Intrauterine use of hyperconcentrated platelet concentrates collected with Trima Accel in a case of neonatal alloimmune thrombocytopenia

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BACKGROUND: Due to the threat of serious or fatal bleedings, fetuses with neonatal alloimmune thrombocytopenia (NAIT) may need intrauterine platelet (PLT) transfusions. To prevent a volume overload or an ABO minor mismatch, standard PLT concentrates need to be washed to increase the PLT concentration and to reduce the plasma content. Hyperconcentrated single-donor PLT concentrates (HCPs) are a therapeutic alternative. The first case of NAIT successfully treated with HCPs collected with the Trima Accel (TA; Gambro BCT) is reported.

CASE REPORT: A 31-year-old woman with a history of NAIT in the preceding pregnancy underwent cordocentesis three times during her third pregnancy (30th, 31st, and 32nd weeks of gestation). NAIT was confirmed by marked fetal thrombocytopenia, a maternal anti-human PLT antigen (HPA)-1a–immunoglobulin G (titer 1:128), and the appropriate HPA genotype of the fetus and the parents. On each cordocentesis procedure, a distinct volume of a HPA-1a-negative HCP with a PLT concentration of 3×10^6 PLTs per μL was transfused resulting in high corrected count increments after 2 hours. The HCPs were transfused within 10 hours after collection. One day after the last cordocentesis procedure, a cesarean section was performed. The newborn did not show any bleeding signs, and the PLT count remained on normal levels and no further PLT transfusions were needed.

CONCLUSION: HCPs collected with TA are a useful alternative to washed standard PLT concentrates without the need for further manipulation of the product after collection. Further in vitro and in vivo studies are needed, however, to make definite recommendations for the shelf life of these HCP.

Neonatal alloimmune thrombocytopenia (NAIT) is a clinical syndrome that is characterized by marked fetal or neonatal thrombocytopenia occurring before or shortly after birth. Three criteria help to distinguish NAIT from other causes of neonatal thrombocytopenia.[1]

1. Severe thrombocytopenia (platelet [PLT] count, $<50 \times 10^3/\mu L$).
2. Antenatal intracranial hemorrhage and/or intracranial hemorrhage accompanied by other signs of bleeding in a baby with birth weight of more than 2.2 kg and an Apgar score greater than 5.
3. The absence of other neonatal complications.

NAIT is caused by the diaplacental transfer of maternal antibodies against human PLT antigens (HPAs) carried by the PLTs of the fetus. Among Caucasian populations, the most common antibodies are directed against HPA-1a and HPA-5b in approximately 80 and 15 to 20 percent of cases, respectively.[2,3] Such maternal antibodies are detectable in approximately 1 in 350

ABBREVIATIONS: HCP(s) = hyperconcentrated single-donor platelet concentrate(s); HPA(s) = human platelet antigen(s); NAIT = neonatal alloimmune thrombocytopenia; SDP(s) = single-donor platelet concentrate(s); TA = Trima Accel.

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pregnancies and lead to NAIT in approximately one-third of cases resulting in an incidence of NAIT of 1 in 1000 live births in the Caucasian population. Up to 25 percent of cases, however, remain clinically silent.[4-6] Up to date and to the best of our knowledge, no country has established a routine screening policy for PLT antibodies during pregnancy. Therefore, the syndrome remains unexpected until a child is affected. Because the risk of recurrence of NAIT in subsequent pregnancies is high (>85%) coupled with a high risk for antenatal intracranial hemorrhage, antenatal treatment must be taken into consideration for subsequent pregnancies of affected women. The optimal antenatal management for NAIT, however, has not been defined and remains controversial.[7-9] Nowadays, the infusion of intravenous immuneglobulin (IVIG) for inhibition of an anti-HPA–immunoglobulin G (IgG) transfer through the placenta with or without additional injection of steroids for suppression of the immune response seems to be the first-line therapy. The invasive approach to perform serial intrauterine PLT transfusions has been used in the past more widely in Europe than in the United States.[7] Facing an overall fetal loss rate of 1.3 percent per procedure and 5.5 percent per affected pregnancy, this approach is currently regarded as salvage therapy in most institutions, that is, used only if medical therapy administered to the mother was not performed or failed to increase the fetal PLT count.[7] Owing to the increased risk for fetal exsanguination at the time of fetal blood sampling, however, PLT transfusion may also be considered in cases with a fetal PLT count of less than 50×10^3 PLTs per μL before extracting the sampling needle.[7] With regard to the kind of PLT concentrate used, several strategies can be considered:

