Evaluation of the Utility of in utero Treatment of Twin Anemia-Polycythemia Sequence

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Key Words

Twin anemia-polycythemia sequence · Twin pregnancy · Monochorionic diamniotic twin pregnancy · Laser coagulation · Fetal transfusion

Abstract

Objective: The aim of this study is to evaluate the interest in the in utero treatment of twin anemia-polycythemia sequence (TAPS). **Methods:** The obstetrical and neonatal data on all cases of TAPS followed up in our institution between 2006 and 2013 were reviewed. Statistical analyses were conducted using Bayesian methods. **Results:** Twenty cases of TAPS were included. Laser therapy or intrauterine transfusion (IUT) was performed on the donor twin in 9 cases. Eleven cases were included in the 'nontreated' group (managed expectantly or diagnosed at birth). The gestational age at diagnosis was lower in the group with treated TAPS [difference (diff) = -22.20 days (-57.13, 14.28), probability (Pr) (diff >0) = 10.6%]. The rate of preterm premature rupture of membranes was higher in the group with treated TAPS [diff = 22.5% (-14, 57), Pr (diff >0) = 89%], but overall mortality was similar. The interval between diagnosis and delivery was longer [diff = 44.37 days (9.41, 77.90), Pr (diff >0) = 99.2%], the TAPS resolution rate was higher [diff = 49.9% (12, 81), Pr

(diff >0) = 99.4%], and the neonatal transfusion rate was lower [diff = -30.5% (-60, 0), Pr (diff >0) = 2.6%] in the treated group. **Conclusion:** In utero treatment for TAPS is associated with a higher resolution rate of TAPS and a longer time between diagnosis and birth, but overall mortality is the same as with expectant management.

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Introduction

Twin anemia-polycythemia sequence (TAPS) is a complication of monochorionic diamniotic twin pregnancies first described in 2007 by Lopriore et al. [1]. Its pathology is characterized by an intertwin difference in hemoglobin levels. It may be diagnosed either in the antenatal or the postnatal period and presents a typical angioarchitecture (slender and rather scanty arteriovenous anastomoses) [2]. It is a heterogeneous disorder, both in terms of its mode of onset [either after laser treatment of twin-twin transfusion syndrome (TTTS) or spontaneously] and its severity. There is no consensus about its antenatal management, and different therapeutic alternatives have been described: simple surveillance, intrauterine transfusion (IUT) of the anemic fetus possibly combined with partial

Table 1. Pre- and postnatal classification of TAPS [2]

	Antenatal stage: findings at Doppler ultrasound examination	Postnatal stage: intertwin Hb difference, g/dl
Stage 1	MCA-PSV donor >1.5 MoM and MCA-PSV recipient <1 MoM without other signs of fetal compromise	>8.0
Stage 2	MCA-PSV donor >1.7 MoM and MCA-PSV recipient <0.8 MoM without other signs of fetal compromise	>11.0
Stage 3	As stage 1 or 2, with cardiac compromise of the donor, defined as critically abnormal flow	>14.0
Stage 4	Hydrops of donor	>17.0
Stage 5	Intrauterine demise of one or both fetuses preceded by TAPS	>20.0

MoM = Multiple(s) of the median; Hb = hemoglobin.

exchange transfusion in the recipient, laser coagulation of the placental anastomoses, selective termination of pregnancy or fetal extraction [2–11]. On account of the low incidence of TAPS (1–5% of monochorionic diamniotic twin pregnancies for spontaneous TAPS [12–15] and 2–13% for iatrogenic TAPS [4, 14–16]), therapeutic options have been presented only in case reports or small-size descriptive cohorts. The objective of our study was to examine obstetrical and neonatal outcomes depending on whether or not an antenatal treatment (IUT or laser) had been provided in a series of TAPS.

Materials and Methods

We carried out a single-center prospective cohort study, with enrollment of all monochorionic diamniotic twin pregnancies complicated by TAPS diagnosed ante- or postnatally and managed at the gynecology and obstetrics hub of the Strasbourg University Teaching Hospitals between December 2006 and August 2013.

