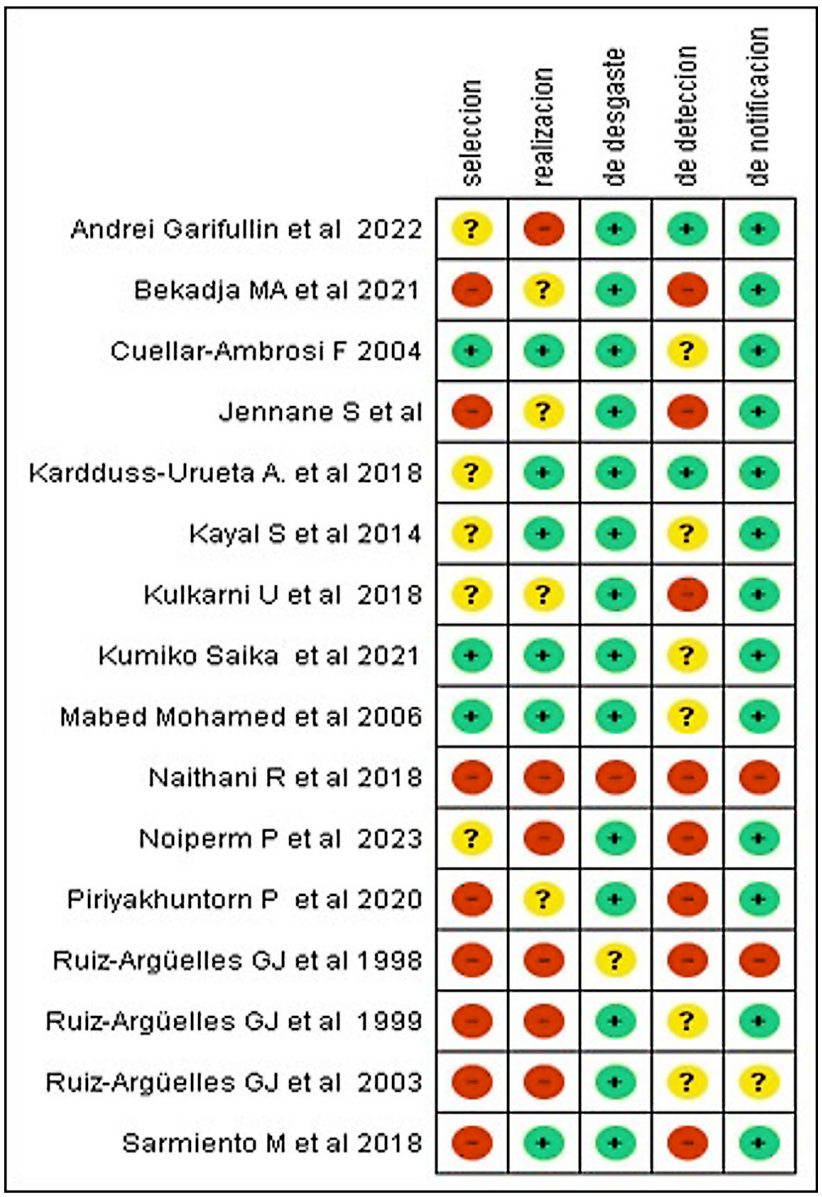


*Own elaboration.

Following the recommendations of the Cochrane Collaboration, a risk of bias assessment was performed for each included study. The articles selected under the PRISMA model (Figure 1) were evaluated using RevMan software. This software, developed by the Cochrane Collaboration, allows for bias analysis based on the following criteria: performance bias, selection bias, detection bias, attrition bias, and reporting bias.

