

# Interfering factors of blood quality of the umbilical cord/ placental for autologous transplantation: integrative review

## *Fatores interferentes da qualidade do sangue de cordão umbilical/ placentário para transplante autólogo: revisão integrativa*

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### RESUMO

Esse estudo tem como objeto os fatores que podem influenciar na qualidade do SCUP e como objetivo apontá-los e defini-los, seguidos da análise de boas práticas na coleta de SCUP, sintetizando, em seguida, informações acerca de boas práticas de coleta. Metodologia: Trata-se de uma revisão integrativa, norteadas pela metodologia PICO. As buscas foram realizadas no Portal da BVS e foram selecionados 15 artigos que abordam a temática. Resultados: Os autores apontam para a associação entre o maior volume de SCUP coletado e o maior número de células nucleadas totais obtidas. O volume da coleta pode ser influenciado pelo peso da placenta, via de parto, tamanho do cordão umbilical, peso e idade gestacional do RN, e também está associado a fatores operacionais, como manuseio incorreto da placenta e cordão umbilical. O número de células nucleadas totais também está associado ao intervalo entre coleta e processamento, via de parto e à temperatura de armazenamento durante o transporte. Conclusão: Para obter-se uma coleta de qualidade, deve-se coletar o maior volume possível, reduzir o intervalo entre coleta e processamento e observar as boas práticas de coleta. O aperfeiçoamento da técnica de coleta pode ser obtido através de um programa de capacitação contínua dos coletadores.

**Descritores:** sangue de cordão umbilical, protocolo clínico, coletadores, qualidade

### ABSTRACT

This study has as object the factors that can influence the quality of the SCUP and aim to identify and define them, followed by the analysis of good practices in the collection of SCUP, then synthesizing information about good practices of collection. Methodology: This is an integrative review, guided by the PICO methodology. The searches were carried out in the VHL Portal and 15 articles were selected that address the subject. Results: The authors point to the association between the highest volume of SCUP collected and the highest number of total nucleated cells obtained. The volume of the collection can be influenced by the weight of the placenta, tract of delivery, umbilical cord size, weight and gestational age of the newborn, and is also associated with operational factors such as incorrect placenta and umbilical cord management. The number of total nucleated cells is also associated with the interval between collection and processing, delivery route and storage temperature during transport. Conclusion: In order to obtain a quality collection, one must collect as much volume as possible, interval between collection and processing and observing good collection practices. The improvement of the collection technique can be obtained through a continuous training program of the collectors.

**Descriptors:** umbilical cord blood, clinical protocol, collectors, quality

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## INTRODUCTION

Embryonic stem cells (ES) have the potential to proliferate indefinitely in culture and can differentiate into any cell type<sup>(1)</sup>. They are able to promote hematopoietic reconstitution and other tissues, being present in the peripheral blood, bone marrow<sup>(2)</sup>, embryonic liver parenchyma<sup>(3)</sup> and cord blood<sup>(4)</sup>.

In 1988, studies with human samples<sup>(5,6)</sup> showed that the Umbilical Cord and Placental Blood (SCUP) has a higher proportion of cells producing immature colonies and progenitors of primitive erythrocytes, when compared to bone marrow, for example. The application of this product was started in therapies to restore the function of hematopoietic stem cells in patients affected by malignant neoplasms and other disorders.

In addition, other studies have been carried out with derivatives of SCUP, such as the Stem Cell Therapy (Stem Cell Educator) method, where a small amount of blood is collected from the patient, passing through a closed circuit, which separates blood cells, exposes the patient's lymphocytes to CB-SC - multipotent stem cells derived from SCUP, promoting their "training" and then returning them to the patient's bloodstream. This type of treatment allows long-term reversal of autoimmunity<sup>(7)</sup>, improvement of metabolic control in individuals with type I diabetes<sup>(8)</sup>, among others.

For autologous transplantation, SCUP should be collected at the time of birth of the baby through puncture of the umbilical cord and placenta, being placed in a reservoir suitable for transport to the Umbilical Cord Blood Bank laboratory, where it will be processed until it is obtained the final product for storage<sup>(9)</sup>.

From the moment of collection to the processing of SCUP, there are several factors that can influence the quality of the same, being the physical factors (such as temperature)<sup>(10)</sup>, obstetric (such as placenta and umbilical cord characteristics)<sup>(11,12)</sup> (such as weight and gestational age at birth) and operational (such as practices performed in the handling of SCUP from collection to transportation and processing)<sup>(13-15)</sup>. The quality, volume, and cellularity (amount of total nucleated cells) of the final product will determine whether it can be classified as viable for cryopreservation (freezing technique for living tissues using preservative substances and protecting cells from them, so that they remain viable after thawing, with the least possible loss)<sup>(16)</sup>.

