The effect of collecting umbilical cord blood during caesarean section on perioperative blood loss and incidence of complications

Wpływ pobrania krwi pępowinowej podczas cięcia cesarskiego na okołoporodową utratę krwi oraz występowanie powikłań

Jakub Młodawski[1], Marta Mlodawska[1], Aleksandra Herman[2], Kinga Kasperek[2], Grzegorz Swiercz[1]

[1]Department of Obstetrics and Gynecology, *Collegium Medicum*, Jan Kochanowski University, Kielce, Poland
Head of the Department: Prof. Marek Sikorski MD, PhD
[2]Student's Scientific Society "Eskulap", Jan Kochanowski University, Kielce, Poland

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Słowa kluczowe: krew pępowinowa, cięcie cesarskie, niedokrwistość poporodowa.

Abstract

Introduction: Collecting cord blood (CB) for banking is a common practice in obstetrics. There are many studies in the literature assessing the use of the obtained stem cells in medicine, however, there are few examining the interference of the collection procedure with the delivery mechanism and maternal blood loss.
Aim of the research: To assess the effect of this procedure on perioperative maternal blood loss during caesarean section (CS).
Material and methods: It was a retrospective, observational study. It included 238 women in whom a CS was performed and umbilical cord blood (CB) was collected using the in utero method. The control group consisted of 1106 patients who underwent CS without CB collection.
Results: We observed statistically significant lower values of hemoglobin (Hb) (11.5 g/dl vs. 11.7 g/dl, $p = 0.04$) and hematocrit (Hct) (33.7% vs. 34.4%, $p = 0.03$) in the study group compared with controls after the surgery. In the study group, we also observed a greater median decrease in the concentration of Hb (1.1 g/dl vs. 0.8 g/dl, $p < 0.001$) and Hct (3.05% vs. 2.2%, $p < 0.001$). Platelet levels did not change. We recorded no difference in the incidence rates of postpartum anemia (Hb < 10 g/dl) and severe postpartum anemia (Hb < 7 g/dl).
Conclusions: In utero CB collection during CS is associated with a statistically significant increase in perioperative blood loss. The difference is small and of no clinical significance in the healthy population of young patients undergoing CS.

Streszczenie

Wprowadzenie: Pobieranie krwi pępowinowej (KP) w celu bankowania jest częstą praktyką w położnictwie. W piśmiennictwie dostępne są badania oceniające użycie bankowanej krwi w medycynie, istnieje jednak niewiele badań oceniających wpływ samej procedury pobrania na mechanizm porodu oraz okołooperacyjną utratę krwi.
Cel pracy: Ocena wpływu procedury pobierania KP na okołoporodową utratę krwi podczas cesarskiego cięcia (CC).
Materiał i metody: Badanie miało charakter retrospektywny, obserwacyjny. Do badania włączono 228 kobiet, u których wykonano CC z pobraniem KP metodą *in utero*. Do grupy kontrolnej włączono 1106 pacjentek, u których wykonano CC bez pobrania KP.
Wyniki: Stwierdzono statystycznie mniejsze wartości stężenia hemoglobiny (Hb) (11.5 g/dl *vs* 11.7 g/dl, $p = 0.04$) oraz hematokrytu (Hct) (33.7% *vs* 34.4%, $p = 0.03$) w grupie badanej w porównaniu z grupą kontrolną po operacji. W grupie badanej zaobserwowano większą medianę spadku stężenia Hb (1.1 g/dl *vs* 0.8 g/dl, $p < 0.001$) oraz Hct (3.05% *vs* 2.2%, $p < 0.001$). Nie wykazano różnic w stężeniu płytek krwi pomiędzy grupami. Nie odnotowano różnic w częstości występowania niedokrwistości poporodowej (Hb < 10 g/dl) oraz ciężkiej niedokrwistości poporodowej (Hb < 7 g/dl).
Wnioski: Pobieranie KP metodą *in utero* podczas CC wiąże się ze statystycznie istotnym zwiększeniem okołooperacyjnej utraty krwi. Różnica jest niewielka i prawdopodobnie klinicznie nieistotna w populacji zdrowych pacjentek poddawanych procedurze CC.