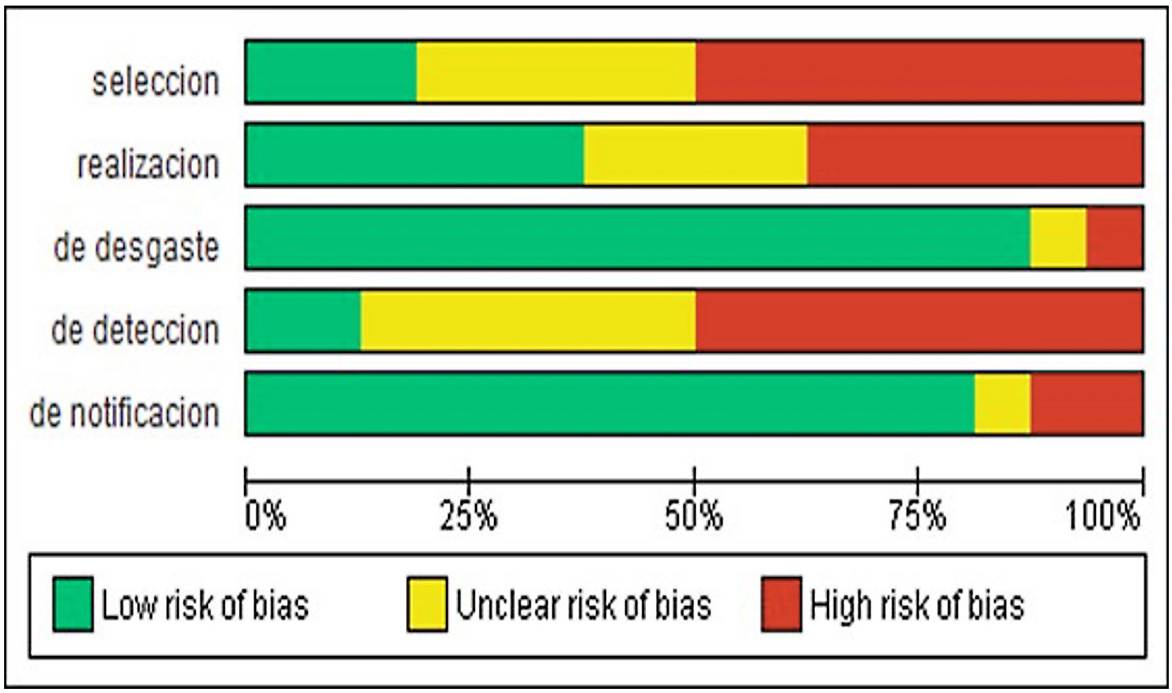
Based on these five criteria, it was determined whether each study had a high, unclear, or low risk of bias. Each article was evaluated by the researchers, who provided a detailed justification for each assigned rating (Figures 2 and 3).

Figure 2. Risk of Bias Assessment



*Own elaboration.

Figure 3. Final Score of the Risk of Bias Assessment



*Own elaboration.

Results

1. Characteristics of the Population in Published Studies:

The target population consists of adults, mostly with multiple myeloma. The average age in the larger studies is not reported, nor is the gender of the participants. In one study, the mean age was not reported, but the population was very specific, including both lymphoma and multiple myeloma patients. It is important to note that the entire studied population is over 30 years of age, which demonstrates the absence of a pediatric population (Table 1).

2. Characteristics of Non-Cryopreserved Storage and Viability Percentage:

The average storage temperature without cryopreservation was 4 °C, defined as optimal. The storage period ranged from 2 to 6 days, without affecting cell viability (1,4).

3. Hospital Stay:

Six publications reported an average of 16.8 days of hospitalization for patients undergoing autologous transplantation without cryopreservation. In one study (9), the hospital stay post-infusion of non-cryopreserved progenitors was longer, with 22 days, compared to another publication (10), where only 10 days of hospitalization were required following progenitor reinfusion.

4. Myeloid and Platelet Engraftment Days by Study Classification:

For Myeloid Engraftment:

- Full sample: Mean of 15.8 days.Dividido por mieloma y linfoma: 10 días para mieloma y 12,5 días para linfoma.
- Divided by myeloma and lymphoma: 10 days for myeloma and 12.5 days for lymphoma.
- Divided by cryopreserved and non-cryopreserved: 16.5 days for cryopreserved and 9.5 days for non-cryopreserved.

For Platelet Engraftment:

- Entire sample: mean of 29.5 days.
- Stratified by myeloma and lymphoma: 11 days for myeloma and 13.5 days for lymphoma.
- Stratified by cryopreserved and non-cryopreserved: 17 days for cryopreserved and 15.5 days for non-cryopreserved.

5. Adverse effects observed after infusion of non-cryopreserved autologous products:

The most common adverse effect was mucositis (grade not specified), followed by febrile neutropenia and, less frequently, gastrointestinal symptoms such as nausea, vomiting, and diarrhea (Table 2). One study reported infections secondary to neutropenia, and another described a case of respiratory failure (13).