There are minimum technical-sanitary criteria that stem cell processing laboratories from SCUP must adopt in order to allow their operation and safety and quality in the processing method (10). The Umbilical Cord and Placental Blood Banks (BSCUP), based on these regulations, formulate Standard Operating Protocols (SOPs) that determine how the procedure for collecting SCUP

should be performed, aiming at both the quality of the procedure and the fulfillment of the specified requirements and the processing of an ideal product for transplantation. If, in addition to the POPs, the professionals also had access to a document that gathered information about factors that could interfere with the quality of the USCUP, the repercussions could be positive, since the combined information would have the potential to improve the procedure.

In view of the presented problem, the present study has as object the factors that can influence in the quality of the UCPU and has as objectives to point out the factors that can influence in the quality of the UCPU collection; to define the factors that can influence the quality of the collection of SCUP and to analyze the good practices in the collection of SCUP, synthesizing, next, fundamental information about good collection practices.

## METHODS

It is an integrative review study, a broad methodological procedure that allows the insertion of experimental and non-experimental research, advising the understanding of the facts evaluated through the combination of data from theoretical and empirical literature, making possible options such as theory review, definitions of concepts and analysis of problems from a particular subject<sup>(17)</sup>.

The search for articles was carried out from May to July 2018, based on the PICO methodology, an acronym for the terms "Patient", "Intervention", "Comparison" and "Outcome", which, are part of the research question<sup>(18)</sup>, with the question posed as follows: "For professionals collecting Umbilical Cord and Placental Blood (SCUPA), the elaboration of a protocol related to factors that interfere in the quality of SCUPA could favor the increase of quality of the materials collected, compared to procedures based only on the POPs of the BSCUPA?".

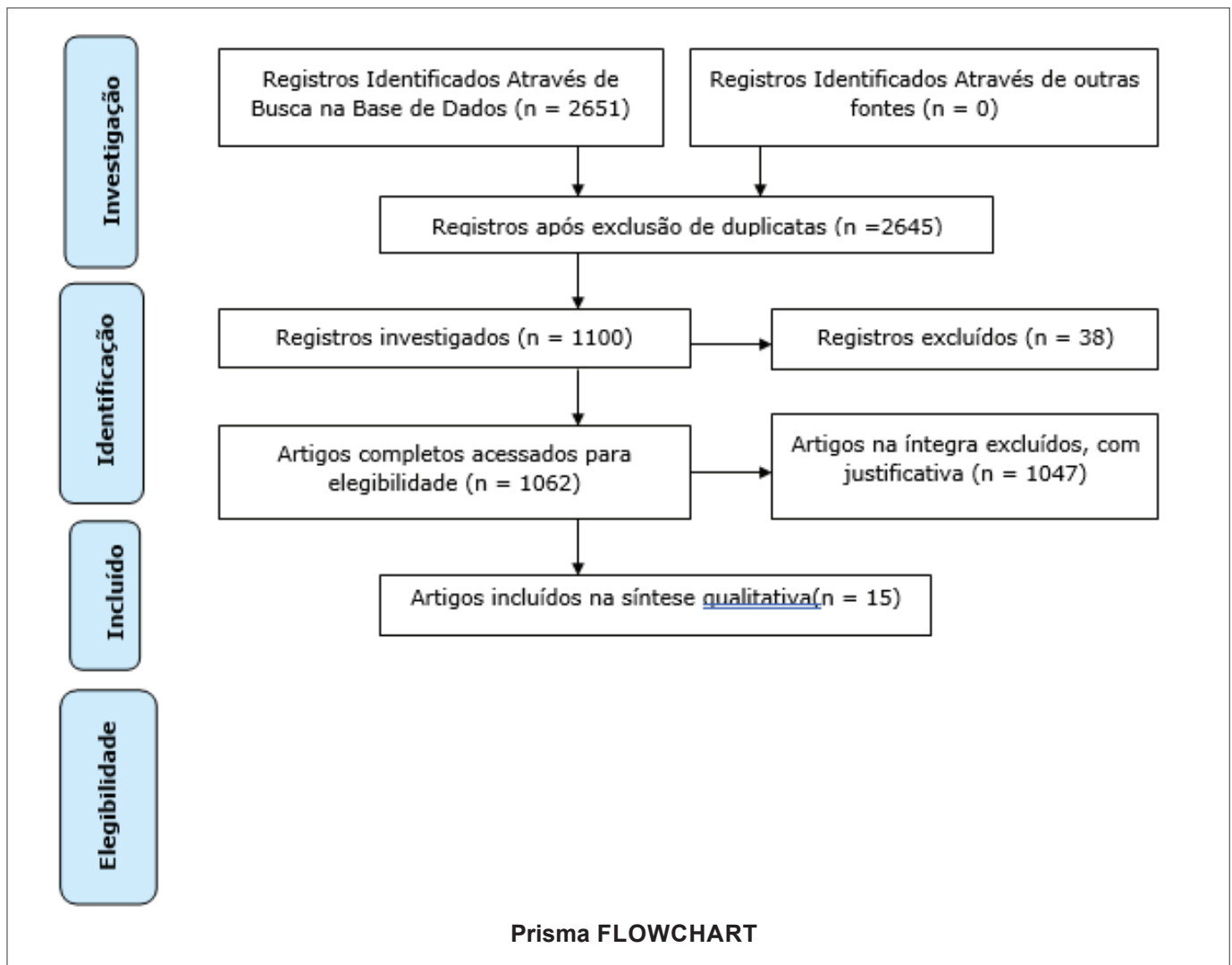
The researches were carried out using the Virtual Health Library (VHL), a platform with 14 bibliographic databases in health sciences, which have scientific articles and documents, as well as reference bases such as the Catalog of Scientific Journals and DeCS. The inclusion criteria were: Publications between 2008 and 2018, made available in full, free of charge, to discuss the topic of cord blood and factors of quality interference. For exclusion criteria: animal studies; Theses and dissertations, studies that promote brands or companies.

