Neonatal outcome using ultrathin fetoscope for laser coagulation in twin-to-twin-transfusion syndrome

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Abstract

Objective: To improve neonatal outcome using ultrathin fetoscope for laser treatment of twin-to-twin transfusion syndrome.

Methods: Retrospective cohort study of a series of 80 cases of twin-to-twin-transfusion syndrome prior to 26 weeks’ gestation subjected to laser coagulation by means of a 1.0/1.2 mm fiber fetoscope with a sheath sectional area 2.65 mm²/3.34 mm² (n=27) and a 2.0 mm classic lens fetoscope with a sheath sectional area: 6.63 mm²/11.27 mm² (n=53).

Results: The survival rates of at least one twin in the compared groups were 94.4% (classic optic) and 100% (ultrathin optic), for both twins: 75.5% and 83.3%, respectively. By decreasing sheath diameter a pregnancy was prolonged by an average of 21.3 days (P=0.0045), with a resulting increase in the recipient’s weight of 389 g (P=0.0049) and an increase in the donor’s Apgar score. However, the intervention with ultrathin optic took 11 min longer (P=0.031).

Conclusion: The reduction of the iatrogenic damage of the amniotic membrane using ultrathin fetoscope with a small sheath, significantly improves the neonatal outcome after laser treatment of twin-to-twin-transfusion syndrome. The operator should only commence working with the 1 mm fetoscope after the learning curve has been accomplished.

Keywords: 1.0 mm Fetoscope; laser coagulation; monochorial pregnancy; neonatal outcome; twin-to-twin transfusion syndrome.

Introduction

Twin-to-twin-transfusion syndrome (TTTS) is a dangerous condition that complicates approximately 8%–15% of monochorial twin pregnancies [13, 17]. Without any treatment the survival rates of both the donor and the recipient are poor. This state is generally associated with a perinatal loss of 70%–90% [13, 23]. In a randomized, controlled study, it could be demonstrated that at least one child survives in 77.1% of cases following fetoscopic laser coagulation (FLC) of placental anastomoses [17]. Preterm premature rupture of membranes (PPROM) turned out to be one of the major complications of fetoscopic surgery, and fetal loss after FLC was still a serious problem [1, 13, 20, 23].

The inherent capability of fetal membranes to repair following injury appears to be limited. Since the fetal membranes in humans are not innervated and only very poorly vascularized, a typical wound healing response that includes inflammation, scar formation, and tissue regeneration – as described for the skin and many other organs – is unlikely to occur [18]. Evidence that has been obtained in sheep and rhesus monkeys confirms that the fetal membranes have a very limited ability to heal [3]. Multiple fetal membrane sealants have been advocated for many years to treat or seal fetal membrane defects; however, at present, neither the safety nor the efficacy of these treatments have been determined [4, 11, 14, 26].

While describing the development of minimally invasive fetoscopic procedures, Hajivassiliou et al. [6] found that there is a relationship between the access hole size and the rate of PPROM as a complication of fetoscopic surgery. This finding was supported by the review of Gratacsos et al. [5] who pointed to a bigger diameter or a greater number of access ports as the reasons for an increased PPROM rate. Beyond this, early work with primates showed that increasing the size of uterine trauma increased the level of postoperative uterine muscular activity, which itself is a risk factor for amniorrhaxis [7, 10]. In the recent review performed by Deprest et al., the link between the bigger diameter of the instrument and the rise in PPROM rate was clearly shown [2].

Fetoscopy, however, is being used increasingly. Despite certain improvements in technique and equipment, between 5% and 30% of fetoscopic procedures are still complicated by PPROM [9, 19, 21, 22, 25]. This limits the clinical use...
of the technique and is a major obstacle to the further development of this field. Based on the available literature and our own experience, we believe that a reduction of the access trauma through the employment of smaller fetoscopic devices, can increase the safety of laser coagulation of placental anastomoses in TTTS and significantly improve the neonatal outcome.

Materials and methods

In the retrospective study presented here, the results of operative interventions performed between 2006 and 2011, using different types of equipment in the Center of Perinatal Diagnosis and Microinvasive Intrauterine Fetal Surgery at the University of Mainz (Germany), have been compared.