The diagnostic criteria for TAPS selected were those drawn up by Slaghekke et al. [2]. In the antenatal period, they associate the absence of twin oligo-polyhydramnios sequence with measurement of a middle cerebral artery peak systolic velocity (MCA-PSV) >1.5 multiples of the median in one fetus (anemic, donor) and <1 multiple of the median in the other fetus (polycythemic, recipient). The MCA-PSV was measured using the technique described by Mari et al. [17] by means of a Voluson 730 or E8 General Electric® device. In the postnatal period, the diagnosis is based on an intertwin hemoglobin difference of >8 g/dl combined with a reticulocyte ratio of >1.7 or the finding of inframillimetric anastomoses. Cases that showed discrepant hemoglobin levels at birth of >8 g/dl but did not meet the other postnatal criteria were also enrolled in the study if there was a strong clinical impression and no evidence of an acute peripartum TTTS [18]. The severity of TAPS was defined using the classification by Slaghekke et al. [2] (table 1).

The follow-up of each monochorionic diamniotic pregnancy consisted of an ultrasound every 2 weeks. In the case of a diagnosis of TAPS before 32 weeks of gestation (WG), in utero treatment was proposed for TAPS stage 3 or 4 or for TAPS stage 1 or 2 with rapid aggravation. As soon as it had been decided to treat a case antenatally, we opted for fetoscopy with laser coagulation of the placental anastomoses, because this is the only causative treatment. For late cases, and if the technical conditions were not favorable (anterior-lying placenta with anticipated incorrect access of the vascular equator and, consequently, risk of incomplete surgery), IUT was performed. After 32 WG, the therapeutic options were expectant management or delivery. Each case was presented at the weekly meetings of the pluridisciplinary prenatal diagnosis center (CPDPN) to validate the in utero management. Two physicians (R.F. and A.-S.W.) performed IUT and laser surgery; they are both well trained in fetoscopic procedures.

The laser photocoagulation technique has already been described in a previous paper [19]. Amniocentesis was always performed to facilitate access to the vascular equator. The preferred photocoagulation technique was complete coagulation of the vascular equator (Solomon technique) [20, 21]. In the case of a technical difficulty, the selective technique was adopted [22]. Follow-up checks of fetal vitality and TAPS status were carried out 24 and 48 h postoperatively, at 1 week and, superseded by conventional checkups, every 2 weeks. For IUT, the sedation and anesthesia protocol was similar to that followed for laser photocoagulation. The procedure was always carried out with a pediatrician being present. Access was by direct transabdominal needling, with puncture of the umbilical vein at the cord insertion. A 20-gauge needle was used for initial sampling of blood (5–10 ml) to obtain the hemoglobin level. Fetal immobilization was obtained by curarization (Nimbex® at a dose of 0.15 mg/kg estimated fetal weight). Transfusion was then carried out using leukocyte-free, irradiated, CMV-negative, 0 rhesus-negative red cell concentrates compatible with the maternal blood group, the volume being calculated on the basis of the gestational age and initial hemoglobin level. MCA-PSV was checked the day after the procedure, at 7 days and every week to 2 weeks thereafter.

Fig. 1. Description of the study population. IUFD = Intrauterine fetal demise; Hb = hemoglobin. * The hematological data on the fetus that was subject to feticide during cesarean section and those on his co-twin were retained for analysis.

After delivery, photographs of both surfaces of the placenta were taken using a Sony-DSC-W220 digital apparatus (12.1 megapixels) after injection of a coloration dye. The placental weight of each child and the number of arteriovenous anastomoses were gathered.

Data on demographics and antenatal care as well as obstetrical and neonatal outcomes were collected prospectively. The term ‘overall mortality’ was used to describe the sum of in utero mortality and neonatal mortality (within 28 days of birth). Unequal sharing was defined by a ratio of the weights of the two hemiplacentas of >1.5 . A difference of $>20\%$ in weight between the two neonates signaled a birth weight discordance [23]. The data were analyzed and compared between ‘treated’ TAPS and ‘nontreated’ TAPS.