The search was carried out using the association of the following descriptors, through the Boolean operators "AND": "umbilical cord blood", "clinical protocol", "collectors" and "quality". MeSH vocabulary has also been used: "cordblood", "quality", "cordclamping", "cordblood banking", "fiscal factors", "temperature", "obstetric factors", "operational factors" and "placenta".

## RESULTS

A total of 2651 articles were analyzed and after applying the inclusion and exclusion criteria, 15 articles were selected:

02 in the Portuguese language, 01 in the Spanish language and 12 in the English language, although the studies are from other countries. The flow chart below shows details of the search.



**TABLE 1 – Selected Articles**

Article Title	Authors	Newspaper / Year	Goal	Results
Good practices for umbilical cord and placental blood collection	Lopes LA, Bernardino E, Crozeta K, Guimarães PRB.	Rev. Latino-Am. Enfermagem/2016	To identify factors related to the quality of umbilical cord and placental blood samples and to define good practices for their collection in a public bank of umbilical cord and placental blood.	There was a correlation in the influence of obstetric and neonatal factors in a smaller scale when compared to the operational factors, resulting in the need to re-adjust the professional practice of the nurse collector and the obstetric team involved in the SCUP collection process.
Correlation between neonatal and maternal physical characteristics com The total count of nucleated cells and CD34 + cells per microliter in umbilical cord blood.	Ordóñez FR, Riaño DP, Martín AL, Zárate AM, Ávila, AR, Villamil CAF, et al.	rev.fac.med, Bogotá/ 2015 2015	To correlate maternal and neonatal variables with the total counts of nucleated and CD34 + cells, measured in $\mu\text{L}$ (microliter).	There is correlation between umbilical cord length and nucleated cell count, total nucleated cells with initial volume and CD34 + cell count in $\mu\text{L}$ and mL was found.
Does the time interval between collection and processing of umbilical cord blood influence the quality of the sample?	Barini R, Ferraz UC, Acácio GL, Machado IN.	Einstein/ 2011	To evaluate the association between time from umbilical cord blood collection to processing and sample quality.	Nucleated cells, viable cells and CD34 + decreased greatly by increasing the time between sampling and analysis, the difference between 24 and 48h being smaller than the difference between 24 and 72h.
Quality rather than quantity: the cord blood bank dilemma	Querol S, Gomez S G, Paugliuca A, Torrabadella M, Madrigal JA	Bone Marrow Transplantation/2010	Determine critical steps of the SCUP process that may affect the final cellular viability; discuss release tests that ensure that the unit is adequate.	Extensive manipulation coupled with factors such as transit time, storage temperature, and cell composition results in viability problems.