6. Mortality and survival associated or not associated with the transplantation of non-cryopreserved autologous products:

Reports on mortality and survival indicate that one study (11) reported 60 deaths within 100 days post-transfusion, while a subsequent publication (11) documented 17 deaths within 30 days post-transfusion, with a survival rate that exceeded mortality among 46 patients. Another study (12) reported 2 deaths within 30 days post-transfusion, while the survival rate was 112 patients. In a separate analysis (9), no deaths associated with the transfusion of non-cryopreserved autologous products were reported; on the contrary,

increased survival was observed. Finally, an additional study (13) reported a transplant-related mortality rate of 2% (Table 3).

The mean of 30-day mortality rate was 2.84% (range: 2–3), as reported in four studies (1,13,17,21). On the other hand, the mean of 100-day mortality rate was 19.41% (range: 2–27).

Table 1. Characteristics of the study populations

STUDY/ REFERENCES	TOTAL SAMPLE (Non-cryopreserved/ Cryopreserved)	MALE/ FEMALE	MEDIAN AGE (Range) Non-cryopreserved/ Cryopreserved	LYMPHOMA/ MYELOMA/. OTHER NON-CRIO/CRIO
Jennane S, 2020 (18)	55.0	31/24	43.0(37-67)	0/55
Naithani R 2018(19)	76.0	44/32	45.0(14-68)	17/59
Sarmiento M 2018(4)	116.0 (42/74)	64/52	52(22-68) // 55(22-69)	9/29/2 40/26/2
Bekadja M. 2016(1)	94.0	0.00	29(25-34)	94/0.0
Noiperm P. 2023(12)	58.0	32/26	57(17-73)	18/40
Ruiz-Argüelles G.(21) 2023	46.0	27/19	33 (8-69)	10/7/29
Piriyakhuntorn P(10) 2020	42.0 (26/16)	11/31	55.7 / 54.9	42/0.0
Ruiz-Argüelles G.J 1998(11)	6.0	2/4	27(9-33)	0.0/0.0/6.0
Kulkarni U 2018 (20)	224	156/68	23-68	0.0/224
Ruiz-Argüelles G.J 1999(21)	29.0	14/15	30.0(9-67)	9/1/19
Ramzi M. 2012(9)	38.0	12/26	50.6 (31-70)	0.0/38/
Kardduss-Urueta A et al 2018 (15)	216	N.R	(29-75)	86/123
Kayal S. et al 2014 (16)	92	61/31	(22-65)	0/92
Cuellar-Ambrosi et al 2004 (24)	47	N.R	(12-67)	21/10/16
Voloshin S.V. Et al 2022 (14)	78 (35/43)	42/36	57(42-72) 57(39-72)	0/35/ 0/43
Mohamed Mabe et al 2006 (25)	28	19/9	30(16-50)	19/0.0

*Non-cryopreserved (Non-CRYO): Autologous transplant with refrigerated, non-cryopreserved progenitor cells.

Cryopreserved (CRYO): Autologous transplant with previously cryopreserved progenitor cells.

*Own elaboration.

Table 2. Adverse Events Associated with Transplantation

STUDY/ REFERENCES	Total Sample Non Crio/Crio	Non Crio/Crio	Mucositis Non Crio/Crio	Febrile Neutropenia	Total Adverse Effects
SAMPLE	55.0	55/0	20.0(36%)	38(69%)	100%
NON CRIO/CRIO	NON CRIO/ CRIO	MUCOSITIS	76	75	100%
NON CRIO/ CRIO	FEBRILE NEUTROPENIA	TOTAL ADVERSE EFfECTS	4(11%) 48(65%)	17(14%) 69(70%)	100%
Bekadja M. 2016(1)	545 94/352	94/351	N.R	N.R	N.R
Noiperm P. 2023(12)	58.0	58/0	26(65%MIELOMA 15(83%) LINFOMA	38(95%) MIELOMA 17 (94.%) LINFOMA	100%
Ruiz-Argüelles G. 2023(21)	46.0	46/0	N.R	N.R	N.R
Piriyakhuntorn P2020 20)	42.0 26/16	26/16	N.R	26/16	100%/ 100%
Ruiz-Argüelles G.J 1998(11)	6.0	6/0.00	N.R	N.R	N.R
Kulkarni U 2018 (20)	224.0	224/0	N.R (23 CULTIVOS POSITIVOS)	N.R	N.R
Ruiz-Argüelles G.J 1999(21)	29.0	29/0	9.00		N.R
Ramzi M. 2012(9)	38.0	38/0	22.0 (57.8%)	23.0 (60.5%)	100%
Kardduss-Urueta A et al 2018 (15)	216	216/0	N.R	N.R	N.R
Kayal S. et al 2014 (16)	92	92/0	66(71.75%)	91(99%)	100%
Cuellar-Ambrosi et al 2004 (24)	47	47/0	N.R	N.R	N.R
Voloshin S.V. Et al 2022 (14)	78	35/43	15(42%)20(46%)	13(37%) 21(49)	100%
Mohamed Mabe et al 2006 (25)	28	38/0	N.R	N.R	N.R