Continuous variables are expressed as means (μ) and standard deviations (σ or SD). Categorical variables are expressed as numbers and percentages. Statistical analyses were conducted using Bayesian methods [24, 25] with R 3.0.0 software and all the required packages in their latest updates at the time of analysis as well as WinBUGS software (estimation using Markov chain Monte Carlo with Gibbs sampling). After a burn-in of 5,000 updates, 100,000 iterations were performed and convergence was checked using trace plots of the sample values for each iteration. Beta distributions $Be(a,b)$ were used to estimate proportions, while means were estimated using normal distribution $N(\mu, \sigma)$. If available, results from previous studies were used to provide informative Bayesian priors. Studies in which some of our cases had already been reported on could not be used as priors to avoid the duplication of data [6, 26]. In the absence of prior information for the estimation of a proportion, a noninformative $Be(1,1)$ prior was adopted. For the estimation of a mean, the prior was derived from the data (empirical Bayes methods) [27]. The same prior was used for both groups in order to minimize the difference of means.

Each result is presented as a difference (diff) [(result of treated group) – (result of nontreated group)] with a 95% credibility interval and a probability (Pr) of exceeding 0 (or 1 for an OR). The priors are presented in supplementary table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000380822). This study received the authorization of the French Commission Nationale de l’Informatique et des Libertés (CNIL) and is registered as No. 1728548.

Results

Our patient population is described in figure 1. In all, 20 patients developed TAPS during the inclusion period, i.e. a global incidence of 4.6% was calculated (433 patients followed up for monochorionic diamniotic twin pregnancy during the inclusion period); 10 had spontaneous TAPS and 10 iatrogenic TAPS after laser. The diagnosis was made in the antenatal period in 17 cases (85%) at a mean gestational age of 24.9 ± 5.9 WG. In utero management included laser treatment in 7 cases (41.1%; 5 photocoagulations using the Solomon technique and 2 selective photocoagulations), IUT in 2 cases (11.8%), expectant management in 5 cases (29.4%), fetal extraction after corticosteroid therapy for pulmonary maturation in 2 cases and as an emergency in 1 case (17.6%; abnormal fetal heart rhythm in the anemic fetus). The 3 cases diagnosed in the postnatal period were included in the nontreated

Table 2. Maternal and diagnostic data for comparisons between the treated and the nontreated group

	Laser (n = 7)	IUT (n = 2)	Treated TAPS (n = 9)	Nontreated TAPS (n = 11)	Statistical analysis, diff (95% CI), Pr (diff >0) or OR (95% CI), Pr (OR >1)
Age, years	31.1±2.5	28±2.8	30.4±2.8	28.4±4.7	2.07 (−1.46, 5.61), 88%
Parity ≥1	6 (85.7)	2 (100)	8 (88.8)	3 (27.3)	51.1% (16, 79), 99.7%
BMI	21.9±5.2	24±5.7	22.3±5.1	24.4±5.1	−2.04 (−6.79, 2.76), 18.5%
GA at diagnosis, WG	22.3±3.6	26±1.3	23.1±3.6	27±7.3	−3.2 (−8.2, 2), 10.6%
Spontaneous TAPS	5 (71.4)	0 (0)	5 (55.6)	5 (45.4)	8.6% (−31, 46), 67.0%
Iatrogenic TAPS	2 (28.6)	2 (100)	4 (44.4)	6 (54.6)	−8.6% (−46, 31), 33.3%
Stage at diagnosis – prenatal					
1	3 (42.8)	1 (50)	4 (44.4)	4 (36.3)	
2	2 (28.6)	1 (50)	3 (33.3)	2 (18.2)	OR = 0.77 (0.24, 2.41),
3	2 (28.6)	0 (0)	2 (22.2)	1 (9.1)	32.6% (prenatal stage)
4	0 (0)	0 (0)	0 (0)	1 (9.1)	
Stage at diagnosis – postnatal					
1	–	–	–	1 (9.1)	–
2	–	–	–	1 (9.1)	–
3	–	–	–	0 (0)	–
4	–	–	–	1 (9.1)	–

Values denote means ± SD or n (%) unless specified otherwise. BMI = Body mass index; GA = gestational age; 95% CI = 95% credibility interval.

group. Of these 3 cases, 2 did not strictly meet all the diagnostic criteria. They were included because the clinical presumption of the diagnosis was strong. Indeed, there was a discrepancy in the hemoglobin levels of >8 g/dl, the two-toned placental appearance – which is typical of TAPS [6] – was present, and we found at least 1 arterio-venous anastomosis per placenta. Besides, delivery took place by cesarean section, which does not suggest an indication of acute peripartum transfusion syndrome. Ultimately, 9 cases of TAPS were included in the treated group and 11 in the nontreated group.