A total of 80 women underwent the FLC procedure. Optics of 1.0/1.2 mm and 2.0 mm diameters were used in 27 and 53 cases, respectively. The diagnosis of TTTS was based on a monochorionic twin pregnancy which had become complicated by polyhydramnios of ≥8 cm in the deepest vertical pocket of the recipient at ≤20 weeks of gestation (or ≥10 cm from 20 weeks of gestation onwards), and oligohydramnios of ≤2 cm deepest vertical pool depth in the donor. Inclusion criteria for FLC were TTTS Quintero stages I through IV and a gestational age of between 16 and 26 weeks [15].

Exclusion criteria were a major fetal anomaly, chromosomal pathology, ruptured amniotic membranes, uncontrolled uterine contractions, and a maternal condition mandating delivery. All TTTS patients who met the above criteria were offered FLC. The protocol for the retrospective cohort study was approved by the institutional review board. All procedures were conducted according to the Helsinki Declaration. Informed consent was obtained from each of the women prior to intervention.

A classical 2.0 mm lens optic 26008AA (0°) together with the 2661U sheath [2.5×3.6 mm, sectional area: 6.63 mm² (here and further outer diameters are stated only) Karl Storz GmbH & Co. KG, Tuttlingen, Germany] were used for the posterior localization of the placenta and a 2.0 mm lens optic 26008BUA (30°) with the 2661UF sheath (3.1×4.3 mm, sectional area: 11.27 mm², Karl Storz GmbH & Co. KG, Tuttlingen, Germany) in cases of anterior placental localization. In 2008–2011, the equipment was changed to a 1.0 mm flexible fiber 11510A fetoscope and a curved modified for anterior placenta 11510 KD sheath with two working channels (1.3×2.6 mm, sectional area: 2.65 mm², Karl Storz GmbH & Co. KG, Tuttlingen, Germany). In 3 cases of women with polyhydramnion >3 L and posterior placentation, and in 1 case of a woman with a BMI >35.0, a 1.2 mm optic 11530AA with a curved fetoscopic 11530KB sheath with two working channels (1.6×2.9 mm, sectional area: 3.34 mm², Karl Storz GmbH & Co. KG, Tuttlingen, Germany) was used. It enabled an essential reduction in the diameter of the instrument.

On the evening before the operation, and on the following day just immediately before the operation, indomethacin suppository, 100 mg was given to the patient.

All fetoscopic laser surgery procedures were performed in the operating room under sterile conditions and local anesthesia using 20 mL 1% Scandicain solution (AstraZeneca GmbH, Wedel, Germany), which was injected up to the peritoneum under sonographic control. Following the performance of a small 2 mm skin incision, the trocar and then the optic itself were inserted (depending on the site of the placenta and operator preference) into the recipient’s amniotic cavity under continuous ultrasound guidance (Philips IU22; Philips Medical, Hamburg, Germany).

The vasculature on the surface of the monochorionic placenta was carefully mapped and anastomoses between the twin circulations were identified. The closure of all anastomoses on the chorionic plate between the twins was performed using a Nd:YAG laser set (Medilas Fibertom 8100; Dornier MedTech, Wessling, Germany) at 50–60 watts and a 0.7 mm laser wire. Excess liquor was drained to a normal pool depth of approximately 4–5 cm. At the end of the procedure, care was taken to ensure that all anastomoses had been closed.

Statistical analysis

The values of the core parameters for the groups were compared using the unpaired t-test and ANOVA. Data are presented as mean±SD. P-values of <0.05 were considered as being significant. Calculations were performed using Statistica® software Version 8.1 (Statsoft, Tulsa, OK, USA).

Results

A total of 80 patients underwent laser surgery and were designated to one of two groups, depending on the type of optic used: 27 patients in the 1 mm optic group and 53 patients in the 2 mm classic optic group. Patients in both groups were comparable as far as age, BMI and medical history were concerned. The mean gestational ages at the time of intervention were 147.35±12.98 days (2 mm optic group) and 140.47±16.38 days (1.0/1.2 mm optic group) (P>0.05). The group in which the thinner optic was used had, on average, deeper changes according to Quintero classification. The I stage was observed in 1 mm optic group in 4% of all patients, the II stage in 28%, the III stage in 60% and the IV stage in 8% of cases. In the group of classical 2 mm optic, we found the I Quintero stage in 6.4%, the II stage in 76.6%, the III stage in 17% and the IV stage in no patients.