* Non-cryopreserved (Non-CRYO): Autologous transplant with refrigerated, non-cryopreserved progenitor cells.Cryopreserved (CRYO): Autologous transplant with previously cryopreserved progenitor cells. N.R.: Not Reported

*Own elaboration.

Table 3. Day of Graft, Survival, and Mortality Associated with Transplantation

STUDY/ REFERENCES	Total Sample	Non Crio/Crio	MRT # (%) Non Crio/Crio	Myeloid Graft Non Crio/Crio	Plaquetinggraft7 Non Crio/Crio
Jennane S, 2020 (18)	55.0	55/0	2(3.6%)	12.0	14.0
Naithani R 2018(19)	76.0	76/0	3(3.9%)	11.0	11.0
Sarmiento M 2018(4)	116.0//42/74	42/74	1(2%) / 0	9/ 12	11/ 14
Bekadja M. 2016(1)	94/351	94/351	(9%) / (7%)	14/ 10	17 / 13
Noiperm P. 2023(12)	58.0	58/0	1(1.7%)	11	11
Ruiz-Argüelles G. 2023(21)	46.0	46/0	1(2%)	14	24
Piriyakhuntorn P2020 (10)	42.0//26/16	26/16	1(2,3%) / 0	12/10.5	14 / 12
Ruiz-Argüelles G.J 1998(11)	6.0	6.00	0.00	21	38
Kulkarni U 2018 (20)	224.0	224/0	7(3.1%)	12	17
Ruiz-Argüelles G.J 1999(21)	29.0	29/0	1.00(3.34%	14.0	20.0
Ramzi M. 2012(9)	38.0	38/0	0	11	13
Kardduss-Urueta A et al 2018 (15)	216	216/0	3(1.4%)	14	16
Kayal S. et al 2014 (16)	92	92/0	3(3.2%)	10	14
Cuellar-Ambrosi et al 2004 (24)	47	47/0	6(12.7%)	11/ 13/ 11	16/15/14
Voloshin S.V. Et al 2022 (14)	78	35/43	0.0	11/ 20(CRIO)	12/ 21(CRIO)
Mohamed Mabe et al 2006 (25)	28	28/0	2	13.0	15.0

*Non-cryopreserved (Non-CRYO): Autologous transplant with refrigerated, non-cryopreserved progenitor cells.Cryopreserved (CRYO): Autologous transplant with previously cryopreserved progenitor cells. N.R.: Not Reported, N.A.: Not Applicable, MRT #(%): Mortality.

*Own elaboration.

Discussion

Despite the positive data reported, it is important to highlight that in this systemic review no randomized clinical trials were found that compared autologous hematopoietic progenitor cell preservation methods—cryopreserved vs. non-cryopreserved. Additionally, a greater number of articles were excluded compared to the one that could be included.

The documented mean viability of non-cryopreserved products ranges from 85% to 96%, while that of cryopreserved products ranges from 93.5% to 95%. However, many studies did not report viability data. Although some studies indicated a high viability percentage, even exceeding that observed with traditional cryopreservation techniques (4), most cases had limitations in data accessibility. Furthermore, the vast majority of studies did not compare both techniques but were limited to reporting case experiences where cryopreservation was not employed. This highlights the lack of data, which introduces a certain degree of information bias, potentially leading to unreliable results.

Most of the included studies were retrospective, though some were prospective with preselected samples, where no randomization process was conducted for intervention assignment. Additionally, in many cases, the application of blinding to both participants and investigators concerning the intervention of interest remains unclear.

Among the positive aspects, the low risk of bias in reporting final outcomes and attrition bias stands out, as more than 70% of the publications indicated that the sample population was not affected by dropout, and the results were presented in full.

Transplant-related mortality, length of hospital stay, hematologic reconstitution, adverse events, and graft failure were similar across the analyzed groups. Additionally, costs were lower in procedures without cryopreservation. However, further studies are needed to corroborate these findings.