The maternal and diagnostic features of TAPS are displayed in table 2. The obstetrical and neonatal data for the entire cohort are reported in table 3. Table 4 concerns the subgroup of pregnancies with two live fetuses: 3 cases of pregnancy complicated by intrauterine fetal demise of one or both twins were excluded from the analysis, whereas the weight and hematological data on a twin pair of which the anemic fetus was subject to feticide during cesarean section were retained for the analysis. The gestational age at the time of diagnosis, in the event of antenatal diagnosis, was 23.1 ± 3.6 WG in treated TAPS versus 27 ± 7.3 WG in nontreated TAPS, with an estimated difference of −3.2 WG (−8.2, 2) [Pr (diff >0) = 10.6%]. The two groups were comparable with regard to the diagnostic stage in the antenatal

period as well as the proportion of spontaneous and iatrogenic TAPS. The rate of preterm premature rupture of the membranes (PPROM) was 44.4% in the treated TAPS group versus 18.2% in the nontreated TAPS group, with an estimated difference of 22.5% (−14, 57) [Pr (diff >0) = 89.0%]. The mean gestational age at delivery (or miscarriage) was 33.4 ± 3 WG in the event of treatment versus 30.4 ± 5.7 WG in the absence of treatment, with an estimated difference of 2.8 WG (−1.1, 6.5) [Pr (diff >0) = 92.4%]. The interval between diagnosis and delivery (or miscarriage) was longer for treated TAPS (10.3 ± 5.7 vs. 2.9 ± 4.1 WG for the other group), with an estimated difference of 6.3 WG (1.3, 11.1) [Pr (diff >0) = 99.2%]. At birth, the rate of TAPS resolution was greater in the event of treatment (71.4 vs. 10% in the absence of treatment), with an estimated difference of 49.9% (12, 81) [Pr (diff >0) = 99.4%, OR = 12.65 (1.7, 155)]. In the treated group, the intertwin hemoglobin difference was 6.2 ± 8.3 g/dl (vs. 13.3 ± 5.6 g/dl in the other group), with an estimated difference of −7.17 g/dl (−14.78, 0.46) [Pr (diff >0) = 3.2%]. Transfusion of the anemic infant during hospitalization was necessary in 89% of the cases in the nontreated TAPS group (vs. 57% in the treated TAPS group), with an estimated difference of −30.5% (−60, 0) [Pr (diff >0) = 2.6%, OR = 5.17 (0.99, 32.34)]. Overall mortality was 17% in the treated and 23% in the nontreated TAPS

Table 3. Obstetrical data for comparisons between the treated and the nontreated group

	Laser (n = 7)	IUT (n = 2)	Treated TAPS (n = 9)	Nontreated TAPS (n = 11)	Statistical analysis, diff (95% CI), Pr (diff >0)
PPROM	4 (57.1)	0 (0)	4 (44.4)	2 (18.2)	22.5% (-14, 57), 89.0%
GA at birth, WG	33.9±3.4	32.1±1	33.4±3	30.4±5.7	2.8 (-1.1, 6.5), 92.4%
Time between diagnosis and birth, WG	11.6±6.4	6.1±0.3	10.3±5.7	2.9±4.1 ^a	6.3 (1.3, 11.1), 99.2%
Live births					
Anemic	5/7 (71.4)	2/2 (100)	7/9 (78)	9/11 (82)	-7.3% (-28, 14), 23.9%
Polycythemic	7/7 (100)	2/2 (100)	9/9 (100)	10/11 (91)	-2.0% (-18, 15), 38.5%
Total	12/14 (85.7)	4/4 (100)	16/18 (89)	19/22 (86)	-6.6% (-19, 7), 15.1%
Overall mortality					
Anemic	3/7 (42.9)	0/2 (0)	3/9 (33)	3/11 (27)	13.1% (-11, 36), 86.1%
Polycythemic	0/7 (0)	0/2 (0)	0/9 (0)	2/11 (18)	-2.3% (-21, 15), 40.1%
Total	3/14 (21.4)	0/4 (0)	3/18 (17)	5/22 (23)	0 (-13, 13), 49.6%
Both children alive (day 28)	4/7 (57.1)	4/4 (100)	6/9 (67)	8/11 (73)	-6.6% (-28, 15), 27.1%
At least one child alive (day 28)	7/7 (100)	4/4 (100)	9/9 (100)	9/11 (82)	6.8% (-4, 20), 89.7%

