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Autologous cord blood harvesting in North Eastern Italy: ethical questions and emerging hopes for curing diabetes and celiac disease

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Background: The Friuli Venezia Giulia (FVG), a region of North Eastern Italy, has passed legislation (Decree No 2324/2010) to regulate the banking of umbilical cord blood samples for personal, autologous, or family-directed use, and to implement the Agreement of the State-Regions Permanent Conference (Decree No 62/CSR/2010). This paper aims to identify the formalities and the reasons why families collect and bank their cord blood in foreign banks for both personal and private use.

Methods: To this end, at the Institute for Maternal and Child Health of Trieste (the regional capital city of the FVG), Italy, which assists about 1800 pregnant women a year, 129 questionnaires, drafted from January 2010 to December 2011 and concerning the granting of authorization to export samples, were examined.

Results: The collected data showed that 75% of involved families had resorted to anonymous public collection, which is available to anyone with therapeutic needs, and provided compatibility and hematologic protocols recognized by the scientific and international community (main indications: leukemia, hemoglobinopaties, and inherited hematologic and immunologic disorders). Conversely, 25.0% requested private storage at a foreign bank for personal or family-dedicated use. The principal motivation by disease was for treatment for diabetes (22.4%) and celiac disease (19.7%) (a multiorgan disease for which the FVG region has provided safeguards by approving a specific law granting support to families; Decree No 561/2007). For these two types of disease we found that information was received from the internet and not from general medical physicians, with a significant difference found using the χ^2 test ($P < 0.01$).

Conclusion: The indication of treating these diseases with cord blood stem cell transplantation appears to be well grounded and encouraging, and has recently been corroborated by the international literature; however, the economic and social motivations promoting cord blood storage, for a fee, in the event of diseases that are still under study, require accurate information through general medical physicians on the actual possibilities of treatment.

Keywords: autologous cord blood harvesting, North Eastern Italy, emerging hopes of therapy

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Introduction

Ever since the first cord blood stem cell (CB-SC) transplantation,[1] placental blood collection has been playing a major role as a source of hematopoietic SCs, acquiring fundamental importance in clinical practice.[1–6] The evidence that the SCs contained in the CB-SCs could offer, at least in children, a viable alternative to bone marrow transplantation from a donor's bone marrow blood, which until then was used in allogeneic bone marrow transplants, opened new therapeutic prospects. This led to the

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creation, throughout Europe, of public banks for the cryopreservation of CB-SC bags from homologous donations for allogeneic use. With the possibility of generating neural, pancreatic, and cardiac tissues from human progenitor cells, and the in vitro differentiation of the derived multipotent cells, the problem of collecting and storing at a private bank the CB-SCs from homologous donation for autologous or family-dedicated use is now being proposed.[7–9] Allogeneic use is now consolidated and documented by the international scientific literature; however, the scientific literature regarding collection for autologous use has not been documented to the same extent.[10–12]

New therapies for celiac disease, diabetes, cystic fibrosis, and other pathologies

Autologous SC transplantation is also becoming an increasingly interesting and effective therapeutic option for autoimmune diseases such as refractory celiac disease, which affects a small proporation (2%–5%) of patients with a celiac disease diagnosis who continue to present with bowel lesions despite a gluten-free diet.[13] The rationale that is frequently offered in favor of placental blood storage programs consists of the hypothesis that, in the future, therapeutic programs will be developed for tissue repair (eg, heart, nervous system, and liver). Thus, patients who have their own SCs available will have greater chances of recovery than patients who have not preserved them, even in many years' time.[14]

SC transplantation is also a subject of study for the cure of type 1 diabetes (T1D), a disease affecting 3% of the population in Italy. In this field, to avoid risks of rejection, it is advisable to use adult autologous SCs harvested from the patient himself/herself.[15] However, this therapy is not likely to be effective for long-term treatment of T1D, and recent studies suggest that alternative approaches using human CB-SCs and mesenchymal stem cells have been shown to modulate immune activity in vitro.[16–18] These initial results indicate that CB-SCs may have important implications for other autoimmune, neurologic, and inflammation-related diseases.[19–21]

The absence of confirmed scientific data and medical trials confirming the possibility of specific therapies for diabetes mellitus and celiac disease, including the transplantation of autologous CB-SCs, and the lack of evidence supporting the integrity and function of cord cells after decades have not stopped the growing storage requests. The recent nuclear disaster of Fukushima, Japan, has influenced the public even more and increased private autologous collection for future therapies with CB-CSs.[22]

The Italian legislation

In Italy, CB-SC storage is exclusively allowed at authorized public facilities (about 15 of them are scattered across the country) and is envisaged either for solidarity purposes (ie, for any patient requiring it, without any discrimination) or for an ad hoc use (donation targeted at a family member affected by a disease and requiring a transplant, and in the case of families at high risk of genetic diseases that are curable by hematopoietic SC transplantation). However, CB-SC storage for autologous use reserved for the donor (who is healthy at the time of birth and is highly likely never to need his/her cord blood) is not allowed. The Italian legislation explicitly forbids private facilities not only to store CB but also to advertise and promote such an activity (ordinance by the Ministry of Health on February 26, 2009).