The time needed for the intervention using the 1.0/1.2 mm optic was significantly longer, requiring, on average, 11 min more than with the 2.0 mm optic (P=0.032). Further basic data is summarized in Table 1.

The difference in the drained amniotic fluid volume in the ultrathin optic group could be explained by the fact that some of the women came from outside of Germany, with severe stages of TTTS, where previous non-effective amniorenages had been prescribed. Additionally, taking into account the shape of the sheaths used with the 1.0/1.2 mm optic (figure-of-eight cut as a result of connection of two tubes), leakage of amniotic fluid into the peritoneal cavity could have occurred.

There was no associated oligohydramnios in the recipient sac, nor any secondary bleeding/abruption. Until now, no twin anemia-polycytemia sequence or re-TTTS have been observed. There were no maternal complications, except for abdominal pain during the first 24 h. We presume that this pain was related to the amount of amniotic fluid that might have passed into the abdominal cavity because of the specific sheath shape. In all cases, it was possible to eliminate the
Table 1  Selected characteristics of the compared groups and the operations performed.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Classic 2 mm optic (n=53, mean±SD)</th>
<th>Ultrathin fiber optic (n=27, mean±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.51±4.5</td>
<td>30.11±3.92</td>
<td>ns</td>
</tr>
<tr>
<td>Gestation term at FLC (days)</td>
<td>147.35±12.98</td>
<td>140.48±16.38</td>
<td>ns</td>
</tr>
<tr>
<td>Estimated weight of the recipient (g)</td>
<td>461.57±164.40</td>
<td>519.02±208.57</td>
<td>ns</td>
</tr>
<tr>
<td>Estimated weight of the donor (g)</td>
<td>344.92±118.81</td>
<td>332.11±128.92</td>
<td>ns</td>
</tr>
<tr>
<td>PI on a.umbilicalis (recipient)</td>
<td>1.32±0.52</td>
<td>1.48±0.51</td>
<td>ns</td>
</tr>
<tr>
<td>PI on a.umbilicalis (donor)</td>
<td>1.65±0.84</td>
<td>1.74±0.58</td>
<td>ns</td>
</tr>
<tr>
<td>Volume of drained amniotic fluid (mL)</td>
<td>2425.53±1241.86</td>
<td>1441.18±684.70</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of the operation (min)</td>
<td>28.09±12.46</td>
<td>39.80±14.67</td>
<td>0.032</td>
</tr>
<tr>
<td>Joule</td>
<td>7926.93±5154.32</td>
<td>8011.18±5890.72</td>
<td>ns</td>
</tr>
<tr>
<td>Anastomoses (total)</td>
<td>10.50±4.62</td>
<td>10.95±4.16</td>
<td>ns</td>
</tr>
<tr>
<td>Anastomoses (Donor&gt;Recipient)</td>
<td>7.21±4.20</td>
<td>8.56±3.98</td>
<td>ns</td>
</tr>
<tr>
<td>Anastomoses (Recipient&gt;Donor)</td>
<td>2.58±1.76</td>
<td>2.40±3.40</td>
<td>ns</td>
</tr>
<tr>
<td>Anastomoses (Undefined)</td>
<td>1.00±0.00</td>
<td>1.67±0.52</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns = Not significant, PI = pulsatility index, FSL = fetoscopic coagulation of placental anastomoses.

pain quite rapidly by encouraging early activity, changes in posture, or a single dose of a non-opioid analgesic.

The perinatal survival rate for at least one child in the group where the straight fetoscope was used amounted to 94.4%. At the same time, in the group of the modified ultrathin sheath and the flexible 1.0/1.2 mm optic, it was 100%.

The perinatal survival rates for both newborns were 75.5% and 83.3% for the 1.0 and 2.0 mm optics, respectively (Figure 1).