Values denote means ± SD or n (%) unless specified otherwise. GA = Gestational age; 95% CI = 95% credibility interval.

^a n = 8; cases diagnosed postnatally excluded.

Table 4. Obstetrical and neonatal data (pregnancies with fetal loss excluded)

	Laser (n = 5/N = 10)	IUT (n = 2/N = 4)	Treated TAPS (n = 7/N = 14)	Nontreated TAPS (n = 10/N = 19 ^a)	Statistical analysis, diff (95% CI), Pr (diff >0)
GA at birth, WG	32.3±2	32.1±1	32.3±1.7	32±2.1	0.3 (-1.7, 2.1), 61.3%
Time between diagnosis and birth, WG	9±5.3	6.1±0.3	8.1±4.6	3±4.9 ^b	4.4 (-0.5, 9), 96.3%
Child born after cesarean section	7/10 (10)	2/4 (50)	9/14 (64.3)	19/19 (100)	-3.3% (-21, 15), 35.2%
Birth weight, g					
Anemic	1,529±464	1,288±187	1,460±404	1,307±378	123.65 (-232.7, 471.5), 76.4%
Polycythemic	1,686±302	1,525±233	1,640±276	1,619±462	15.7 (-320.8, 345.3), 54.4%
Birth weight discordance	2/5 (40)	0/2 (0)	2/7 (29)	6/10 (60)	-21.6% (-54, 13), 10.8%
Unequal sharing	0/3 (0)	1/2 (50)	1/5 (20)	6/10 (60)	-29.6% (-67, 13), 8.9%
Hb, g/dl					
Anemic	12.8±6.4	10.2±6.9	12±6	7.2±2.5	4.75 (-0.54, 9.97), 96.4%
Polycythemic	17.3±3	19.7±6.6	18±3.8	20.5±3.6	-2.56 (-6.48, 1.33), 9%
Hb discordance >8 g/dl	1/5 (20)	1/2 (50)	2/7 (28.6)	9/10 (90)	-49.9% (-81, -12), 0.6%
Hb delta, g/dl	4.8±7.1	9.6±13.5	6.2±8.3	13.3±5.6	-7.17 (-14.78, 0.46), 3.2%
Reticulocyte ratio	0.8±0.4	1.1±0.5	0.9±0.4	1.6±0.5	-0.7 (-0.46, 0.3), 33.3%
Postnatal stage					
No TAPS	4/5 (80)	1/2 (50)	5 (71.4)	1 (10)	49.9% (12, 81), 99.4%
1	0 (0)	0 (0)	0 (0)	2 (20)	-
2	0 (0)	0 (0)	0 (0)	2 (20)	-
3	0 (0)	0 (0)	0 (0)	1 (10)	-
4	1 (20)	1 (50)	2 (28.6)	4 (40)	-
Blood transfusion – anemic	2/5 (40)	2/2 (50)	4/7 (57.1)	8/9 (88.9)	-30.5% (-60, 0), 2.6%
Exchange transfusion – polycythemic	0/5 (0)	1/2 (50)	1/7 (14.3)	4/10 (40.0)	-29.7% (-57, 1), 2.8%

Values denote means ± SD or n (%) unless specified otherwise. n = Number of cases; N = number of newborns; GA = gestational age; Hb = hemoglobin; 95% CI = 95% credibility interval.