The ordinance, however, allows women who want to preserve their CB for their child to do so, for a fee, at accredited foreign banks, subject to a previous authorization by the Ministry of Health. In compliance with the Italian national legislation, the Friuli Venezia Giulia (FVG) region of North Eastern Italy has regulated CB-SC collection, transport, and storage. It has identified the Institute for Maternal and Child Health of Trieste (the regional capital city) as the center responsible for the regional public collection program, and the Cord Blood Bank of Padua (a city located in the neighbouring Veneto region) as the storage center, by means of an operational transport protocol entrusted to the civil protection volunteers. Furthermore, the FVG region has entrusted the health care boards of birth centers with the responsibility of granting authorization for the banking of CB-SCs in foreign states for private use, by establishing a fee to cover collection costs (€300) to be added to the approximately €2000 a year charged by the foreign bank (Decree No 2324/2010).

Aim

Therapies for autoimmune diseases such as diabetes and celiac disease are still under study and often create false expectations as they still require further scientific evidence.

The aim of this paper is to evaluate the questionnaires submitted to the health care board of the Institute for Maternal and Child Health of Trieste, for the private collection of CB-SCs during the 2010–2011 period, to identify the formalities and the reasons why families collect and bank their cord blood in foreign banks, for both personal and private use, and in order to study and prepare for an update meeting with the general practitioners (GPs) and specialist physicians of the FVG region on the actual possibilities of treatment with autologous CB-SCs and the information that the mass media give to pregnant women regarding the storage and therapeutic use of CB-SCs.

Patients and methods

Approximately 1800 deliveries take place at the Institute for Maternal and Child Health every year. In the years 2010–2011, 386 applications were submitted for collection and storage at a public CB-SC bank and 129 applications for private collection. Of these 129, the examined questionnaires, which had been approved by the bioethical committee of the institute, were filled out during the interview with the health care board physician for the granting of authorization to export to a foreign bank. The interview was confidential and took place after confirmation tests were performed and information on the pregnancy provided, as requested by the general medical physician (GM). In addition to including the regulations for CB-SC collection and storage issued by the FVG region, the questionnaire specified the bank where samples were to be sent, the collection and storage methods certified according to the European Community regulations, as well as the possibility of noncollection in the event of premature births or bacterial contamination, the date of the delivery, manner of transport, country of destination, and presence of genetically determined disease in the family (Figure 1).[31] Once both parents had given their consent and the required certifications (sent to the family by the foreign bank where the deposit was to be made), the health care board physician issued the authorization and thoroughly explained the possible therapies, for final approval by both parents. Every 6 months, data were collected and sent to the central health directorate of the FVG region and the Ministry of Health. The data and the information about the two pathologies (diabetes and cystic fibrosis) were studied with a χ^2 test to determine whether the two groups had significant differences of information source (internet or GM) and were applied to cross-tabulations.

Results

From January 2011 to December 2012, a total of 3650 deliveries took place at the Institute for Maternal and Child Health. A total of 25.0% of these mothers did not choose public, anonymous collection for solidarity and therapeutic purposes, which is approved by the European regulations, but instead chose private use. In total, 129 families (two of which were from neighboring countries, Slovenia and Austria) applied for private collection at a foreign nonpublic bank (Table 1). The most frequent motivations concerned the general possibility of storage for personal use (84), excluding donations to subjects outside the family without particular therapeutic needs. Information and news on CB-SC collection had been supplied by the internet (78.29%) or by gynecologists (5.42%), nurses (3.87%), friends and family members (2.32%), hematologists (0.77%), volunteer associations (0.77%), or the media (0.77%). Only ten pregnant women (7.75%) had received information from their GPs on

1. *The donation of umbilical cord blood cells is on a voluntary basis and the public collection is available for who ever needs transplantation. Did the general medical physician inform you about the possibility of the donation of the umbilical cord blood cells?*
   YES ☐ NO ☐
2. *Does she/he know the existence of a network of public banks, in Italy for patients who need cord blood cells transplantation?* YES ☐ NO☐
3. *By which way or modality of information has she/he been informed about the possibility of preserving cord blood cells for autologous use?*
   INTERNET☐ PARENT-FRIEND ☐ NURSE ☐ GYNECOLOGIST ☐
   MEDICAL JOURNAL ☐ GENERAL MEDICAL PHYSICIAN ☐ OTHER ☐
4. *Why does he/she choose the autologous preservation in order to send to a foreign private bank?*
   ....
5. *Does she/he know the motivations which did not allow the harvesting due to medical problems?*
   ….….……………………………………………...
6. *Date of delivery*………………………………………
7. *Manner of transport*…………………………………
8. *Country of destination*……………………………..
9. *Presence of genetically determined disease in family*…………………………………………..

Figure 1 Private family questionnaire (translated).