Introduction

Cord blood (CB) can be a source of stem cells used in the treatment of many diseases, both neoplastic and non-neoplastic ones. There is also ongoing worldwide research on the use of autogenous stem cells in regenerative medicine, however, current scientific evidence in support of these indications is limited [1].

CB is commonly regarded as medical waste, which, if it is stored in banks, is disposed of along with the postpartum material. Therefore, its collection, even in the case of a low chance need to utilize it in the future, does not raise objections among the community of clinicians. Yet, it should be remembered that the procedure of collecting cord blood units (CBU) may potentially influence the perinatal loss of maternal blood and interfere with procedures that have proven to have long-term benefits for the baby, such as the delayed cord clamping (DCC). Few studies in the literature assess the effect of CBU collection on the perinatal loss of maternal blood during cesarean section (CS), we decided to assess this based on two potential reasons. Firstly, CBU collection by "in utero" (collection before delivery of placenta) method may prolong time from neonate delivery to the beginning of suturing the uterine muscle. Secondly, there are data in the literature indicating a small but statistically significant blood loss in the case of vaginal delivery and CBU collection [2, 3].

Aim of the research

Comparison of the morphotic parameters of maternal peripheral blood after surgery and occurrence of specific maternal complications during CS with and without CBU collection.

Material and methods

The study had an observational and retrospective character. We analyzed the medical records of 1,344 women who gave birth by CS in the Department of Obstetrics and Gynecology of the Provincial Combined Hospital in Kielce. In 238 patients who had delivered between January 2016 and December 2020, umbilical cord blood was collected using the in utero method. The control group consisted of the consecutive 1106 patients who had delivered by CS at the same facility in 2020. CS was performed using the Misgav Ladach technique [4]. Oxytocin at a dose of 10 IU or carbetocin at a dose of 100 µg by intravenous bolus was used as an uterotonic drug during CS. The choice of a tocomimetic drug was dependent on the operator's request. The standard postoperative procedure was carried out for each patient. We excluded patients with multiple pregnancies from the study. All patients had their peripheral venous blood counts performed not earlier than 24 h before the procedure and between 12 and 24 h after the procedure. We compared the groups with regard to demographic data, peripheral venous blood counts, and the absolute value of their postoperative changes versus preoperative values (Δ) as well as the percentage of adverse events, such as the need for using misoprostol 600–800 µg rectally postpartum due to uterine atony/subatony, as well as the percentage of patients with hemoglobin (Hb) < 7 g/dl (the threshold below which symptomatic patients are offered red blood cell transfusions) and < 10 g/dl (a commonly used definition of "postpartum anemia") [5]. The study was approved by the bioethics committee at the Jan Kochanowski University in Kielce (consent number 38/2021).

Statistical analysis

Statistical analysis was conducted using the Statistica 13.3 program (TIBCO Software Inc., Palo Alto, CA). On account of non-fulfilment the assumption about the normal distribution of variables, the median was used as the measure of the central tendency and the interquartile range was used as the measure of dispersion. Continuous variables were compared using the Mann-Whitney *U* test. Qualitative variables were presented as a percentages and Pearson's χ^2 test was used to compare the groups. For the qualitative variables that measure the outcome, we calculated the odds ratio (OR) of the event occurrence for the patients in the study group versus the control group. The size of the control group was selected based on the sample size estimation with the given parameters – a difference of at least 0.2 g/dl between the medians of ΔHb (difference in hemoglobin concentration after the procedure versus concentration before the procedure) in the groups, with a power of 90%. The differences were considered statistically significant if $p < 0.05$.

Results

The demographic data for the groups are presented in Table 1. The groups did not differ significantly in terms of the initial parameters capable of affecting the final results, such as the concentration of the morphotic parameters of blood before CS, the newborn's birth weight and length, the number of patients after previous CS, and the percentage of patients who received carbetocin during CS. The a priori groups differed in age. The patients deciding on the collection were significantly older (33 vs. 31 years old). Most of the collections in the analyzed period (68%) were CBU collections for private banks.