In spite of the fact that the group in which the thinner optic was used had more serious changes according to the Quintero stages, the duration of the pregnancy was significantly prolonged. The birth weight of the recipients and the donors’ Apgar score for the first minute were significantly increased. The average values of the donors’ weights and recipients’ Apgar scores were not significantly different (Table 2).

Comment

In the present study, it was shown that it is possible to achieve good survival rates after fetoscopic laser coagulation of placental anastomoses in TTTS using an ultrathin optic. At least one child survived during 28 days in 100% of cases (compared to 94.4% in the 2.0 mm optic group), and both children survived in 83.3% of cases (compared to 75.5% in the 2.0 mm group). According to Morris et al. [9], the only independent factor of significance for increased perinatal survival is gestational age at delivery. By decreasing the diam-

Figure 1  Fetal survival rates after usage of the 1.0/1.2 and 2.0 mm optics.
Table 2  Neonatal outcome after fetal laser coagulation.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Classic 2 mm optic (n = 53, mean ± SD)</th>
<th>Ultrathin fiber optic (n = 27, mean ± SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at birth (in days)</td>
<td>226.53 ± 28.06</td>
<td>247.79 ± 17.37</td>
<td>0.0045</td>
</tr>
<tr>
<td>Apgar score of the recipient (1st min)</td>
<td>7.52 ± 1.85</td>
<td>7.88 ± 1.17</td>
<td>ns</td>
</tr>
<tr>
<td>Apgar score of the recipient (5th min)</td>
<td>8.56 ± 1.38</td>
<td>8.77 ± 1.47</td>
<td>ns</td>
</tr>
<tr>
<td>Apgar score of the donor (1st min)</td>
<td>6.25 ± 2.51</td>
<td>7.87 ± 1.41</td>
<td>0.023</td>
</tr>
<tr>
<td>Apgar score of the donor (5th min)</td>
<td>8.05 ± 1.73</td>
<td>8.72 ± 1.20</td>
<td>ns</td>
</tr>
<tr>
<td>Weight of the recipient (g)</td>
<td>1845.00 ± 670.9</td>
<td>2233.95 ± 640.2</td>
<td>0.0049</td>
</tr>
<tr>
<td>Weight of the donor (g)</td>
<td>1638.81 ± 711.03</td>
<td>1991.76 ± 787.2</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns = not significant.

eter of both the optic and sheath in our center, it was possible to prolong the pregnancy by an average of 21.3 days, which resulted in an average increase in the recipient's weight of 389.0 g and an average increase in the donor's Apgar score. In contrast to our results, however, a research group from Brazil could find no benefit from using the 1.0 mm optic for TTTS treatment [16]. In our opinion, there are a number of possible reasons for this difference, which will be outlined here. First of all, from a technical point of view, the reduction of the 2 mm lens optic to the 1.0/1.2 mm fiber optic fetoscope should – at least intuitively – worsen the area of the image received from the camera. In our laboratory we tried to verify this possibility and to compare the images obtained by the 1.0/1.2 mm and 2 mm optics. Unexpectedly, image comparison showed the areas of view to be practically the same. As an example, the working area at a distance of 2 cm totals approximately 706.5 mm² for both optics (with no sheath), in spite of the fact that the light spot was visually bigger in the 2 mm optic. It is, however, clear that the quality of the picture received from 1.0 mm fetoscope is worse (Figure 2). In our opinion, this is related to the different core-principles of receiving the image (lens vs. fiber), although it turned out to be not the only reason.

We found that the flexible sheaths (7–8 F) used for the 1.0/1.2 mm optic could provide truncation and displacement of the image in the case of observation at an angle. Thus, both (the optic and sheath) should be thoroughly mutually adjusted, otherwise the parallax of the image will be substantial. Additionally, it was noted that in cases where the light power was not well-regulated (e.g., with excessive light), a sizeable ‘blind zone’ at the center of the image resulted, which could not be seen while working in the amniotic cavity because of the liquid environment. This blind spot could become a considerable obstacle for an untrained operator, so this issue should be kept in mind.