^a The hematological data and weight of the fetus that was subject to feticide during cesarean section and those of his co-twin were retained for analysis.

^b n = 7; cases diagnosed postnatally excluded.

Fig. 2. Evolution of MCA-PSV. **a** Polycythemic twins in expectant management. **b** Anemic twins in expectant management. **c** Polycythemic twins treated with IUT. **d** Anemic twins treated with IUT. **e** Polycythemic twins after laser. **f** Anemic twins after laser. † Intrauterine fetal demise. * Delivery.

group. A nil estimated difference was retrieved after integration of priors [i.e. the priors pejorated our result; estimated difference = 0% (−13, 13), Pr (diff > 0) = 50.4%].

The changes in MCA-PSV in the polycythemic and anemic fetuses in relation to each therapeutic option (expectant management, IUT or laser) are shown in figure 2. In the expectant management group, the data concern 4

of the 5 cases (a single measurement was made for the fifth case prior to delivery). For the cases treated with laser, the first measurement corresponds to the MCA-PSV before laser treatment. Three patients were referred back to their gynecologist for ongoing surveillance (cases No. 2, 4 and 7). For the other 4 patients, delivery took place at most 2 weeks after the last measurement.

Of the 7 cases of TAPS treated with laser, 3 placentas were not exploitable. In 2 cases, maceration occurred due to in utero death of one of the two fetuses. An analysis of the third placenta was impossible because of a fixation error; unfortunately, this was the single case in which there was a difference in hemoglobin level at birth, reflecting a failure of laser photocoagulation. Of the 13 cases of TAPS not treated with laser, 12 placentas could be analyzed (1 case was excluded because of early in utero death of both fetuses). Comparative analysis revealed an absence of residual anastomoses in the 4 cases treated with laser, whereas arteriovenous anastomoses were detected in 75% of the cases of nontreated TAPS [estimated difference = 54.6% (12, 84), $Pr(>0) = 99.3\%$, $OR = 18.48 (1.65, 665.37)$].

Discussion

Our study suggests that antenatal treatment resolves most cases of TAPS and prolongs the interval between diagnosis of TAPS and delivery at the expense of a rise in PPRM. Overall, there was no difference in terms of overall mortality.

As far as we know, there are limited data in the literature that would enable a rigorous evaluation of the utility of antenatal therapy of TAPS; this is due to the rarity of this sequence and the lack of randomized studies. A multicenter study (including some of our data) on the feasibility of laser for treating TAPS has recently been published [26]. Rather than opting for a specific treatment, this study examined the utility of a therapeutic strategy for treating TAPS with laser or IUT depending on local conditions. Indeed, although laser has the advantage of being an etiological treatment, technical conditions are such that it is not always feasible; IUT would then appear to be an alternative, even if it is only a purely symptomatic treatment.

Our study did not show any benefits of antenatal treatment with regard to fetal and neonatal mortality. Nevertheless, we found that in the treated TAPS group, the rate of TAPS resolution was higher, the interval between diagnosis and delivery was longer, and the gestational age at delivery was more advanced. In addition, the intertwin hemoglobin difference at birth was less marked, and recourse to postnatal hematological treatments was less frequent. There also was birth weight discordance in more than half of the nontreated TAPS cases, whereas this affected only 29% of the treated TAPS cases. Zhao et al. [28], too, found a more marked tendency towards discrepant birth weights in the event of TAPS versus uncomplicated

monochorionic diamniotic twin pregnancies. Correction of anemia therefore appears to be associated with improved growth of the anemic fetus. Nevertheless, birth weight discordance could also be a consequence of unequal sharing, which was more frequent in nontreated TAPS. We did not study the neurological development of these infants, but it should be noted that neurological lesions have been reported in both anemic [5] and polycythemic fetuses [29, 30].

Performing an in utero procedure was associated with an increased risk of PPRM: this reflects the iatrogenicity associated with any invasive therapeutic act. Nevertheless, the gestational age at delivery was higher if antenatal treatment was provided. It is noteworthy that none of the 4 patients in our series who underwent two invasive procedures (laser for TTTS and laser or transfusion for TAPS) had PPRM.