Optimizing Donor Selection for Public Cord Blood Banking: Influence of Maternal, Infant and Collection Characteristics on Cord Blood Unit Quality.	Page KM, Mendizabal A, Staleinb B, Wease S, Shoulars K, Gentry T et al.	Transfusion/2014	Describe the characteristics that identify high quality CBUs, which can be used to inform CBU collection strategies for public banks.	The other high quality CBUs are those with higher levels of TNCC and CD34 + + UFC. Higher CD34 + or CFU content was associated with a lower collection interval at processing, lower gestational age; Caucasian race, greater weight of the RN and higher volume collected.
Effects of obstetric factors and storage temperatures on the yield of endothelial colony forming cells from umbilical cord blood.	Coldwell KE, Lee SJ, Kean J, Khoo CP, Tsaknakis JS, Smythe J et al.	Angiogenesis/2011	Examine possible obstetric selection criteria to achieve higher UCB ECC yields, and to determine if the storage temperature of UCB and cryopreservation affected the performance and function of the ECFC.	Placental weights were the only statistically significant obstetric factor that predicted the frequency of ECFC in SCU. Temporary storage of fresh UCB at 4°C reduced the ECFC yield compared to at 22°C. Cryopreservation of UCB MNCs reduced ECFC recoveries.
A new strategy for umbilical cord blood collection developed at the first Colombian public cord blood bank increases total nucleated cell content.	Vanegas D, Triviño L, Galindo C, Franco L, Salguero G, Camacho B, et al.	Transfusion/2017	Analyze data from UCB's Colombian public bank (Col CBB), including variables that affect blood volume and TNC counts.	There is correlation between neonatal birth weight and cellularity. The new collection method increased cellularity by about 26% and did not alter pre-cryopreservation and recovery, viability or post-thawing clonogenic capacity. In addition, it showed a remarkably low microbial contamination rate.
Maternal obesity associated with increase in natural killer T cells and CD8+ regulatory T cells in cord blood units.	Espinosa LOG, Cervantes LAM, Márquez AM, Juárez KP, Maldonado ER, Ojeda JV.	Transfusion/2016	To determine if obstetric, maternal and fetal factors modify the number of lymphocyte subsets in UCB units.	Mean number of CD34 + cells was $4.45 \times 10^6$ , NKT, CD3 +, CD4 +, CD4 +, CD8 + and CD8 + CD25 + FoxP3 + Treg cells were much higher in overweight or obese mothers and decreased CD34 + cells. The number of iNKT and CD34 + cells decreased in the newly born of greater weight.
Pre-birth selection of umbilical cord blood donors.	Urcioli P, Passeri S, Ceccarelli F, Luchetti B, Paolicchi A, Lapi S, et al..	Blood Transfusion/2010	Provide basis for selection of SCUP donors who would provide CBU with sufficient volume and white blood cell count, reducing collection, transfer and storage costs. Analyze CBU to be unsuitable for transplantation.	The average birth weight of newborn donors was $3484 \pm 389$ grams and mean gestational age was $40 \pm 1$ weeks. Physiological parameters of the newborn donors are presented in Table I. The mean CBU volume was $118.2 \pm 21.8$ mL and the mean total nucleated cell (TNC) content of the CBU was $1.51 \times 10^9$ .
Umbilical Cord Blood: Counselling, Collection, and Banking	Armson B A, Allan D S, Casper R F.	J ObstetGynaecol-Can/2015	Review of counseling, collection, BSCUP services, guidelines for health professionals on patient education, consent, procedural aspects and options for BSCUP in Canada.	Counseling, collection and services of BSCUP, education of health professionals, indications for the collection of SCUP, short- and long-term risk and benefits, maternal and perinatal morbidity, parental satisfaction and medical care costs.
Time related variations in stem cell harvesting of umbilical cord blood.	Mazzoccoli G, Miscio G, Fontana A, Copetti M, Francavilla M, Bosi A, Perfetto F, et al.	ScientificReports/2016	To evaluate the variations related to umbilical cord blood volume (CTB), UCC TNC and CD34 + cells content in relation to obstetric, neonatal and collection factors that influence the volume and content of hematopoietic cells of CBU.	The temporal immobility influences the number of SCUP and number of TNC and CD34 + cells. The mean age of birth, gestational age, birth rate, sex / weight of the newborn was associated with: year, month, time of birth, gestational age, birth weight, MVC, TNC, CD34 + negatively related to Apgar score at 1 and 5min.
Factor predicting total nucleated cell counts in cord blood units	Al-Qahtani R, Al-Hedythi S, Arab S, Al-Juhani A, Jawdat D.	Transfusion/2016	To optimize clinical use of stem cells in our population, this study aims to address several variables that affect TNC counts.	Of the 16 maternal and infant variables evaluated, three factors demonstrated statistically significant predictive value for the level of TNC accepted. The CBU volume was the best predictive factor, followed by the birth weight of the newborn and the way of delivery.
Optimizing cord blood collections: Assessing the role of maternal and neonatal factors.	Philip J, Kushwaha N, Chatteerjee T & Mallhi R S.	Asian Journal of Transfusion Science/2015	To determine maternal and neonatal factors affecting TNC and CD34 + cell counts in cord blood to assist in the proper selection of cord blood units for cryopreservation	Volume of SCU correlated with yields of TNC, CD34 + and CFU-GM cells. Heavier placenta and heavier baby were associated with a significantly greater volume of cord blood, while the age, parity of the mother and the sex of the baby had no significant effect.

