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Original Article

A prospective pilot study of fetoscopic laser surgery for twin-to-twin transfusion syndrome between 26 and 27 weeks of gestation



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ABSTRACT

Objective: The aim of this study is to clarify the feasibility and efficacy of fetoscopic laser photocoagulation of placental vascular communicating vessels (FLP) on twin–twin transfusion syndrome (TTTS) after 26 weeks of gestation.

Materials and Methods: This is a prospective pilot study investigating all cases of TTTS between 26 weeks and 27 weeks during 2012 and 2013 in Japan. The primary endpoints in this study were the feasibility of FLP and rate of harmful complications for the mother's health. Also, perinatal prognosis was investigated.

Results: Six cases were enrolled and underwent FLP. Two of the six cases were classified preoperatively as Quintero Stage II and four cases were Stage III. FLP was completely achieved in all six cases. No severe maternal complications were noted during and immediately after the surgery. All but one case continued the pregnancies > 14 days after FLP. The median gestational age at delivery was 33.4 weeks (28.0–36.6 weeks). All 12 fetuses survived at the 28th day in the neonatal period. No case was diagnosed with cerebral lesion at the neonatal period.

Conclusion: This prospective pilot study shows that FLP could be a therapeutic option for TTTS between 26 weeks and 27 weeks of gestation.

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Introduction

Twin-to-twin transfusion syndrome (TTTS) occurs in ~10% of monochorionic (MC) twin pregnancies and carries a high risk of perinatal morbidity and mortality [1,2]. The precise etiology of TTTS remains uncertain, although unbalanced blood flow between two fetuses via placental vascular anastomoses, resulting from a net transfusion of blood flow from the donor twin to the recipient twin, attributes the pathophysiology of TTTS. If left untreated, perinatal

mortality rates reach 90% [3]. Fetoscopic laser photocoagulation of placental vascular communicating vessels (FLP) has been proven as the best therapeutic option in TTTS with significant perinatal outcomes [4–7].

Most published studies on FLP for TTTS were limited to pregnancies treated before 26 weeks of gestation [5–8]. The reason for this limitation is that fetoscopic procedure itself was initially considered as a more invasive therapeutic approach than palliative amnioreduction or elective delivery if gestational age was enough to gain fetal viability [9]. However, fetoscopic procedure has gained wide acceptance almost two decades after the first publications on FLP for TTTS [10]. Recently a few investigators have reported the introduction of FLP for TTTS beyond 26 weeks of gestation [11], but there is still little evidence to support the feasibility and efficacy of FLP after 26 weeks of gestation.

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The aim of this study was to evaluate the feasibility and efficacy of FLP for TTTS diagnosed after 26 weeks of gestation.

Materials and methods

This is a prospective pilot study, investigating all cases of MC twin pregnancies complicated with TTTS between 26 + 0 weeks and 27 + 6 weeks of gestation, who underwent FLP at three institutions in Japan from January 2012 to December 2013. The study was approved by the ethics committee in each institution and patients provided written informed consent. This clinical study was registered under Number UMIN000007208 (<http://www.umin.ac.jp/>).

Gestational age was calculated by the last menstrual period and corrected by the first trimester ultrasound. Chorionicity was established at the first trimester ultrasound. The diagnostic criteria of TTTS were defined as polyhydramnios with a maximum vertical pocket (MVP) ≥ 10.0 cm in the recipient fetus and oligohydramnios with an MVP ≤ 2.0 cm in the donor fetus according to the Eurofetus criteria [9]. Preoperative ultrasound evaluations including fetal biometry, amniotic fluid volume estimation, and pulsed Doppler examination were performed to stage patients according to the Quintero staging system [12]. FLP was performed on the basis of previously described methods [7,13,14]. A 3.5-mm diagnostic fetoscope and a 3-mm operating fetoscope (Richard Wolf, Knittlingen, Germany) or a 2-mm fetoscope with a 3-mm cannula (Karl Storz, Tuttlingen, Germany) were used according to the physician's predilection. All vascular anastomoses were interrupted selectively using a Nd:YAG laser. The amniotic fluid was subsequently drained through the cannula until the MVP reached < 8 cm. All patients gave written informed consent to undergo FLP. Perioperative tocolysis as well as prophylactic antibiotics were provided. Postoperative care with weekly ultrasound evaluation, including pulsed Doppler assessment and delivery and neonatal management was provided by the referring perinatal centers. Delivery was determined according to obstetrical indications by the attending physician. Neonates were routinely examined by cerebral ultrasonography. Magnetic resonance imaging was performed when clinical examination or ultrasonography was suggestive of an abnormality. All infants were examined by neonatologists at 28 days of age. A color dye injection test of the placenta was prospectively planned to investigate the presence or absence of residual vascular anastomoses.

The primary endpoints in this study were the feasibility of FLP and the rate of harmful complications for the mother's health. Other measurement outcomes were the rate of surviving twins, the survival of at least one twin, and the rate of major neurological complications in survivors at 28 days of age. Major neurological complications were defined as severe intraventricular hemorrhage (Grade 3 or 4) and/or cystic periventricular leukomalacia.