The laser procedure is the only etiological treatment, as shown by the graphs which display modifications in MCA-PSV and by placental analysis. In a recent study by Slaghekke et al. [26] on the effect of laser photocoagulation on TAPS ($n = 8$) as compared to no treatment ($n = 27$) or IUT ($n = 17$), the survival rate after laser was 94% (vs. 83 and 84% with expectant management and IUT, respectively; $p = 0.30$), with a prolonged diagnosis-delivery interval (11 vs. 5 and 8 WG; $p < 0.01$) and no severe hematological complications (vs. 72 and 52%; $p < 0.01$). It should be noted that placental photocoagulation for TAPS is more complicated than for TTTS due to the absence of polyhydramnios, a less tense uterine wall, more opaque amniotic fluid as well as slender and often marginal anastomoses [6, 28]. In the particular case of iatrogenic TAPS after laser treatment, the rationale for repeating the laser procedure should be carefully considered; if the anastomoses were not visualized during the first laser treatment for TTTS, it is unlikely that they will be identified any better during a second procedure. Changing the access route may be helpful, since it may be easier to visualize persisting anastomoses from a different viewpoint. In any event, if a laser treatment is performed, the Solomon technique should be preferred insofar as it is feasible [21].

IUT is a symptomatic treatment, and it sometimes needs to be repeated; this was the case with one of our patients. Study of the MCA-PSV changes illustrates that TAPS recurs at some point following the procedure. However, one of our cases presented a less typical progress, with resolution of TAPS following IUT and no relapse. A similar case was described by Robyr et al. [4]. Absence of anastomosis on placental analysis may sug-

gest an anastomotic thrombosis, as has been suggested by Lopriore et al. [31]. In any event, IUT should be preferred in cases of TAPS occurring at a later stage, in order to avoid (if possible) having to repeat this procedure. In our cohort, it is noteworthy that the MCA-PSV readings in the recipient fetuses did not show any significant post-procedural modifications, although increased polycythemia is a complication commonly described with IUT and it may give rise to complications [4], especially of a neurological type [32]. Some authors have described partial exchange transfusion of the polycythemic fetus to be associated with IUT of the anemic twin, with the advantage of reducing the potential risk of complications due to polycythemia. However, this procedure is symptomatic and requires double needling [5]. Expectant management is part of the armamentarium for selected cases [8]. A very early case of TAPS, i.e. inaccessible to any in utero therapy, ought to be monitored before any decision is made in order to perform the appropriate procedure at the appropriate time. In our cohort, the course was unfavorable, with double intrauterine fetal demise at 14 WG, underlining the considerable prognostic variability of this disorder. A slowly progressing stage 1 or 2 TAPS, especially if diagnosed after 30 WG, may also benefit from closer monitoring at least twice monthly or even weekly, as has recently been proposed by our team [33], with antenatal corticosteroid therapy and fetal extraction at what seems

to be the right time [7, 34]. Finally, the decision to proceed with fetal extraction should be discussed after 32 WG whenever there is recurrence or worsening of TAPS. Selective feticide or termination of pregnancy can be considered as a therapeutic option for the more severe cases.

The observational design of our study introduced a potential bias into our analysis, since TAPS cases receiving antenatal treatment are not necessarily comparable with TAPS cases for which expectant management has been selected. There was no difference between the groups with regard to grade of severity, but TAPS cases undergoing in utero treatment were those occurring earliest in pregnancy. It would therefore appear that our study minimized the utility of an antenatal treatment strategy, since those cases treated were the most severe. The size of our cohort was limited, but nonetheless relatively large in view of the incidence of TAPS. Small-size samples generally provide little information. Our Bayesian approach, integrating some previously published data into the priors, would therefore appear to be of particular relevance.

In conclusion, antenatal treatment appears to be an option for selected cases of TAPS even if there is no evidence that it improves overall (fetal and neonatal) mortality rates. Laser photocoagulation of the placenta is the sole etiological treatment, but IUT may be considered if there are technical difficulties. Studies are needed to investigate the neurodevelopmental effects of in utero intervention.

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