Neonatal Polycythemia : Effects of Partial Exchange Transfusion Using Fresh Frozen Plasma, Haemaccel and Normal Saline

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Abstract

Background: Neonatal polycythemia remains a significant clinical problem in Thailand. Partial exchanges transfusion (PET) with fresh frozen plasma (FFP) has been the mainstay of management for this condition in Thailand. Since FFP is difficult to find in certain areas and can cause concerns of transfusion related diseases, this study was undertaken to investigate the possibility of using plasma substitute and normal saline (NSS) for PET in the newborn infant with polycythemia.

Objective:

1. To compare the rate and duration of decrease of venous hematocrit (Hct) before and after PET with FFP, Haemaccel and NSS.

2. To compare any complications from using FFP, Haemaccel and NSS such as coagulation defect, electrolytes change, etc. in PET.

Methods and Subjects: A randomized prospective trial was conducted in Neonatal Unit, Department of Pediatrics, Ramathibodi Hospital.

The first phase of study : July 1, 1993 to June 30, 1994 : randomized prospective trial using FFP or Haemaccel for PET in 26 newborn infants with polycythemia.

The second phase of study: July 1, 1994 to June 30, 1995 : consecutive enrollment trial using NSS for PET in 38 consecutive newborn infants with polycythemia.

Results: There was significant decrease in Hct in both groups after PET but there was no statistically significant difference in the rate of decrease of Hct.

There was no significant difference in biochemical profiles in both groups of infants 24 hours after PET.

In the NSS group, there was significant decrease of Hct level after PET. There was no significant change of biochemical profiles and coagulation activity in these patients 24 hours after exchange transfusion. There were 2 patients with complications related to umbilical venous catheter and PET.

Conclusion: Haemaccel and NSS can be safely used for PET to treat neonatal polycythemia. However, the attending physician should be aware of possible complications related to umbilical venous catheterization and PET.

Key word : Polycythemia, Partial Exchange Transfusion, Newborn

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Background

Polycythemia remains one of the common causes of admission to neonatal intensive care unit in Thailand. The incidences of neonatal polycythemia were 1.8 to 4 per cent[1]. Neonatal polycythemia is defined by the venous Hct that is higher than 65 per cent in the newborn infant. Neonatal polycythemia can cause morbidities including poor feeding, lethargy, altered level of consciousness, convulsions and apnea. Severe morbidities which occur from venous thrombosis include acute renal failure and cerebral infarction which may lead to neurological handicaps. Although those morbidities are relatively rare, all can be prevented with partial exchange transfusion (PET)[2-10].

In the past, PET with fresh frozen plasma (FFP) remains one of the most common and effective methods of management of neonatal polycythemia. However, FFP is not always available and also relatively expensive compared to normal saline (NSS). Giving FFP transfusion also carries the risk of transfusion related infections. Using certain plasma substitute such as Plasmanate®, which is a synthetic colloid, has proven effective[11]. Haemaccel, another plasma substitute is available in Thailand. The ingredients of Haemaccel are shown in Table 1. NSS has been proven equally effective with low complications and would be a perfect choice because of the cost, availability and safety. The umbilical venous catheter route for PET is best suited because it can be easily done anywhere in Thailand with little training or experience.

Table 1. The ingredients of Haemaccel.

Haemaccel :
3.5 per cent colloidal infusion solution for volume substitution
Active ingredient : Polygelin
Composition : 100 ml contain

	mmol	g
Na^+	145	3.33
K^+	5.1	0.20
Ca^{2+}	6.25	0.25
Cl	145	5.14

Traces of phosphate ions and sulphate ions, plus serionic polypeptides up to the isoionic point
Water for injections : 1,000 ml
Physio-chemical data :
Mean molecular weight : 35,000 Dalton
Relative viscosity (35°C) : 1.7 - 1.8
pH of the infusion solution : 7.3 ± 0.3

Population and study protocols

The first phase of the study was done to compare the effectiveness and safety of FFP and Haemaccel. The study was done in a prospective randomized controlled trial in newborn infants who were born during July 1, 1993 to June 30, 1994 in the newborn service of Department of Pediatrics, Ramathibodi Hospital.