1. Transfusion of maternal washed single-donor PLTs concentrates (SDPs).
2. Transfusion of selected SDPs negative for the presence of the involved HPA.
3. Transfusion of random-donor PLT concentrates.

In prenatal life, volume overload of the fetus is a major concern. For this purpose, the volume of the transfused PLT component should be low, even more so, if an ABO minor-mismatched transfusion might be necessary. Therefore, standard PLT concentrates need to be washed for plasma reduction and resuspended with saline. Such a washing procedure, however, may be associated with a loss of PLTs as well as reduced PLT quality.[10] The use of apheresis-derived hyperconcentrated single-donor PLT concentrates (HCPs) may represent a solution for this problem.[11] We would like to report the first case of NAIT treated with intrauterine transfusion of HCPs collected with the Trima Accel device (TA; Gambro BCT, Lakewood, CO).

MATERIALS AND METHODS

HCPs were collected with the TA with its accompanying software (Version 5.1, Gambro BCT) from two healthy cytapheresis donors (HPA-1a-negative) according to the relevant guidelines.[12-14] TA is an apheresis device with a single-stage filler collecting PLTs continuously.[15] One individual donated twice with an interval of 2 weeks and the other individual once in between. We programmed the machine to collect 3×10^{11} PLTs in a volume of 100 mL and an additional plasma unit of 500 mL. The collected by-plasma was used for fractionation purposes because this is routinely done in our center. Furthermore, because the whole-blood flow rate is controlled by the quantity of anticoagulant (acid citrate dextrose, solution A [ACD-A]) infused per minute and per liter of the donors' total blood volume, the collection of by-plasma enables the machine to increase the blood flow rate during the time of plasma collection, thus increasing the mean blood flow rate of the entire procedure and shortening the overall procedure time.[16] No further procedural modifications were needed for the collection of the HCPs. The preprocedure blood cell count of the donor was used for programming the device. The ratio of total inlet to ACD-A was set to 1:11. Peripheral blood samples for donors' cell counts were drawn from the IV line before and after each cytapheresis procedure. All HCPs were leukoreduced with the leukoreduction system technique.[17]

For determination of the donor's hematocrit and PLT count as well as for the PLT count in HCPs, we used automated blood cell counters (Sysmex K-1000 and K-4500, TOA Medicals, Kobe, Japan). White blood cell (WBC) counts were performed with a modified Nageotte chamber (Poly Labo, Strasbourg, France) as previously described.[17-19] The corrected count increment (CCI) was defined as

$$(\text{posttransfusion} - \text{pretransfusion PLT count}/\mu\text{L}) \times \text{body surface area}\,(\text{m}^2)/\text{number of transfused PLTs} \times 10^{-11}.$$[20]

The body surface area was calculated in accordance to Mosteller:[21]

$$\text{Body surface area} = \sqrt{(\text{body height [cm]} \times \text{body weight (kg)}/3600)}.$$

HCPs were stored for 30 minutes without agitation and then transferred to a flat-bed shaker (50-60 cycles/min; Helmer Laboratories, Nobesville, IN) at 20 to 24°C. After at least another 30 minutes and when no PLT aggregation was visible, a sample for blood cell count was taken from each collected unit. The HCPs were stored in containers of citrated polyvinylchloride (Citroflex, Gambro BCT) on the above-named flat-bed shaker at 20 to 24°C until transfusion. Immediately before transfusion, the

products were connected to an IV line, a three-way stopcock, and a syringe. Thereafter, the umbilical vein at the placental insertion was sampled and the fetal PLT count was determined with a blood cell counter (CellDyn Ruby 3500, Abbott Laboratories, Abbott Park, IL). Meanwhile, the system was connected to the cordocentesis needle for transfusion of the HCPs.

