Placenta 36 (2015) 599–602

Contents lists available at ScienceDirect

Placenta

journal homepage: www.elsevier.com/locate/placenta

Intrauterine transfusion combined with partial exchange transfusion for twin anemia polycythemia sequence: Modeling a novel technique

F. Slaghekke [a,*], J.P.H.M. van den Wijngaard [b,c], J. Akkermans [a], M.J.C. van Gemert [b], J.M. Middeldorp [a], F.J. Klumper [a], D. Oepkes [a], E. Lopriore [d]

[a] Division of Fetal Medicine, Department of Obstetrics, Leiden University Medical Center, Leiden, The Netherlands
[b] Biomedical Engineering and Physics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
[c] Department of Clinical Chemistry and Laboratory Medicine, Leiden University Medical Center, Leiden, The Netherlands
[d] Division of Neonatology, Department of Pediatrics, Leiden University Medical Center, Leiden, The Netherlands

ARTICLE INFO

Article history:
Accepted 26 January 2015

Keywords:
Twin anemia polycythemia sequence
Intrauterine transfusion
Partial exchange transfusion
Mathematical model

ABSTRACT

Introduction: Twin anemia-polycythemia sequence (TAPS) is a newly described disease in monochorionic twin pregnancies, characterized by large inter-twin hemoglobin differences. Optimal management for TAPS is not clear. One of the possible treatment modalities is intrauterine blood transfusion (IUT) in the donor with or without combination of partial exchange transfusion (PET) in the recipient.
Methods: We applied a computational model simulation to illustrate the mechanism of IUT with and without PET in TAPS occurring after laser surgery for twin–twin transfusion syndrome (TTTS). Model simulations were performed with the representative anastomotic pattern as observed during laser intervention, and after placental dye injection.
Results: The model was tested against different cases where IUT was combined with PET for the treatment of post-laser TAPS. Model simulations using the observed anastomotic pattern showed a significant reduction of hyperviscosity in the recipient after IUT/PET compared to IUT without PET.
Discussion: In this model simulation we show that the addition of PET to IUT reduces the severity of polycythemia in the recipient. PET may thus be important to prevent complications of hyperviscosity.
Conclusion: This model simulation shows the beneficial effect of PET for the recipient in TAPS cases treated with IUT.

1. Introduction

Monochorionic twin pregnancies can be complicated by the twin anemia-polycythemia sequence (TAPS), which is a chronic form of feto-fetal transfusion. TAPS is characterized by large inter-twin hemoglobin (Hb) differences but without signs of the oligo-polyhydramnios sequence. TAPS placentas are characterized by the presence of only few, miniscule vascular anastomoses [1]. The incidence of TAPS varies between 1 and 5% in spontaneous TAPS [2–5] and up to 16% in post-laser TAPS [6,7]. TAPS can be diagnosed antenatally or postnatally. Prognosis of TAPS can vary from two healthy neonates with hematological problems to severe neonatal morbidity, such as limb necrosis, severe cerebral injury or perinatal death. Antenatal management options include expectant management, induction of labor, intrauterine blood transfusion (IUT) with or without combination of partial exchange transfusion (PET), selective feticide or (repeat) fetoscopic laser surgery [8–11]. Treatment with IUT at least temporarily improves the condition of the donor twin, however, the transfer of transfused red cells to the already polycythemic recipient may worsen its hyperviscosity and increases the risk for associated complications such as limb necrosis and severe cerebral injury [6,12]. The PET procedure implies replacement of the polycythemic fetal blood with saline solution and leads to a reduction of hyperviscosity. In this study we tested a model simulation against different cases of IUT in combination with PET. With this model we illustrate the mechanism of IUT with PET compared to IUT without PET.

2. Methods

We selected different post-laser TAPS cases treated with IUT in combination with PET with full details of vascular anastomotic pattern during laser treatment and

* Corresponding author. Division of Fetal Medicine, Department of Obstetrics, K6, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands. Tel.: + 31 (0) 71 5262896; fax: +31 (0) 71 5266741.
E-mail address: f.slaghekke@lumc.nl (F. Slaghekke).

http://dx.doi.org/10.1016/j.placenta.2015.01.194
0143-4004/

Table 1
Hematological measurements and management information.

GA (weeks)	Anatomic pattern during laser for TTTS	Intervention	Twin A Hb before	Twin A Hb after	Birthweight twin A	Amount of blood exchanged (ml)	Twin B Hb before	Twin B Hb after	Birthweight twin B	Amount of blood transfused (ml)
Case 1										
22 + 2 (laser for TTTS)	2 AV, 4 VA									
26 + 3		1st IUT & PET	18.2	15.0		32 out + 32 in	5.0	8.0		23 iv + 20 ip
27 + 5		2nd IUT & PET	17.4	13.9		38 out + 40 in	6.6	10.9		47 iv + 30 ip
28 + 6		3rd IUT & PET	16.3	14.6		26 out + 20 in	10.9	13.1		27 iv + 10 ip
31 + 5 (at birth)			23.4		1445 g	reticulocyte count 28‰	9.3		1715 g	reticulocyte count 115‰
Case 2										
21 + 5 (laser for TTTS)	4 AV, 3 VA									
23 + 4		1st IUT & PET	17.9	n/a		6 ml out, 5 ml in	1.9	7.5		N/A
24 + 4		2nd IUT & PET	19.3	11.2		50 ml	2.6	8.6		12 ml
25 + 6		3rd IUT & PET	18.6	17.6		30 ml out, 25 ml in	3.7	10.7		N/A
26 + 6		4th IUT & PET	20.6	13.1		94 ml out, 100 ml in	3.5	11.5		50 ml iv +30 IP
27 + 5 (at birth)			21.5		980 g	reticulocyte count 39‰	9.3		1235 g	reticulocyte count 143‰
Case 3										
25 + 1 (laser for TTTS)	4 AV, 4 VA									
27 + 2		1st IUT & PET	18.9	15.0		30 ml out, 30 ml in	4.3	9.3		30 ml IV + 25 ml IP
29 + 3		2nd IUT	–	–		–	7.0	9.3		20 ml IV + 30 ml IP
32 + 3 (at birth)			23.0		1664 g	reticulocyte count 43‰	12.8		1615 g	reticulocyte count 94‰
Case 4										
15 + 3 (laser for TTTS)	2 AV, 3 VA									
28 + 2		1st IUT & PET	18.2	14.7		55 ml out, 55 ml in	5.0	13.8		65 ml IV + 50 ml IP
29 + 1		2nd IUT & PET	17.8	14.6		57 ml out, 45 ml in	9.6	13.6		45 ml IV + 50 ml IP
31 + 1 (at birth)			26.1		1520 g	reticulocyte count 29‰	12.0		1759 g	reticulocyte count 108‰