1. All newborn infants with high risk of neonatal polycythemia (i.e. plethoric, intrauterine growth retardation, small for gestational age, hyperbilirubinemia or cyanosis) had a capillary Hct done and if the result was higher than 65 per cent then venous Hct was performed.

2. PET would be considered for the newborn infants if venous Hct was >70 per cent or if venous Hct was >65 per cent with the observed clinical symptoms of cyanosis, convulsions or apnea.

3. Those infants who required PET for therapy were randomized into two groups, one using FFP and another using Haemaccel.

4. Informed consent was obtained from parents who had treatment protocol explained to them and who were kept abreast of the baby's condition.

5. Data regarding the pregnancy, delivery, birth record were reviewed and collected.

6. PET *via* UVC was done using umbilical catheter size 5 or 8 F. The volume would be approximated using the following formula : Volume for exchange = BW x 80 x (actual Hct - desired Hct)/actual Hct.

Desired Hct was 55 per cent

7. Hct was checked at 2, 6, 12, and 24 hours after PET.

8. Blood for plasma biochemical profiles was collected pre, post and 24 hours post PET.

9. Oxygen saturation was continuously monitored before PET until one hour after the PET.

During the second phase of the study, all newborn infants in the neonatal service of Department of Pediatrics, Ramathibodi Hospital during July 1, 1994 to June 30, 1995 who required PET using the above mentioned criteria were consecutively enrolled to receive PET with NSS *via* UVC. Inform consent was obtained before the treatment. Coagulation profiles, platelet count, whole blood viscosity study using Wells Brookfield cone plate microviscometer[3] were also performed in the second phase

due to the concern regarding diluted coagulation factor.

Statistics

Student's *t*-test was used for comparison of continuous variables. Chi-square and Fisher's exact test was used for proportional variables. Statistical significance was accepted at $p < 0.05$.

RESULTS

Phase I

There were 26 newborn infants who required PET due to neonatal polycythemia during the 1-year period. Eleven received PET with FFP and 15 received Haemaccel. There was no statistical dif-ference between the clinical information for either group regarding birth weight, age, gestational age, Apgar score, sex or delivery methods (Table 2).

Table 2. Clinical information of FFP and Haemaccel groups.

Variable	FFP (n = 11) (mean ± SD)	Haemaccel (n = 15) (mean ± SD)	P value
Gestational age (wk)	37.9 ± 0.7	38 ± 2.12	NS
Birth weight (g)	2737 ± 579	3022 ± 990	NS
Age (h)	12.8 ± 27.8	16.6 ± 21.8	NS
Age of mother (yr)	28.4 ± 46.4	28.3 ± 4.1	NS
Sex, Male : Female	5 : 6	7 : 8	NS
Delivery, NL : C/S	8 : 3	9 : 6	NS

NL = normal labour, C/S Cesarean section

Means of Hct in FFP group was 75 per cent and Haemaccel group was 70 per cent. There were significant decrease of Hct to the target of 55 per cent in both groups. There was no significant difference in the value of Hct in the two treatment groups except at 2 hours of age in which FFP group had slightly lower Hct than Haemaccel group. (Table 3)

Serum sodium, chloride and calcium in Haemaccel group were significantly higher immediately after PET compared to FFP group but the level of those electrolytes remained in the normal range. Those differences, however, normalized without need for intervention 24 hours after PET.

Phase II

Thirty-eight infants were enrolled in the second phase of the study. Thirty-six or 94.7 per cent of the studied population had venous Hct > 70 per cent. Two or 5.3 per cent had venous Hct > 65 per cent. One patient had persistent hypoglycemia and one other patient had hyperbilirubinemia from polycythemia.

Levels of venous Hct were significantly lower in all babies after PET and the mean Hct at 24 hours after PET with NSS was 55.6 per cent (Table 3). There were no significant changes in the level of serum electrolytes, coagulation profiles pre- and post-PET. There was a significant decrease of blood viscosity after PET in 6 patients who were randomly measured (Table 4). There was one baby who developed necrotizing enterocolitis after PET *via* UVC. There was one baby who developed hemo-

Table 3. Serial central venous Hct (mean ± SD) before and after PET using FFP, Haemaccel and NSS.