For HPA typing and analysis and titration of the HPA antibody we used a sequence-specific priming kit ("HPA-TYPE," BAG, Lich, Germany) and a Capture-P test (Immucor, Rödermark, Germany), respectively. Both tests were performed according to the manufacturer's instructions.

CASE REPORT

A 31-year-old woman (third pregnancy) presented herself in her current pregnancy with a dichorial-diamniotic twin pregnancy at 22 weeks of gestation in our outpatient clinic. The patient was known to have polyarthritis and Sjögren's syndrome since 2000 and 2006, respectively. In 1994, the patient had given birth to a healthy child from a different partner at term after an uneventful pregnancy. The first child with the current partner was born in 2002 at 38 weeks of gestation. Whereas the course of pregnancy was without any complications, the newborn showed petechial bleedings and hematoma formation during the first hours postpartum. Further workup revealed old and fresh parenchymal bleeding with lateral ventricle asymmetry as well as bleeding in the brain stem and the cerebellum. Because the PLT count was only 12×10^3 PLTs per μL, the newborn was transfused twice with 50 mL of random-donor PLT concentrates on Days 1 and 3 of life. In addition, one dose of 1.3 g of IVIG was administered on Days 2, 3, and 4 of life. On Day 12 of life, the PLT count was stable with 245×10^3 PLTs per μL, and the baby was discharged. There were no more bleeding periods and the further development of the baby was normal. Blood analysis of the mother confirmed the suspected diagnosis of a NAIT with an antibody against HPA-1a, her genotype being HPA-1b/1b.

In the current pregnancy, the first ultrasound investigation at 22 weeks of gestation demonstrated intrauterine death of one twin most likely having occurred several weeks before. The live fetus was of normal size and did not show any visible morphologic abnormality. Owing to the positive history of NAIT, we performed a HPA genotyping of the parents. The genotype of the mother was HPA-1bb, -2ab, -3aa, -4aa, -5aa, -15ab and of her partner HPA-1aa, -2aa, -3aa, -4aa, -5aa, -15aa. Additionally analysis performed for maternal antibodies against HPA confirmed the finding of an anti-HPA-1a–IgG (titer 1:128). Based on these findings, we offered a therapy with IVIG to the mother, which was refused by her. The patient was lost to follow-up until 30 weeks of gestation when we performed a cordocentesis to measure the fetal PLT count and to transfuse PLTs into the umbilical vein. To accelerate fetal lung maturation, betamethasone (2×12 mg intramuscularly) was administered. In parallel, the blood bank was contacted to provide HPA-1a-negative PLT concentrates. Because two HPA-1a- and cytomegalovirus-negative apheresis blood donors were easily available, we did not consider use of the pregnant mother as PLT donor. Furthermore, washing procedures to minimize the HPA-1a antibody containing plasma in the final product would have been unavoidable in that case. Because this may cause PLT loss and damage,[10] we are not very enthusiastic to wash the PLTs in general. Both available blood donors, however, had blood group O. Because the ABO blood group of the fetus was not known at the time, we still aimed for a very low volume of the plasma-stored PLT concentrate to prevent a possible ABO minor mismatch. We considered a simple saline replacement procedure to reduce the amount of plasma in the SDP. For this approach, however, an additional spinning procedure and further manipulation steps of the product are also unavoidable. Therefore, we decided to collect HCPs from the male donors with the TA. The first collection was started at 8:00 AM on November 7, 2006. Serologic and nucleic acid test screening for human immunodeficiency virus, hepatitis C virus, and hepatitis B virus was started immediately after we had obtained the blood sample from our donation site close to the university hospital. The testing was finished by 2:00 PM, and the HCP was released for transfusion at 3:00 PM. The maternity ward was informed immediately after release of the HCPs, and in the late afternoon of the same day, cordocentesis was performed. The PLT concentration of the fetus was 12.9×10^3 PLTs per μL, and 12 mL of the first HCP was transfused. Approximately 2 minutes after the transfusion, the fetal PLT concentration was 154×10^3 PLTs per μL. Analysis of the ABO blood group of the fetus revealed blood group O. Thus, we were able to exclude the possible threat of hemolysis due to an ABO minor mismatch transfusion. In addition, the HPA typing of the fetus was performed with the result HPA-1ab, -2ab, -3aa, -4aa, -5aa, -15aa.