In Table 2 we have presented the outcome data. We observed statistically significant differences between the values of some morphotic parameters of blood after CS. Postoperative Hb and hematocrit (Hct) values were statistically lower in the group of patients whose umbilical cord blood had been collected (11.5 g/dl vs. 11.7 g/dl, $p = 0.04$, 33.7% vs. 34.4%,

Table 1. Demographic and initial data of the groups

Demographic	Cord blood donors	Control group	*P*-value
Age [years] (median, IQR)	33 (7)	31 (6)	0.000003
Newborn weight [g] (median, IQR)	3410 (530)	3400 (630)	0.946204
Newborn length [cm] (median, IQR)	54 (4)	54 (4)	0.206945
Carbetocin administration	63.87%	58.79%	0.14
Induced labor	3.78%	4.53%	0.61
Number of patients after previous CS	38.66%	42.86%	0.23368

Table 2. Hematological and clinical outcome in both groups

Parameter	Cord blood donors	Control group	*P*-value	OR (95% CI)
Baseline Hb [g/dl] (median, IQR)	12.6 (1.3)	12.5 (1.4)	0.082952	N/A
Baseline Hct [%] (median, IQR)	36.9 (3.7)	36.6 (3.9)	0.173438	N/A
Baseline Plt [× 1000/µl] (median, IQR)	204 (67)	207 (77)	0.140922	N/A
Postpartum Hb [g/dl] (median, IQR)	11.5 (1.7)	11.7 (1.6)	0.042209	N/A
Postpartum Hct [%] (median, IQR)	33.7 (4.6)	34.4 (4.6)	0.030516	N/A
Postpartum Plt [× 1000/µl] (median, IQR)	179 (67)	190.5 (74)	0.051598	N/A
ΔHb (median, IQR)	–1.1 (1.3)	–0.80 (1.2)	0.000020	N/A
ΔHct (median, IQR)	–3.05 (3.8)	–2.2 (3.8)	0.000308	N/A
ΔPlt (median, IQR)	– 17 (34)	–16 (33)	0.575431	N/A
Need for postpartum misoprostol administration	3.36%	4.26%	0.52	0.91 (0.45–1.81)
Hb < 7 g/dl	0%	0%	1	N/A
Hb < 10 g/dl	7.17%	8.02%	0.65	0.88 (0.51–1.52)
Hb < 11 g/dl	31.22%	26.25%	0.11	1.27 (0.92–1.73)

Hb – hemoglobin concentration, Hct – hematocrit, Plt – platelet concentration, ΔHb – difference between Hb after and before delivery, ΔHct – difference between Hct after and before delivery, ΔPlt – difference between Plt after delivery and before delivery, IQR – interquartile range.

p = 0.03 respectively). In both groups, we observed a decrease in Hb and Hct concentration after CS compared to the value before the surgery. The absolute values of the median ΔHb and ΔHct were statistically greater in the group of patients whose CBU had been collected. We did not observe any changes in the concentration of platelets. There was no difference between the groups regarding the percentage of patients with Hb < 7 g/dl and < 10 g/dl postpartum, as well as the percentage of patients requiring the administration of postpartum misoprostol due to uterine atony/subatony.

Discussion

Cord blood collection is a fairly common procedure used in obstetric practice, both for vaginal deliveries and CS.

Every year, more and more data on its potential applications in allo- and autogenous therapy are published in the databases of scientific literature. Still, scientific evidence does not justify the routine recommendation of private banking in obstetric practice, as reflected in the recommendations of the American College of Obstetricians and Gynecologists [1]. Meanwhile, in numerous countries, we are faced with relentless marketing of cord blood banking companies, which overestimate the current potential of umbilical cord blood use while lacking objective evidence of benefit in many of the advertised clinical indications [2, 6]. Considering the above, first of all, due diligence should be applied to comply with the standards of perinatal care and to appropriately apply procedures with a documented positive impact on the child's development (such as DCC) [7, 8]. Research should also be carried out in order to assess whether the CBU collection procedure has an adverse effect on the mother.