	Before transfusion	After transfusion			
		2 hours	6 hours	12 hours	24 hours
FFP	74.6 ± 2.1	56.2 ± 2.9	55.1 ± 2.4	54.2 ± 1.9	56.7 ± 5.6
Haemaccel	72.6 ± 2.3	54.6 ± 5.9	57.6 ± 3.4	55.2 ± 2.3	54.1 ± 1.6
NSS	72.5 ± 2.3	60.6 ± 5.9	58.8 ± 5.3	56.3 ± 4.9	55.6 ± 4.2

Table 4. Blood viscosity pre- and post-PET with NSS in 6 randomly selected patients.

Shear rate (sec^{-1})	1.15	2.3	5.75	11.5	23	46	115	230
Blood viscosity pre PET	92.17	58.20	33.77	23.13	16.91	12.54	9.95	8.18
Blood viscosity post PET	75.33*	47.00*	25.10*	17.32*	13.02*	10.37*	7.89*	6.44*

* $p < 0.05$

rrhagic gastritis and blood coagulogram which was similar to hemorrhagic disease of the newborn. The baby was well afterward four hours after PET.

DISCUSSION

This study demonstrated that plasma substitute (Haemaccel) and NSS can safely be used for PET to treat neonatal polycythemia *via* UVC. One patient with NEC was related to the procedure of PET *via* UVC rather than the solution being used. There were no significant changes in the level of serum electrolytes, serum protein or coagulation profiles in those babies who received NSS. The whole blood viscosity was also significantly decreased but still abnormal for age. There was one study performed previously that also used NSS for PET but the investigator opted to use radial arterial catheter to draw the blood out and gave NSS *via* peripheral vein. No complications were observed. Black et al[1] had also observed cases of NEC post PET *via* UVC using FFP. Therefore, using FFP for PET would not decrease this complication. Hein[5] had suggested to use UVC to remove the blood and give NSS back to the baby *via* peripheral vein. He expected that this method would decrease the incidence of NEC. Furthur investigation is needed to confirm that recommendation. At the present time, our studies demonstrate that using NSS or Haemaccel instead of FFP via UVC can effectively manage neonatal polycythemia.

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REFERENCES

1. Black VD, Runiack CM, Lubchenko LO, et al. Gastrointestinal injury in polycythemic term infants. Pediatrics 1985; 76:225-31.
2. Singh M, Singhal PK, Paul VK, et al. Polycythemia in the newborn: do asymptomatic babies need exchange transfusion? Indian Pediatr 1990; 27: 61-5.
3. Thomas E, Wiswell MC, Deun CJ, et al. Neonatal polycythemia: frequency of clinical manifestations and other associated findings. Pediatrics 1986; 78:26-30.
4. Shohat M, Merlob P, Reisner SH. Neonatal polycythemia: I. early diagnosis and incidence relating to time of sampling. Pediatrics 1984; 73: 7-10.
5. Hein HA, Lathrop SS. Partial exchange transfusion in term, polycythemic neonate : Absence of association with severe gestrointestinal injury. Pediatrics 1987; 80:75-8.
6. Charlton V, Phibbs R. Peripheral venous partial exchange transfusion for neonatal polycythemia. Clin Pediatr 1980; 22:59-60.
7. Murphy DJ, Reller MD, Meyer RA, Kaplan S. Effects of neonatal polycythemia and partial exchange transfusion on cardiac function : an echocardiographic study. Pediatrics 1985; 76:909-13.
8. Goldberg K, Wirth FH, Hathaway WE, et al. Neonatal hyperviscosity : effect of partial plasma exchange transfusion. Pediatrics 1982; 69: 419-31.
9. Black VD, Lubchenco LO, Koops BL, Poland RL, Powell DP. Neonatal hyperviscosity : Randomized study of effect of partial plasma exchange transfusion on long-term outcome. Pediatrics 1985; 75:1048-53.
10. Oh W. Neonatal polycythemia and hyperviscosity. Pediatr Clin North Am 1986; 33:523-33.
11. Rosenkrantz TS, Oh W. Cerebral blood flow velocity in infants with polycythemia and hyperviscosity: effects of partial exchange transfusion with plasmanate. J Pediatr 1982; 101:94-8.