The procedures of the second and third cordocentesis 1 and 2 weeks later, respectively, were performed likewise. The quality data of the transfused HCPs and the pre- and posttransfusion fetal PLT concentration are given in Table 1. On the occasion of Procedures 2 and 3, the volume of the transfused HCP was doubled (23 and 25 mL, respectively) because we usually yield a posttransfusion fetal PLT count of 200×10^3 to 300×10^3 PLTs per μL.[22] The transfused volumes are very similar to those we usually apply when we use modified, plasma-reduced, or washed PLT concentrates because the final PLT concentration in these preparations is similar to those in the HCPs. Use of unmodified standard SDPs with a PLT concentration of 1.0×10^6 to 1.4×10^6 PLTs per μL, however, would have

TABLE 1. Quality data of transfused HCPs and fetal PLT count

Variable	Number of cordocentesis procedures 1	2	3
Gestational age (week + days)	29 + 6	30 + 6	31 + 6
PLT concentration of HPCs ($\times 10^6$ per μL)	2.353	2.731	3.181
Volume of HPCs (mL)	105	103	105
PLT content of HPCs ($\times 10^{11}$)	2.47	2.81	3.34
WBC content of HPCs ($\times 10^6$ per unit)	0.0042	0.0041	0.0042
Transfused volume of HPCs (mL)	12	23	25
Transfused number of PLTs ($\times 10^{10}$)	2.82	6.28	7.95
Hemoglobin pretransfusion (g/dL)	16.1	15.7	15.9
Mean cell volume before transfusion (fL)*	113.8	111.6	110.0
Pretransfusion PLT concentration (/μL)	12,900	19,000	25,900
Posttransfusion PLT concentration (/μL)	154,000	†	280,000
Increment (per μL)	141,100	†	254,100
CCI‡ (per μL)	64,596	†	41,263

* Mean cell volume is given to prove the fetal origin of the umbilical blood sample (>90 fL).
† Umbilical blood sample coagulated = no value.
‡ Calculated with body weight = 1.5 kg; body height = 40 cm; body surface = 0.1291 m^2.

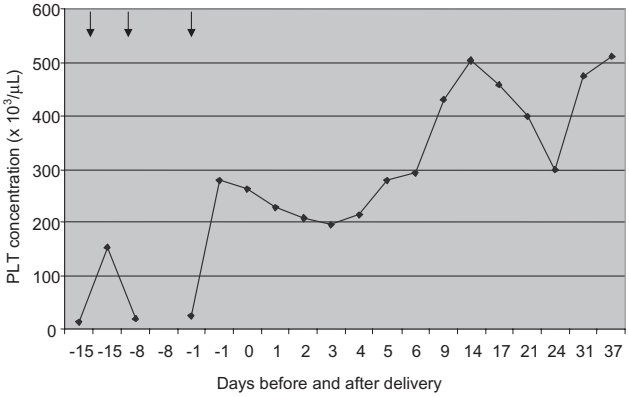

Fig. 1. PLT concentration before and after delivery. Arrows = transfusion of HCP. PLT concentration after the second HCP transfusion due to coagulation of the umbilical blood sample not available.

been associated with the need to transfuse at least a twofold volume to reach a similar increase in fetal PLT count. No adverse reactions were noticed in context with the performed cordocentesis and transfusions.