GA: gestational age; AV: arterio-venous anastomosis; VA: veno-arterial; IUT: intrauterine transfusion, PET: partial exchange transfusion, Hb: hemoglobin (g/dL); iv: intravenous; ip: intraperitoneal.

from postnatal placental injection studies [13]. Details on IUT and PET were recorded, including the amount of blood transfused and exchanged. Cases were selected based on completeness of data (gestational age at laser, at re-intervention: IUT and PET and gestational age at birth, placenta anastomotic pattern at time of laser therapy, amount of transfused and exchanged blood, hemoglobin levels at time of IUT and PET and postnatal hemoglobin levels, birth weight and neonatal outcome). Simulations of the effect of IUT and PET were performed in our computational model of monochorionic twin pregnancies [11].

2.1. Mathematical model simulation

The model as used for the simulations was based on the previous twin–twin transfusion syndrome (TTTS) models with nonpulsating circulations [14,15] as was previously applied to predict development of hydrops in the TTTS recipient [16] and the presence of a discordant hematocrit in the presence of normal amniotic fluid volumes after incomplete laser therapy of vascular anastomoses [11]. In brief, the model applies 13 coupled differential equations for each twin to describe changes in volumes of fetal arterial and venous blood, volumes of interstitial, intracellular, and amniotic fluid, colloid osmotic pressures of fetal blood and interstitial fluid, osmolality of fetal blood and amniotic fluid, the concentration of vasoconstrictive peptides in the fetal blood, blood hematocrit, arterial wall elastin content, arterial wall thickness, as well as measures of brain and placental vascular resistances. The differential equations of the nonpulsatile model are programmed in Delphi 5.0 (Borland Interprise Corp., Cupertino, CA) and are numerically solved for 12–36 weeks with a time step of approximately 0.6 s. Input variables for computation of anastomotic flow include the type of anastomosis, i.e. arterio-venous (AV), veno-arterial (VA), arterio-arterial (AA) or veno-venous (VV) and the anastomosis resistances. Following the application of Ohm's law of each of the resistances, multiple parallel placental anastomoses of identical type can be computationally represented by a single corresponding replacement resistance. Laser intervention of a set of anastomoses combined with amnioreduction is simulated as cessation of fetofetal transfusion of blood and constituents through the anastomoses and the normalization of the recipient amniotic fluid volume. IUT as well as PET are simulated by instantaneous increase or replacement of blood volume and its constituents respectively with blood of normal properties.

3. Results

Four cases fulfilled the inclusion criteria and all required data were available for the model simulation. In one case IUT in combination with PET was performed four times, in one case three times and in two cases twice (Table 1). Overall perinatal survival was 88% (7/8). One donor (case #2) died after six days of life due to extensive cerebral injury. Detailed information regarding this case has been previously been reported [9]. The recipient in case #2 had normal cerebral ultrasound findings and was discharged from the hospital after a few weeks. All neonates in cases #1, # and #4 had normal cerebral ultrasound findings and were discharged from the hospital in good clinical condition.

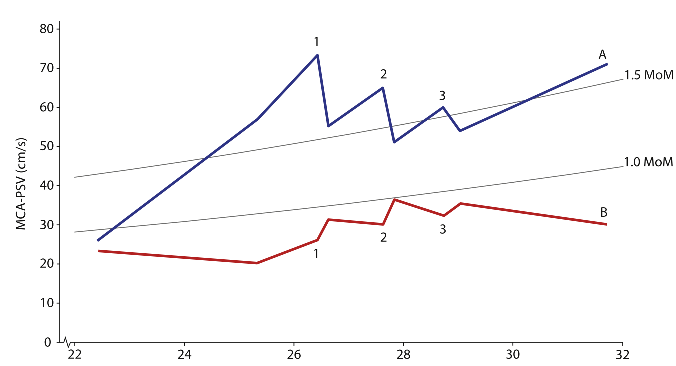

Fig. 1. Doppler measurements of Middle Cerebral Artery – Peak Systolic Velocity (MCA-PSV) in cm/sec and gestational age in weeks. In blue the MCA-PSV measurements of the ex-TTTS recipient and post-laser TAPS donor (A). In red the MCA-PSV measurements of the ex-TTTS donor and post-laser TAPS recipient (B). The numbers indicate the time points of intrauterine blood transfusion and partial exchange transfusion.