Four phases of checks for exclusion of umbilical cord blood donors.	Volpe G, Santodioco M, Di Mauro L, Miscio G, Boscia FM, Muto B, et al..	Blood Transfusion/2011	To analyze umbilical cord blood collection (SCU) in a year between October 2008 and September 2009, looking for ways to improve the number of convenient UCB units.	The volume of SCU collected after cesarean section was higher than after vaginal delivery. After vaginal delivery they contained a larger number of total nucleated cells than after cesarean section.
Optimizing umbilical cord blood collection: impact of obstetric factors versus quality of cord blood units	Mancinelli F, Tamburini A, Spagnoli A, Malerba C, Suppo G, Iasorella R et al.	Transplant Proc./2006	Determine if obstetric factors influence the UCBs collected.	Weight of RN was the main factor for total volume, TNC, CD34, and CFU-GM. Weight of the placenta > 600 g had higher volume and no TNC. IG > 39 weeks increased CD34% Caesarean production > volume and <no leukocytes Females had WBC and CD34 (+) counts higher than the male.

In the analysis of the studies demonstrated above, several conditions were identified that interfere in the quality of the UCPU collection, which were distributed in five items. The first one represents the characteristics of the Obstetric Factors; the second, the Neonatal Factors; the third addresses the Maternal Factors; the fourth, the Operational Factors and the fifth, Physical Factors.

### I. Obstetric factors

#### a) Placenta

A descriptive research with a quantitative approach has shown that placental weight interferes with the amount of nucleated cells and the volume of SCUP collected, inferring that the larger the size and weight of this organ, the greater the volume collected<sup>(20)</sup>. This manifesto was reaffirmed by others authors, who add that the higher the volume, the greater the number of nucleated cells obtained from the sample<sup>(21-23)</sup>.

A study with 365 USCUPA adds that there is still a correlation between placental weight and the amount of CFU (Colony Forming Cells), also called precursor cells, in SCUP<sup>(24)</sup>. Some authors add that volume and cellularity improved when placental weight was between 600 and 700g<sup>(22,25)</sup>.

However, there is a study that found no relationship between placental weight / size and number of nucleated cells, but corroborated with the statement that the larger the volume collected, the greater the cellularity obtained<sup>(26)</sup>.

#### b) Umbilical cord

There is information about the characteristics of the umbilical cord and how it can be associated with the collected volume, arriving at the conclusion that the larger the gauge of the cord and the more filled it is, the greater the volume collected and the cellularity of the USCUPA<sup>(20,26)</sup>. In addition, there is a relationship between umbilical cord length and sample volume, establishing a direct relationship between cord length, volume and, also, cellularity<sup>(26)</sup>. There is evidence that umbilical cord length must be equal to or greater than 30 cm to provide adequate blood volume and that there is increased cellularity and volume of SCUP collected in cords with lengths greater than 55 cm<sup>(22,25)</sup>.

There are also factors associated with the reduction of umbilical cord blood volume, such as maternal hypertension, smoking during pregnancy, multiple gestation, preterm birth, intrauterine growth restriction, abnormal placentation, maternal transferrin<sup>(22)</sup>.

## 2. Fatores Neonatais

### a) Weight

There are reports that the weight of the newborn is directly related to the volume of SCUPA collected and also to the cellularity, and strong positive correlations between the waist circumference and the volume of UCPU, as well as the number of CFU, and better results were found in newborns weighing between 3390g and 3500g<sup>(27,23,25,22,20,24)</sup>.