According to published recommendations,[7] a cesarean section 1 day after the last intrauterine PLT transfusion was performed at 32 weeks of gestation. The male newborn was vital and did not show any bleeding signs. Furthermore, a cranial ultrasound was performed to exclude an intracranial hemorrhage. The PLT concentration of the newborn was 262×10^3 PLTs per μL. Although IgG-HPA antibodies with a $t_{1/2}$ of 23 days can persist for weeks, the PLT count was stable (Fig. 1) and no further PLT transfusions were needed during the following days and weeks. We assume that after the placental transfer of the antibodies was stopped, the titer of the antibodies might have been too low to cause thrombocytopenia again after the $t_{1/2}$ of the transfused HPA-1a-negative PLTs. Owing to respiratory failure, the application of surfactant factor (100 mg/kg) and mechanical ventilation became necessary. After a rapid recovery, no further clinical problems occurred and the child was discharged from hospital.

DISCUSSION

To the best of our knowledge, ours is the first published case of NAIT successfully treated with intrauterine transfusion of HCPs collected with the apheresis device TA. This therapeutic approach has several advantages compared with already published and well-known alternatives. First of all, there is no need to further manipulate a standard SDP. The PLT concentration of those preparations usually varies between 1.0×10^6 and 1.4×10^6 PLTs per μL and requires an additional plasma-reducing procedure to prevent volume overload of the fetus. Such a washing procedure must be performed even more intensively when a maternal PLT concentrate is used because all antibody-containing plasma must be removed. Besides the time-consuming effect, this can result in deterioration of PLT quantity and quality.[10] Each additional manipulating step might also increase the risk of bacterial contamination. As a consequence the production of HCPs appears to be more appropriate.[11] Experience with collection of HCPs is currently increasing. Several modern apheresis devices seem to have the potency to collect HCPs without the need of specific changes in the apheresis system as has been described for the apheresis device Spectra (Gambro BCT).[23] One of these apheresis devices is the TA, which is used for plateletpheresis procedure in our department routinely. We had chosen TA to collect HCPs in the particular case for several reasons. First of all, we did not have any experience collecting HCPs with the modified Spectra technique as described by Dumont and coworkers.[23] Furthermore, we were able to demonstrate that HCPs can be collected with the TA without any further changes in the hard- or software even up to a target PLT concentration of 5×10^6 PLTs per μL without leading to a significantly increased PLT activation level.[24] At such high target PLT concentrations, however, the efficiency of the TA system has been found to be low. Because a PLT concentration between 2.5×10^6 and 4.0×10^6 PLTs per μL is usually sufficient to achieve a satisfactory posttransfusion PLT count in the transfused fetus,[9] in our case we decided to collect HCPs with a target PLT concentration of 3×10^6 PLTs per μL. Although the number of HCPs is of course very low, the achieved PLT concentration in the HPCs (Table 1) seems to come very close to the target level. Also, the adequate

rise of the fetal PLT count may prove a good in vivo quality of the transfused HCPs.