Table 1 Foreign country of autologous cord blood destination

Foreign country	Total number	%
Switzerland	38	29.4
Germany	30	23.2
England	28	21.7
St Marino Republic	25	3.1
Poland	4	2.3
Slovakia	3	2.3
Belgium	1	0.8

Table 3 Motivation for request for pathology

Pathology	Total number	%
Diabetes	29	22.4
Celiac disease	25	19.3
Cystic fibrosis	23	17.8
Alzheimer's disease	22	17.0
Cardiovascular disease	11	8.5
Hematology disease	10	7.7
Other	9	6.9

the possibility of collecting CB-SCs, and of these everybody had forgotten private collection to opt for public collection (Table 2). Among the prevailing motivations was the hope of curing diabetes (22.4%) and celiac disease (19.3%) (a multiorgan disease for which the FVG region has provided safeguards by approving specific legislation to support families [Decree No 561/2007]), then cystic fibrosis (17.8%), Alzheimer's disease (17.0%), cardiovascular diseases (2.0%), and other pathologies. For the first two groups of diseases, information was supplied by the internet and not by GPs ($P < 0.01$) (Table 3).

Families who during pregnancy had turned to their GPs stated that they were not given precise and thorough information on the existence of transplantation therapies for diabetic and other diseases; some families had asked, without obtaining it, for information on the therapies for celiac disease by which they were affected. This condition excluded them from public collection by law. The results show that GMs did not inform families about autologous CB harvesting and the therapeutic hematologic applications. The families did not receive information about the possibility of cure in future pathologies not yet included in the common international protocols. The answers were described as evasive and incomplete, and ranged from a concrete possibility of therapy to exclusion. Information obtained from the internet was prevalent. That happens because these issues are more often described than others and marketing is prevalent by private banks. The importance and the relevant social cost of curing severe autoimmunity pathologies, such as refractory Crohn's disease, include medical support about pharmaceutical treatment and actual therapies.[32]

Table 2 Type of information

Source	Total number	%
General medical physician*	10	7.76
Gynecologist physician	7	5.43
Nurses	5	3.88
Parents/friends	3	2.33
Voluntary associations	1	0.77
Hematology physician	1	0.77
TV, journals, magazines, media	1	0.77
Internet*	101	78.29

Note: *P-value < 0.01.

Conclusion

In Italy, public collection allows "… storage for an ad hoc use, for newborns affected by a disease at the time of collection or previously, for which the use of cord blood stem cells is scientifically grounded and clinically appropriate … it is also allowed for an ad hoc use in the case of families at risk of having children affected by genetically determined diseases … and/or … also within the framework of clinical experimentations approved according to the existing legislation."[37] In these cases, samples are stored in public banks at the expense of the regional health care service.

In addition to this law, the possibility of preserving a sample for autologous use is currently allowed only at private facilities abroad, subject to authorization by the region of origin (ordinance of the Ministry of Health on February 26, 2009).

Around the world, the number of placental samples stored at private banks and for personal (autologous) use is three times larger than that of samples donated for public use.[23] These procedures subvert the concept of a solidarity use for the collection of blood and its components, including SCs, and can considerably damage it. However, the psychological pressure exerted by the media on the radiation damage caused by the recent Japanese tsunami and the possibility of bone marrow and SC transplantation develops an emotional tension that is reminiscent of other nuclear tragedies, such as Hiroshima, Nagasaki, and, more recently, Chernobyl. Emotion, fear, and selfishness often prevail over the reasonableness of correct information and "counselling" to future parents, and families request the donation for autologous use in the hope of taking advantage, in the future, of treatments to cure diseases such as T1D, celiac disease, and other degenerative diseases with a high social impact, which have not yet been confirmed by clinical trials but only by experimental data.

Discussion

GM and specialist physicians are called to deal with this topic with the awareness of being the first suppliers of information for the collection of CB-SCs, according to the program introduced by the FVG region and to specific international clinical protocols to treat leukemia, hemoglobinopaties, and immunologic disorders. Furthermore, international literature draws attention to the difficulties of autologous CB transplant in particular situations. For example, genetic alteration, already present in CB cells, makes CB use unsuitable for leukemia caused by chromosomal abnormalities; in the case of an autologous transplant, there is no beneficial "graft versus host leukemia" effect.[24] With regard to public cord collection, the probability for donors to find, in case of need, their own placental blood units still available exceeds 97%.[25,26] Furthermore, private collection discriminates between families who can afford it and families who cannot, thereby causing great damage to the cryopreservation of samples at public banks that are available to anyone needing them.[27–29] The donations for private use do not always meet the same criteria of public storage (ie, number of cells, human T-cell lymphotropic virus type III). These differences among CB-CS units can lead to confusion about the curable pathologies by CB-CS disease.

The inclusion of placental blood collection into a specific program introduced by the National Health Service is of fundamental importance for future developments in this sector. The authors think the discussion should not be about banning private initiative to the advantage of State monopolies but about being able to get sufficient and effective means to treat future patients. This can be done successfully only through public–private collaboration.[30] This shows the added value of storage for potential use within the family, ie, for autologous and related allogeneic uses.[33–36] To GMs goes the task of first providing the correct information on ethical themes and therapeutic possibilities, which are often incorrect and inappropriate, advertised by the media, often for money-making purposes, and without real evidence of confirmed efficacy.

Disclosure

The authors report no conflicts of interest in this work.

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