There are authors who also report that every 500g of newborn weight, there is a 28% increase in CD34 + cells (phenotype found in hematopoietic stem cells) and that every 500 g of deviation from the mean weight of the newborn there was a 40% greater chance of producing a TNC count that would be accepted for clinical use<sup>(21,28)</sup>.

### b) Gestational age

Term babies had a significantly higher cell count in UCP compared to preterm infants. In addition, a positive (although described as a modest) correlation was found between the cellularity obtained from the collected SCUP and the gestational age, obtaining better results in neonates with gestational age of at least 39 weeks<sup>(23,22,25)</sup>.

It has been reported that with the advent of placental aging, due to the advancement of gestational age, there may be progressive fetal hypoxia and one of the defense mechanisms of the baby would be the increase in hematopoietic cells and circulating blood volume<sup>24</sup>.

On the other hand, others report that gestational age babies had lower cell counts, however, a higher CD34 + count<sup>(29,23)</sup>.

### c) Ethnicity

A study with 5267 SCUPAS evaluated that Caucasian babies tend to provide SCUPAS with greater potency (SCUPA ability to go through all stages of processing with as little cell death as possible) and higher amount of CFU when compared to afro-descendant infants<sup>(29)</sup>.



#### d) Gender

Regarding gender, one of the studies denies having found a significant influence, however, it admits that previous studies diverge in this information, sometimes positively correlating male infants to larger volume samples, and positively correlating female infants<sup>(28)</sup>.

#### e) Stress conditions at birth

It is a consensus among some authors that situations that generate stress and neonatal hypoxia at the time of delivery, such as prolonged labor, reduced APGAR index at the 1st and 5th minutes, are related to the increase in the volume and cellularity of the SPUP<sup>(30,22)</sup> and (which leads to neonatal stress) and also (low) the baby's blood pH positively influence the volume and cellularity of UCPB<sup>(25)</sup>.

### 3. Maternal factors

In the context of maternal obesity, there is a correlation between the reduction of iNKT cells in the liver (cells that recognize lipid and glycolipid antigens) and their increase in the adipose tissue of the babies. This would function as a compensatory mechanism since these cells have the ability to identify and respond to changes in adipose tissue lipid homeostasis and then culminate in an increase in the number of CD34 + cells in lower birth weight (<3000g) compared to infants (under normal conditions)<sup>(31)</sup>.

### 4. Operational Factors

The best described way to obtain high cellularity in a collection is to extract as much volume as possible during umbilical cord and placenta puncture. In this context, undue practices can occur that culminate in the reduction of the collected volume and, consequently, in the lower cellularity of the collected SCUP<sup>(20)</sup>. The practices are:

#### a) Clamping time and incorrect cord cutting

In the present study, we examined the effects of umbilical cord clamping in the collection of Umbilical cord blood and its use in the collection of Umbilical cord blood, findings have shown that early cord clamping (30 seconds postpartum) is directly related to a collection with higher volume and cellularity available in the UCPU and, in contrast, when the cord is clamped late (1 to 3 minutes after delivery) there is a reduction in the volume of SCUP available for collection<sup>(22)</sup>. Umbilical cord clamps between 30 and 60 seconds after delivery showed better numbers of cellularity<sup>(25)</sup>.

#### b) Incorrect handling of the placenta

High pressure when handling the placenta was one of the factors that impaired the integrity of the placenta and occurred in 23.43% of the collections<sup>(20)</sup>;

#### c) Rupture or laceration of the umbilical cord

In the period of expulsion of the placenta, when ex-

erting pressure to assist the process, rupture or laceration of the cord occurred, damaging 21.60% of the collections<sup>(20)</sup>;

#### d) Time between collection and processing

SCUPA samples have a higher nucleated cell rate when processed within 24 hours after collection. Samples processed within 12 hours after collection had a better final yield in the laboratory compared to samples processed within 24 hours after collection, which hours have significant progenitor cells and CFU losses compared to samples processed within 10 hours of collection<sup>(20,29)</sup>.

Statistical data on the interval between collection and processing of SCUPA showed that samples processed within 24 hours had an average of 1.1 billion nucleated cells, while samples processed in 48 hours showed an average of 967 million and processed in 72 hours showed an average of 711 million nucleated cells<sup>(13)</sup>.

The initial cellularity percentage of the sample is inversely proportional to the time from collection to processing, from the point of view that the collection bag material is unsuitable for storing the product, in theory. This hypothesis comes from a reflection based on a study that indicates that the collection bags were made in material ideal for the storage of red blood cells and that when other types of cells (the study in question tested platelets) are stored in the same, it occurs progressive cell death in the course of hours. In theory, the same would occur with SCUPA (it is suggested that within 24 hours of collection there is no significant loss of cellularity, but the same cannot be stated after this period)<sup>(32)</sup>.