It is worth mentioning that the existing 7/8 F flexible sheaths with figure-of-eight cut do not fully satisfy the needs of the operator. The possibility of amniotic fluid leaking into the peritoneal cavity by way of the chute of the sheath has already been mentioned. Similarly, the passage of blood from the uterine tissues and abdominal wall into the uterine cavity can be envisaged. If this occurs, it can result in a substantial

Figure 2  Comparison of the section areas of the 11510 KD sheath used for 1 mm optic and the 2661UF sheath used for 2 mm optics.

a – Image received from the flexible 1 mm fetoscope.

b – Image received from the straight 2 mm fetoscope.
decrease in the transparency of the amniotic fluid (as well as the preceding amniодrainage), leading to a prolongation of the intervention. For this reason, we have contacted Karl Storz GmbH (Tuttlingen, Germany) with recommendations for changes which would result in an improvement of the instrument (the new sheath has been already developed). We do not use ports for sheath introduction as we believe that the additional use of cannulae changes the shape of the hole and inherently increases the total outer diameter.

To conclude, it should be stressed that the experience of the operator plays a great part in the success of fetoscopic laser coagulation. According to the literature, between 15% and 30% of anastomoses are missed even when a 2.0 mm optic is used [13, 23]. Obviously, the reduction of the image quality with the ultrathin optic, could negatively contribute to the final results of the surgery. It could also be the reason for the 11 min longer duration of the intervention in the ultrathin optic group. In our center, additional time is always invested during the operations to avoid placental anastomoses being overlooked and indeed, no instances of re-TTTS or TAPS have been observed in our patients, as these complications never occur if all potentially dangerous communications are coagulated in a carefully selective manner. Accordingly, we consider that the operator should only commence working with the 1 mm fetoscope after the learning curve has been accomplished.

It could be hypothesized that a continuation of the use of the 2.0 mm optic could result in a further improvement, due to the operator gaining more and more experience.

Nevertheless, taking into consideration the fact that the diameter of the hole in the amniotic membrane following surgical or diagnostic intervention might be directly related to the PPROM risk, we hope to be on the right path to finding a compromise between the minimal instrument diameter and an acceptable quality of the fetoscopic image. For example, the difference between the inlets of the 11510 KD sheath for the 1 mm optic (2.65 mm²) and the 2661UF sheath for the 2 mm optic (11.27 mm²) seem to be dramatic. Unfortunately, we had no complete data regarding the rate of PPROM in our patients, as some of them gave birth in other countries and it was sometimes impossible to receive reliable information about the circumstances of onset of a labor. This fact could be considered as the limitation of the study. Nevertheless, the duration of pregnancy was significantly longer in ultrathin optic group and among other reasons, it could be also due to decreased rate of iatrogenic rupture of membranes.

As already mentioned, the amniotic membranes are known to have only poor regenerative abilities. It would appear that we are confronted with a biological protective mechanism established by natural evolution which is aimed at preventing the mother’s death as a result of intrauterine infection due to healing of damaged fetal membranes. We look optimistically to the future since numerous attempts to improve the state of the field by means of in-depth studies of amniotic membranes have been undertaken over the past 5 years [8, 12, 24]. It is definitely important to develop strategies enabling a membrane defect to be sealed, or to stimulate the spontaneou repair mechanisms of the fetal membranes. Until these goals have been reached and been proven to be effective, many children’s lives will be lost. We are convinced that it would be reasonable to start with some simple measures aimed at improving the safety of currently available fetoscopy.

As shown in this study, the usage of ultrathin optic with a small sheath seems to be beneficial, but requires a highly experienced surgeon and the thorough fine-tuned arrangement of technical parameters (light, laser power) since the occlusion of all placental anastomoses is a precondition for the long-term success of the operation. In the worst case, the reduction of the quality of the picture using the ultrathin optic may lead to anastomoses being missed and a worsened neonatal outcome.

In conclusion, the utilization of ultrathin fetoscope with a small sheath significantly improves the neonatal outcome after laser treatment of TTTS. The learning curve of laser coagulation must however be accomplished before the use of ultrathin optic commences.

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from the determination of physical properties. Placenta. 2006; 27:1037–51.


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