There are few studies available in the literature, which assess the effect of umbilical cord blood collection on perinatal blood loss. In 2011, the results of a retrospective study covering data from a register maintained in 14 countries were published. They indicate an increased volume of blood lost in the case of blood collection during the third stage of labor (321 ±273 vs. 255 ±237 ml; $p = 0.02$), the difference was more pronounced in the case of instrumental deliveries (469 ±276 vs. 334 ±250 ml; $p = 0.007$). In the study, no differences were noted in the percentage share of the patients who received red cell mass transfusions on account of anemia [3]. Another study assessing blood loss during vaginal delivery with in utero CBU collection shows a significantly greater reduction in hemoglobin and hematocrit concentration in the group of patients who have had their cord blood collected and amount patients with postpartum anemia defined as Hb < 10 g/dl (15.9% vs. 10.64%, $p = 0.05$). However, the differences in the reduction of hemoglobin and hematocrit were small and clinically insignificant in young, otherwise healthy women (the decrease in Hb was 1.4 g/dl in the study group vs. 0.9 g/l in the control group, $p < 0.001$). No differences were found in the rates of maternal complications such as the percentage of patients with postpartum hemorrhage, postpartum curettage, manual removal of placenta, percentage of severe anemia (Hb < 7 g/l), or blood transfusion requirement [2].

In the literature, we have found no studies evaluating blood loss and the percentage share of complications during CS. The results of our study indicate increased blood loss in the study group compared to the control group. Despite the statistical significance, from a clinical point of view, this loss seems to be not relevant, taking into account that the vast majority of patients undergoing CS constitutes a population of women who are not burdened with chronic diseases. However, this information may be important in the case of patients with severe anemia, for whom a caesarean section should be performed before the correction of morphotic blood elements deficits.

In our study, the collection of CBU was performed using the in utero technique. This means that CBU is collected by inserting a needle into the umbilical vessels before separating the placenta. Such a procedure extends the time from neonate birth to placenta delivery and may increase bleeding from the unsutured uterine muscle. In utero CBU collection is not the only possibility for cord blood collection during CS. The second method is ex utero collection. In this case, CB should be collected within 10 min due to the rapid formation of clots within the umbilical cord. Research indicates that in both types of collection, the quality of the sample, measured by indicators such as the volume of the preparation, the number of CD34+ cells, and CFU-GM cells is the same [9]. In the case of ex utero collection, contamination of the sample with bacteria and the formation of clots has been observed less frequently [9, 10]. Also when accounting for the lower interference with the activities performed by the operator during CS, due to the lack of influence on the time elapsing to the moment of placenta delivery, this method seems to be safer from the perspective of perioperative blood loss. These two methods, however, require a direct comparison in the context of the blood loss in delivering patients.

Our study had an observational and retrospective character. The authors are aware of the limitations of random sampling in such a study, however, we included all patients from specific time intervals in our study, which allowed us to reflect the general population and reduce the impact of confounding factors. The limitation of the study is due to the lack of data on the patients' body mass index, which may have an impact on the difficulty level of the surgery and the perioperative blood loss. Another limitation is the significant difference between one of the initial parameters – the groups differed in terms of age, which, in our opinion, does not translate into confounding the values of the final parameters. The lack of visual assessment of the volume of blood lost can also be considered a limitation, but in our assessment, the visual assessment of blood loss, especially when mixed with amniotic fluid, is highly subjective, therefore we selected the objective parameters of the patient's peripheral blood.

Conclusions

In utero blood collection during CS is associated with a small but statistically significant increase in maternal blood loss. The difference is small and of no clinical significance in the healthy population of young patients undergoing CS.

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The data that support the findings of this study are openly available in OSF Storage at https://osf.io/qbdh6/

Conflict of interest

The authors declare no conflict of interest.

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Address for correspondence:

Jakub Młodawski MD
Department of Obstetrics and Gynecology
Collegium Medicum
Jan Kochanowski University
Kielce, Poland
E-mail: jakub.mlodawski@ujk.edu.pl