Conclusions

Autologous hematopoietic progenitor cell transplantation without cryopreservation is a feasible and safe alternative, particularly in institutions with limited resources.

The studies analyzed reported positive outcomes regarding viability, time to hematologic reconstitution, adverse events, length of hospital stay, and early mortality.

The ideal storage temperature is 4 °C, allowing for the preservation of progenitor cells for up to 6 days while maintaining an average viability of no less than 90%. The average time to hematologic recovery is comparable to that observed with cryopreserved products. In one study, this recovery time was even shorter (14); however, other studies reported longer hematologic recovery periods (1, 4, 10). Notably, despite the prolonged recovery time, the length of hospital stay was shorter in studies that used non-cryopreserved progenitors (4, 10).

The most frequent adverse events following infusion were mucositis and febrile neutropenia. No evidence was found linking the incidence of adverse events to any specific method of progenitor cell storage. Transplant-related mortality was similar in both groups and significantly lower in the more recent studies.

In conclusion, short-term storage of autologous hematopoietic progenitor cells at 4 °C is a safe and effective practice. This method achieves hematologic reconstitution within the average timeframe observed in patients receiving cryopreserved progenitors. In contrast, the costs associated with refrigeration are significantly lower than those of cryopreservation. Furthermore, avoiding cryopreservation eliminates potential complications and toxic effects related to the administration of dimethyl sulfoxide during reinfusion. It also reduces economic costs related to the cryopreservation, freezing, storage, and thawing of progenitor cells.

This technique represents a viable alternative for centers with limited financial resources that lack the infrastructure for cryopreservation but have trained personnel and the necessary facilities to manage hemato-oncologic diseases and their complications. This could significantly improve access to this therapy for a larger number of patients.

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References

1. 1.Bekadja MA, Boumendil A, Blaise D. Non-cryopreserved hematopoietic stem cells in autograft patients with lymphoma: A matched-pair analysis comparing a single center experience with the use of cryopreserved stem cells reported to the European Society for Blood and Marrow Transplantation registry. Cytotherapy 2021;23(6):483-7.
2. 2.Mahajan S, Tandon N, Kumar S. The evolution of stem-cell transplantation in multiple myeloma. Ther Adv Hematol 2018;9(5):123-33.

3. 3.Gaytán F. Trasplante de células progenitoras hematopoyéticas en pediatría. Gac Mex Oncol 2013;12(3):174-81.

4. 4.Sarmiento M, Ramírez P, Parody R, Salas MQ, Beffermann N, Jara V, et al. Advantages of non-cryopreserved autologous hematopoietic stem cell transplantation against a cryopreserved strategy. Bone Marrow Transplant 2018;53:960-6.

5. 5.Philip T, Armitage JO, Spitzer G, et al. High-dose therapy and autologous bone marrow transplantation after failure of conventional chemotherapy in adults with intermediate-grade or high-grade non-Hodgkin's lymphoma. N Engl J Med 1987;316:1493-8.

6. 6.Philip T, Guglielmi C, Hagenbeek A, et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med 1995;333:1540-5.

7. 7.Reich-Slotky R, Vasovic LV, Land KJ, Halpenny M, Woeltz J, Mathew AJ, et al. Cryopreserved hematopoietic stem/progenitor cells stability program-development, current status and recommendations: A brief report from the AABB-ISCT joint working group cellular therapy product stability project team. Transfusion 2022;62(3):651-62.

8. 8.Hahn S, Sireis W, Hourfar K, et al. Effects of storage temperature on hematopoietic stability and microbial safety of BM aspirates. Bone Marrow Transplant 2014;49(3):338-48.

9. 9.Ramzi M, Zakerinia M, Nourani H, Dehghani M, Vojdani R, Haghighinejad H. Non-cryopreserved hematopoietic stem cell transplantation in multiple myeloma: A single center experience. Clin Transplant 2012;26:117-22.

10. 10. Piriyakhuntorn P, Tantiworawit A, Rattanathammethee T, Hantrakool S, Chai-Adisaksopha C, Rattarittamrong E, et al. Outcomes of non-cryopreserved versus cryopreserved peripheral blood stem cells for autologous stem cell transplantation in multiple myeloma. Ann Transplant 2020;25:e927084.