Results

Six cases were enrolled and underwent FLP during the study period. Perioperative characteristics are presented in Table 1. Four of six cases were classified as Quintero Stage III, and intravenous administration of tocolytic agents such as magnesium sulfate and/or ritodrine hydrochloride was given in four patients due to threatened premature labor. FLP was completed for all six cases without major maternal complications during the surgery. The median operating time was 47 minutes (range, 25–72 minutes).

Detailed perinatal outcomes are presented in Table 2. No fetal demise was noted in all six cases. The median gestational age at delivery was 33.4 weeks (range, 28.0–36.6 weeks). All but one case delivered > 2 weeks after FLP. One patient delivered 3 days

Table 1
Perioperative characteristics of six patients.

Maternal age	30.7 (26–39)
Para	2 (0–4)
ART, n	0
Quintero stage, n	
I	0
II	2
III	4
IV	0
No. of gestational wks at FLP	26.9 (26.1–27.6)
MVP in recipient sac (cm)	11.4 (10.2–12.0)
Tocolysis before operation	4 (67)
Operation time (min)	47 (25–72)
Anterior placenta	1 (17)
Volume of amniotic fluid reduction (mL)	2110 (1050–3350)

Data are presented as median (range) or n (%), unless otherwise indicated.

ART = assisted reproductive technology; FLP = fetoscopic laser photocoagulation of placental vascular communicating vessels; MVP = maximum vertical pocket.

after FLP because of tocolysis failure followed by maternal pulmonary edema. This required intensive care but the patient improved soon after the delivery (Case 6). Five patients could continue pregnancy > 2 weeks after the surgery and improvement of polyhydramnios and oligohydramnios in each twin was confirmed. The incidence of preterm delivery < 32 weeks was 50% ($n = 3$). The number of extremely low birth weight infants (< 1000 g) was two (17%) of 12 live-born twins. Overall, perinatal survival at 28 days was 100%. Four twins were complicated with respiratory distress syndrome (Case 3 and 6). One twin born with extremely low birth weight suffered with small-intestine perforation (Case 6). All twins survived without neurological complications at 28 days of age. Pathological examination of delivered placenta showed no residual anastomoses in all cases.

Discussion

This study shows that FLP for TTTS after 26 weeks of gestation is feasible and provides a good prognosis compared with standard therapeutic strategy for TTTS before 26 weeks of gestation [7]. As a result, all twins survived after FLP.

Recently, several studies on FLP for TTTS after 26 weeks of gestation have been published in the literature. Middeldorp et al [11] reported the possibility of FLP instead of amnioreduction in 2007, and then only two reports were published. Valsky et al [15] reported 28 cases of FLP between 26 + 0 weeks and 28 + 6 weeks of gestation with a 92% rate of at least one survivor and other reports on 18 cases also showed a 94% rate of at least one survivor [16]. Our results were similar to these results. In these reports, gestational age at delivery ranges from 31 weeks to 33 weeks of gestation, which is compatible with our results.

We were initially concerned with surgical and perinatal complications, but these complications were less than anticipated. In fact, premature rupture of membrane at less than 32 weeks occurred in two of six cases, resulting in premature delivery before 32 weeks, but this was compatible with previous reports. Unfortunately, one case resulted in early delivery (3 days after FLP). In this case, more than one tocolytic agent had been administered even before FLP, and tocolysis failure was not considered preventable. Most of our cases were complicated with premature preterm labor and amnioreduction for the improvement of polyhydramnios was required, in which the median volume of reduced amniotic fluid was > 2000 mL. This might indicate that TTTS after 26 weeks could manifest more typical features of twin polyhydramnios–oligohydramnios sequence than that

Table 2
Perinatal outcome.

Case	Quintero stage	GA at FLP	GA at delivery	Interval from FLP to delivery (d)	Reason for delivery	Recipient Twin		Donor Twin		survival (n)
						BW (g)	complication	BW (g)	complication	
1	3	26.1	36.0	69	PIH	2292	—	2262	—	2
2	3	26.1	36.6	73	planned delivery	2170	—	2580	—	2
3	2	26.7	30.0	23	PROM	1310	RDS	1400	RDS	2
4	3	27.7	30.9	22	PROM	1612	—	1806	—	2
5	3	27.0	36.4	66	tocolysis failure	2154	—	2166	—	2
6	2	27.6	28.0	3	tocolysis failure, pulmonary edema	822	RDS, small-intestine perforation	977	RDS	2

BW = birth weight; FLP = fetoscopic laser photocoagulation of placental vascular communicating vessels; GA = gestational age; PIH = pregnancy-induced hypertension; PROM = premature rupture of membrane; RDS = respiratory distress syndrome.

before 26 weeks, and could have more maternal complications such as premature preterm labor.

In this study the criterion of TTTS for FLP was changed from our previous study, which focused on TTTS between 26 weeks and 27 weeks of gestation [7]. Specifically, polyhydramnios of the recipient twin was defined as MVP > 10 cm. The reason for this was because according to Eurofetus criteria, 8 cm is not considered to be enough to manifest clinical features of the recipient twin [9].

A limitation of our study is that the number of cases is small. Precise prevalence of TTTS after 26 weeks is still unclear but a number of cases are limited. In the 2 years of the study period, we enrolled almost 200 cases of TTTS before 26 weeks treated with FLP (unpublished data). This might imply the rarity of the cases.

In conclusion, our prospective pilot study shows that FLP could be a therapeutic option for TTTS between 26 weeks and 27 weeks of gestation.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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