Several questions, however, remain open. First of all, we do not know how long HCPs can be stored ex vivo without addition of plasma or additive solutions. It has recently been shown that already up to a storage period of 8 hours after PLT collection an increased anaerobic metabolism was detectable compared to a hold time of 2 hours until addition of a storage solution.[25] Because the target PLT concentration (4×10^6 PLTs/μL) in this study was higher than in our case, these results, however, may not be directly transferable. In the current case, we planned that the collection and transfusion of the HCPs had to be performed within the same working day. This time limitation seemed to be necessary to us as validated storage data on the in vitro quality of the particular HCPs had been missing. This decision was also influenced by the above-named finding that PLTs stored in HCPs for 8 hours already showed an increased anaerobic metabolism compared to those stored for only 2 hours. Finally, all HCPs were transfused within 10 hours. Therefore, we did not measure the pH of the HCPs or perform any additional in vitro quality screening assays such as hypotonic shock response, extent of shape change, PLTs' P-selectin expression, or PLT morphology score. Several logistic reasons, for example, restricted availability of antigen-negative apheresis donors, delayed release of products due to technical problems with screening methods, or difficulties with sampling of the umbilical vein, might result in a prolonged storage of HCPs. Therefore, it might facilitate treatment if HCPs could be stored for up to 1 or 2 days without a significant deterioration in PLT quality. For HCPs collected with the apheresis device Spectra, Dumont and colleagues[23] were able to show a decrease in pH value (22°C) in association with the PLT content of the HCPs.[23] For a PLT content of not more than 1.6×10^{11}, between 1.6×10^{11} and 2.2×10^{11}, and more than 2.2×10^{11}, they reported that the pH was maintained above 6.2 for more than 3 days, less than 2 days, and less than 24 hours, respectively. It is also noteworthy that some of the other tested in vitro parameters in their study indicated a decreased in vitro PLT quality in the intermediate-yield and especially high-yield HCPs. Based on these findings, Dumont and coworkers recommended that HCPs with a volume of 60 mL can be stored up to 3, 2, and 1 days dependent on the PLT content as classified above. The calculated PLT concentration numbers are not more than 2667×10^3, between 2667×10^3 and 3667×10^3, and more than 3667×10^3 PLTs per μL, respectively. The Spectra-derived HCPs were stored in the same citrated polyvinyl storage bag modified by folding it in half widthwise once and secured with clips to reduce the surface area by half. This modification of the overall bag size resulted in a proportional drop in the total gas exchange rate. In our case, we did not modify the storage bag because the volume of our HCPs was 100 mL and therefore within the relevant storage limit recommendations.[26] Furthermore, we were aware of our former finding that PLTs stored as HCPs show an increased glykolytic activity.[25] This might result in a higher pCO_2 in the HCP accelerating a decrease in pH if the total gas exchange rate is reduced. Taking the data of Dumont and colleagues into account, however, we assume that our TA-derived HCPs with a PLT concentration between 2353×10^3 and 3181×10^3 PLTs per μL are suitable for ex vivo storage for at least 2 days. However, further in vitro and in vivo studies are urgently needed to increase the feasibility of this collection method and to make definite recommendations for the shelf life of HCPs as used in our case.

REFERENCES

1. Bussel JB, Zacharoulis S, Kramer K, McFarland JG, Pauliny J, Kaplan C. Clinical and diagnostic comparision of neonatal alloimmune thrombocytopenia to non-immune cases of thrombocytopenia. Pediatr Blood Cancer 2005;45:176-83.
2. Mueller-Eckhardt C, Kiefel V, Grubert A, et al. 348 cases of suspected neonatal alloimmune thrombocytopenia. Lancet 1989;1:363-6.
3. Ouwehand WH, Smith G, Ranasinghe E. Management of severe alloimmunte thrmbocytopenia in the newborn. Arch Dis Child 2000;82:173-5.
4. Kaplan C. Alloimmune thrombocytopenia of the fetus and the newborn. Blood Rev 2002;16:69-72.
5. Davoren A, Curtis BR, Aster RH, McFarland JG. Human platelet antigen-specific alloantibodies implicated in 1162 cases of neonatal alloimmune thrombocytopenia. Transfusion 2004;44:1220-5.
6. Mandelbaum M, Koren D, Eichelberger B, Auerbach L, Panzer S. Frequencies of maternal platelet alloantibodies and autoantibodies in suspected fetal/neonatal isoimmune thrombocytopenia, with emphasis on human platelet antigen-15 alloimmunisation. Vox Sang 2005;89:39-43.
7. Berkowitz RL, Bussel JB, McFarland JG. Alloimmune thrombocytopenia: state of the art 2006. Am J Obstet Gynecol 2006;195:907-13.
8. Kaplan C, Murphy MF, Kroll H, Waters AH. Feto-maternal alloimmune thrombocytopenia: antenatal therapy with IVIgG and steroids—more questions than answers. European Working Group on FMAIT. Br J Haematol 1998;100: 62-5.
9. Murphy MF, Waters AH, Doughty HA, et al. Antenatal management of fetomaternal alloimmune thrombocytopenia—report of 15 affected pregnancies. Transfus Med 1994;4:281-92.
10. Ringwald J, Althoff F, Zimmermann R, et al. Washing platelets with new additive solutions—aspects on the in vitro quality after 48 hours of storage. Transfusion 2006;46:236-43.
11. Allen DJ, Samol J, Benjamin S, Verjee S, Tusold A, Murphy MF. Survey of the use and clinical effectiveness of HPA-1a/