การรักษาภาวะเลือดข้นในทารกแรกเกิดด้วยการถ่ายเปลี่ยนเลือดแบบหาส่วน โดยการเปรียบเทียบการใช้พลาสม่าแช่แข็ง, ฮีแมคเซล และน้ำเกลือนอร์มัล

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ภาวะเลือดข้นในทารกแรกเกิดเป็นปัญหาทางคลินิกที่สำคัญในประเทศไทย การศึกษาโดยการถ่ายเปลี่ยนเลือดแบบบางส่วนโดยใช้พลาสม่าแช่แข็งนั้น เป็นวิธีการรักษาที่ใช้กันอย่างแพร่หลาย แต่พลาสม่าแช่แข็งอาจจะหาไม่ได้ในบางสถานที่ และสามารถแพร่เชื้อโรคบางชนิดที่ติดต่อทางเลือดได้ ได้ทำการศึกษาเพื่อทดสอบน้ำเกลือนอร์มัล และ Haemaccel เปรียบเทียบกับการใช้พลาสม่าแข็งในการถ่ายเปลี่ยนเลือด

จุดประสงค์

1. หาอัตราการลดลงของฮีมาโตคริต (Hct) ก่อนและหลังการเปลี่ยนถ่ายเลือด โดยใช้พลาสม่า น้ำเกลือนอร์มัล และ Haemaccel

2. เปรียบเทียบผลข้างเคียงจากการรักษา โดยใช้สารทั้ง 3 ชนิดข้างต้น เช่น ภาวะเลือดออกง่าย การผิดปกติของระดับเกลือแร่ในเลือด

วิธีการรักษา

ทำการศึกษาในผู้ป่วยเด็กทารกแรกเกิด ในโรงพยาบาลรามาธิบดี เป็น 2 ระยะดังนี้

ระยะที่ 1 1 กรกฎาคม 2536–30 มิถุนายน 2537 ทำการศึกษาในผู้ป่วยเด็ก 26 คน แบ่งเป็น 2 กลุ่ม เป็นการศึกษาแบบสุ่มกลุ่มผู้ป่วยโดยใช้พลาสม่าแช่แข็งเทียบกับ Haemaccel ในการเปลี่ยนถ่ายเลือด

ระยะที่ 2 1 กรกฎาคม 2537–30 มิถุนายน 2538 ทำการศึกษาผู้ป่วย 38 ราย โดยใช้สารน้ำเกลือนอร์มัลอย่างเดียว

ผลการศึกษา

ค่า Hct ในทุกกลุ่มรักษา มีการลดลงอย่างไม่มีความแตกต่างกันทางสถิติ ในทั้ง 3 กลุ่มผู้ป่วย ไม่มีความแตกต่างทางผลข้างเคียงจากการรักษาในทั้ง 3 กลุ่ม ในการศึกษากลุ่มน้ำเกลือนอร์มัล มีผู้ป่วย 2 คน มีอาการลำไส้น่าตายอย่างเฉียบพลัน คิดว่าเกี่ยวข้องกับสายน้ำเกลือที่ต่อกับหลอดเลือดดำสายสะดือ (UVC) 1 คน และอีก 1 คนมีเลือดออกในกระเพาะอาหาร

สรุปผลการศึกษา

สามารถใช้น้ำเกลือนอร์มัล, Haemaccel และพลาสม่าแช่แข็งทดแทนกันได้ สำหรับถ่ายเปลี่ยนเลือดเพียงบางส่วนผ่านหลอดเลือดดำสายสะดือในการรักาภาวะเลือดข้นในทารกแรกเกิด

คำสำคัญ : ภาวะเลือดข้นในทารกแรกเกิด การเปลี่ยนถ่ายเลือดเพียงบางส่วนโดยใช้น้ำเกลือนอร์มัล, ฮีแมคเซล และพลาสม่าแช่แข็ง

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