#### e) Type of collection

The intrauterine technique (collection performed prior to placental delivery/delivery) produces slightly larger volumes of UCPV and higher yields of total nucleated cells compared to the extra uterus technique (after placental delivery/delivery)<sup>(22,11)</sup> and studies show that merging intrauterine collection with extra uterine collection has a significant increase in blood volume collected, compared to separate intrauterine and extra uterine collections. The intrauterine technique has 75% success while the extra uterus has 67%. Extra uterus collection may be associated with lower volumes and cellularity due to the fact that there are haemorrhagic foci and clots in the umbilical cord veins after deportation<sup>(27,25)</sup>.

#### f) Type of birth

After the cesarean delivery, a greater volume of UCPU was collected for vaginal delivery (95.4 mL versus 85.0 mL, respectively), but it was found in the collection after vaginal delivery that greater cellularity was obtained in the UCPU (9.70x10<sup>8</sup> cells versus 8.74x10<sup>8</sup> cells). After Cesário's delivery, there was a 40% reduction in the probability of cellularity being satisfactory<sup>(25, 28,29)</sup>.

## 5. Physical factors

### a) Temperature

The consensus about the ideal temperature is that when stored between 4 and 22°C in 24 hours, there is little or no influence on cellular viability<sup>(21)</sup>. On the other hand, current Brazilian regulations recommend the “material to remain at 4°C (plus or minus 2°C)”<sup>(10)</sup>.

## DISCUSSION

It is agreed by the authors that the volume of SCUP collected at the time of delivery has a strong relation with the initial cellularity of the sample (20-27). This information leads us to believe that in order for a collection to be successful, the professional responsible for collecting must, in addition to observing the norms that involve the collection of SCUP and ensuring the quality of the procedure, collect the largest volume of SCUP possible, in order to assure a sample rich in nucleated cells that can go through all processing steps and maintain sufficient cellularity to be eligible for storage and transplantation.

In addition to the volume of SCUP, other factors were identified as preponderant for the quality and success of a collection. Some situations and procedures that involve the collection that can interfere in the quality / quantity of the sample. For the scientific technical improvement of the collecting professionals, the information considered most relevant were recommendations of good practices aimed at guaranteeing a collection of quality and greater volume and cellularity. Among them we observe:

1. The size of the umbilical cord is a factor that can be influenced by the obstetrics professional and is directly related to the volume and cellularity of the UCPB<sup>(20,22,25,26)</sup>. Thus, it is important to emphasize the importance of monitoring and also the instruction of the obstetric team by the collecting professional during the clamping and umbilical cord section, so that the largest cord size can be obtained (if possible, greater than 30 cm).
2. The integrity of the umbilical cord and the placenta significantly interfere in the volume of SCUP available for collection, since when there is laceration of one or the other, there is formation of clots and bleeding foci<sup>(25)</sup>. Once again, the obstetrics team is advised. The more delicate cord management during induced placental debridement, the lower the chances of trauma with impairment of the integrity of both.
3. Umbilical cord clamping time is the focus of several studies, with some authors agreeing that there are several benefits to the baby when one to three minutes after childbirth to do so. In contrast, other authors have shown that the optimal cord clamping time after delivery, in order to obtain satisfactory

volume and cellularity in a UCPB collection, would be between 30 and 60 seconds<sup>(22)</sup>. Thus, although there is no contraindication to the collection of SCUP after the late cord clamping, the ideal is to guide the parents of the baby before birth about the possible repercussions of late cord clamping in the collection of Umbilical Cord Blood Spreads, as well as the benefits of late decision and leave the final decision at their discretion;

4. The interval of Processing time between the collection and the processing proved to be relevant. The authors' understanding of the optimal range varies, but all suggest that the shorter the interval, the lower the cell loss that occurs during processing<sup>(13,20,29)</sup>, the maximum limit being established by Brazilian standards of 48 hours;
5. The type of collection was divided between intrauterine and extrauterine. The former was described as being the source of a larger volume collected<sup>(22)</sup>. But one of the authors mentioned that the combination of the two techniques could cause an even more voluminous collection, when compared to the separated techniques<sup>(27)</sup>. Only one of the authors correlated the intrauterine technique with the increase of cellularity of the collected SCUP<sup>(11)</sup>. Thus, since it is possible for the collecting professional to be able to perform the two techniques simultaneously or still unable to perform it, giving preference to intra-uterine collection, the chance of obtaining a sample richer in volume and cellularity it's bigger;
6. The temperature at which SCUP is maintained between collection and processing has also been shown to be important for cell preservation and viability<sup>(10,21)</sup>.