5b-negative platelet concentrates in proven or suspected platelet alloimmunization. Transfus Med 2004;14:409-17.
12. German Medical Association and Paul Ehrlich Institute. Guidelines for the collection of blood and blood components and the use of blood products (Hemotherapy). Cologne: Deutscher Aerzteverlag; 2005.
13. German Society for Transfusion Medicine and Immunohematology. Performance of preparative cellular hemapheresis for the collection of blood cell concentrates. II. Recommendations for preparative white cell and platelet apheresis. Infusionsther Transfusionsmed 1998;25:376-82.
14. Guide to the preparation, use and quality assurance of blood components. Strasbourg: Council of Europe Press; 2006.
15. Ringwald J, Zingsem J, Zimmermann R, Strasser E, Antoon M, Eckstein R. First comparison of productivity and citrate donor load between the Trima version 4 (dual-stage filler) and the Trima Accel (single-stage filler) in the same donors. Vox Sang 2003;85:267-75.
16. Zingsem J, Weisbach V, Zimmermann R, Glaser A, Bunkens H, Eckstein R. Preparation of FFP as a by-product of plateletpheresis. Transfusion 2002;42:81-6.
17. Zingsem J, Zimmermann R, Weisbach V, Glaser A, van Waeg G, Eckstein R. Comparison of COBE white cell-reduction and standard plateletpheresis protocols in the same donors. Transfusion 1997;37:1045-9.
18. Lutz P, Dzik WH. Large-volume hemocytometer chamber for accurate counting of white cells (WBCs) in WBC-reduced platelets: validation and application for quality control of WBC-reduced platelets prepared by apheresis and filtration. Transfusion 1993;33:409-12.
19. Moroff G, Eich J, Dabay M. Validation of use of the Nageotte hemocytometer to count low levels of white cells in white cell-reduced platelet components. Transfusion 1994;34:35-8.
20. Davis KB, Slichter SJ, Corash L. Corrected count increment and percent platelet recovery as measures of posttransfusion platelet response: problems and a solution. Transfusion 1999;39:586-92.
21. Mosteller RD. Simplified calculation of body-surface area. N Engl J Med 1987;317:1090-9.
22. Kroll H, Maier HF. [Diseases of fetus and newborn]. In: Mueller-Eckhardt C, Kiefel V, editors. [Transfusion Medicine]. 3rd ed. Berlin: Springer Verlag; 2004.
23. Dumont LJ, Krailadsiri P, Seghatchian J, Taylor LA, Howell CA, Murphy MF. Preparation and storage characteristics of white cell-reduced high-concentrations platelet concentrates collected by an apheresis system for transfusions in utero. Transfusion 2000;40:91-100.
24. Ringwald J, Duerler T, Frankow O, et al. Collection of hyperconcentrated platelets with Trima Accel. Vox Sang 2006;90:92-6.
25. Ringwald J, Haager B, Krex D, et al. Impact of different hold time before addition of platelet additive solution on the in vitro quality of apheresis platelets. Transfusion 2006; 46:942-8.
26. Gambro BCT platelet storage recommendations. Lakewood (CO): Gambro BCT, Inc.; 2005.