11. Ruiz-Argüelles GJ, Ruiz-Argüelles A, Pérez-Romano B, Marín-López A, Delgado-Lamas JL. Non-cryopreserved peripheral blood stem cells autotransplants for hematological malignancies can be performed entirely on an outpatient basis. Am J Hematol. 1998 Jul;58(3):161-4.

12. Noiperm P, Julamanee J, Viboonjuntra P, Lekhakula A. Non-cryopreserved peripheral blood stem cell graft for autologous hematopoietic stem cell transplantation in multiple myeloma and lymphoma patients. Ann Transplant. 2023 Jan 17;28:e938595.

13. Ruiz-Argüelles GJ, Gómez-Rangel D, Ruiz-Delgado GJ, Ruiz-Argüelles A, Pérez-Romano B, Rivadeneyra L. Results of an autologous noncryopreserved, unmanipulated peripheral blood hematopoietic stem cell transplant program: a single-institution, 10-year experience. Acta Haematol. 2023;110(4):179-83.

14. Voloshin SV, Garifullin AD, Kuzyaeva AA, Sinitsina NN, Alekseeva NN, Schmidt AV, Linnikov SY, Shuvaev VA, Kuvshinov AY, Potikhonova NA, Seltser AV, Balashova VA, Chubukina ZV, Bogdanov AN, Sidorkevich SV. The use of non-cryopreserved hematopoietic stem cells for autologous transplantation in multiple myeloma patients. Oncohematology. 2022;17(2):82-94. (In Russ.)

15. Kardduss-Urueta A, Gale RP, Gutierrez-Aguirre CH, Herrera-Rojas MA, Murrieta-Álvarez I, Perez-Fontalvo R, et al. Freezing the graft is not necessary for autotransplants for plasma cell myeloma and lymphomas. Bone Marrow Transplant. 2018.

16. Kayal S, Sharma A, Iqbal S, Tejomurtula T, Cyriac SL, Raina V. High dose chemotherapy and autologous stem cell transplantation in multiple myeloma: a single institution experience at All India Institute of Medical Sciences, New Delhi, using non-cryopreserved peripheral blood stem cells. Clin Lymphoma Myeloma Leuk. 2014;14:140-7.

17. Saika K, Gatellier L. Age-specific lymphoma incidence rate in the world. Jpn J Clin Oncol. 2021;51(10):1599-1600.

18. Jennane S, Hasnaoui N, Mahtat EM, Merimi F, Bougar S, El Maaroufi H, Belmekki A, Zafad S, Essakalli M, Mikdame M, Doghmi K. Non-cryopreserved peripheral blood stem cells autologous transplantation in multiple myeloma: bicentric study. Transfus Clin Biol. 2020 Aug;27(3):152-6.

19. Naithani R, Dayal N, Pathak S, Rai R. Hematopoietic stem cell transplantation using non-cryopreserved peripheral blood stem cells graft is effective in multiple myeloma and lymphoma. Bone Marrow Transplant. 2018 Sep;53(9):1198-1200.

20. Kulkarni U, Devasia AJ, Korula A, Fouzia NA, Nisham PN, Samoon YJ, Lakshmi KM, Abraham A, Srivastava A, Mathews V, George B. Use of non-cryopreserved peripheral blood stem cells is associated with adequate engraftment in patients with multiple myeloma undergoing an autologous transplant. Biol Blood Marrow Transplant. 2018 Dec;24(12):e31-e5.

21. Ruiz-Argüelles GJ, Lobato-Mendizábal E, Ruiz-Argüelles A, Pérez-Romano B, Arizpe-Bravo D, Marín-López A. Non-cryopreserved unmanipulated hematopoietic peripheral blood stem cell autotransplant program: long-term results. Arch Med Res. 1999 Sep-Oct;30(5):380-4.

22. Curado MP, Oliveira MM, Silva DR, Souza DLB. Epidemiology of multiple myeloma in 17 Latin American countries: an update. Cancer Med. 2018;7(5):2101-8.

23. Cuellar-Ambrosi F, Karduss UA, Gomez WR, et al. Hematologic reconstitution following high-dose and supralethal chemoradiotherapy using stored, noncryopreserved autologous hematopoietic stem cells. Transplant Proc. 2004;36:1704-5.

24. Mabed M, Shamaa S. High-dose chemotherapy plus non-cryopreserved autologous peripheral blood stem cell transplantation rescue for patients with refractory or relapsed Hodgkin disease. Biol Blood Marrow Transplant. 2006;12:942-8.4o mini