In addition to the factors described above, maternal and neonatal characteristics that can predict the volume of a sample have been described by several authors. On the other hand, when there is a need to select only one baby to collect SCUP (in the case of twins and only one collector, for example), they become fundamental in the orientation of the professional. In this type of situation, the collector must pay attention to the following aspects:

1. Weight at birth: It was agreed among the authors that the heavier the baby, the greater the volume of SCUP collected. Thus, the collector should give preference to the larger baby, who appears to have the highest weight<sup>(20,22-25,27)</sup>;
2. Placenta Size: As well as the weight of the newborn, it was determined that placental size and weight positively influence the amount of collected volume, characterizing a larger and heavier placenta as the best collection option<sup>(20-25)</sup>;

3. **Umbilical Cord Characteristics:** A larger umbilical cord, with more flow, greater caliber and better preserved integrity, is more likely to provide an adequate volume of blood for collection <sup>(20,22,25,26)</sup>;
4. **Gestational age:** There is controversy when it comes to outcomes related to gestational age, but most authors report that a baby of greater gestational age is more likely to provide more volume and, especially, greater cellularity in UCPD <sup>(22-25)</sup>, in a situation where there is more than one labor in progress or even in a gestation where there are babies of different gestational ages (when more than one ovulation takes place, with fertilization of both ovules at different times), it is interesting that the collector evaluate other aspects before making the decision.
5. **Gender/Ethnicity:** There are many controversies related to the sex of the baby and little information about ethnicity regarding its involvement with higher volume and cellularity of UCPB <sup>(29)</sup>. Thus, they do not have the necessary reliability for decision making;
6. **Maternal BMI:** There is evidence that maternal obesity during pregnancy positively changes the volume and cellularity of UCPB <sup>(31)</sup>. A study of 109 mothers who presented with preterm birth showed that 42.20% of these women were overweight and 32.11% were obese at the end of gestation <sup>(33)</sup>. These data show a significant relationship between obesity and preterm birth and, consequently, low neonatal weight. In the context of SCUP collection, this combination of characteristics could point to a more viable collection, since it brings together three important predictors of higher cellularity.
7. **Type of Delivery:** The agreement between the authors about the type of delivery is that after the cesarean section there is a greater volume of SPUP available for collection. With regard to vaginal delivery, the collection performed after the same has higher cellularity <sup>(25, 28, 29)</sup>. As it was already verified in the present study that there is a correlation between Umband volume and cellularity, it is necessary to exercise caution when giving par-

ents guidance on the ideal delivery type to collect a quality UCPU;

It was also described, in this study, that prolonged labor, low fetal pH, stress situations and neonatal hypoxia were predictors of greater cellularity in UCPB <sup>(22,24,25)</sup>, however, the possibility of there is compromise of the safety of the mother and the baby in these cases, which would constitute a strong contraindication to the UCPB collection.

In addition, some authors have approached an interesting proposal: to place the baby in the lap of the mother immediately after the birth. This action, according to their studies, benefits not only the link between the two, but also showed an increase in the number of CD34 + cells and the volume of recovery of the SCUP collected <sup>(22,25)</sup>.

Another factor of excellent importance to be considered is the implementation of continuing education at the service, which provides the health professional with a technical-scientific update, consolidation of technical-professional skills and improvement of the communicative aspects between staff and family, strengthening the commitment with the life of the other. This set of characteristics makes Continuing Education an important factor for achieving quality health care/procedures <sup>(33)</sup>.

## CONCLUSION

In agreement with other authors, this study concluded that to optimize a collection, one must obtain the largest possible volume of SCUP, since, in this way, the final cellularity will be increased. For this, there are neonatal and maternal characteristics that can be observed, procedures that can be improved and specific techniques that can be performed during the collection.

Thus, a service that provides access to a document that gathers the information pertinent to good practices and quality of collection and maintains a continuous training program of collecting and obstetrical professionals about the appropriate procedures would not only bring optimization of collections and a higher quality service, but could also avoid the main errors that lead to poor quality (volume/cellularity) collection <sup>(20,22,34)</sup>.

In addition, knowing the factors that predict the greatest volume of UCPU, professionals would have ownership in decision-making in the face of multiple births and would still be able to adequately guide parents before the baby is born.



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