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What is the impact of placental tissue damage after laser surgery for twin-twin transfusion syndrome? A secondary analysis of the Solomon trial

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ABSTRACT

Background: The introduction of the Solomon technique for the treatment of twin-twin transfusion syndrome (TTTS) increased placental exposure to laser energy. This study aims to identify the impact of power and energy used in laser treatment on placental tissue and pregnancy outcome.
Methods: Pictures of all dye-injected placentas since the start of the Solomon trial were analyzed. Placental damage was scored using a grading system including visual scar depth and affected proportion of the vascular equator. Parameters analyzed included laser power and total energy, gestational age (GA) at laser, GA at birth, laser-to-delivery interval and preterm prelabor rupture of membranes (PPROM).
Results: We included 122 cases in the analysis. More placental damage occurred more often in the Solomon group (42%) compared to the selective group (15%) ($p < 0.001$). In multivariate analysis, more placental damage was associated with higher laser energy (regression coefficient B 0.002) but not with higher power setting (regression coefficient B −0.442). More damage was associated with earlier GA at birth (regression coefficient B −0.167), higher incidence of PPROM <32 weeks (regression coefficient B 0.003) and a shorter laser-to-delivery interval (regression coefficient B −0.168).
Conclusions: Placental damage is positively associated with more laser energy but negatively associated with higher power setting. More placental damage was associated with a lower GA at birth, shorter laser-to-delivery interval and higher PPROM rate. Whether these results should lead to a change in surgical technique requires more research, both further ex-vivo experiments on human placentas and clinical studies.

1. Introduction

Monochorionic (MC) twin pregnancies are high-risk pregnancies, often (10%) complicated by twin-twin transfusion syndrome (TTTS). Untreated, this condition is associated with approximately 90% perinatal mortality and severe morbidity [1–3]. Survival rates increase significantly after treatment with fetoscopic laser therapy up to 88% for at least one twin and 62% for survival of both twins, in experienced centers [4].

In 2008, the Solomon technique was introduced as an adaptation of the selective fetoscopic laser coagulation technique for the treatment of TTTS complicated MC pregnancies [5]. The rationale behind the Solomon technique is to eliminate even the smallest anastomoses by coagulating a line between the visible anastomoses, thereby avoiding residual anastomoses leading to recurrence of TTTS or occurrence of post-laser twin anemia polycythemia sequence (TAPS). We concluded that the Solomon technique significantly reduces the incidences of recurrent TTTS and post-laser TAPS [5].

A possible drawback of the Solomon technique is a larger surface area of the placenta being exposed to laser energy, compared to the selective laser coagulation technique (Fig. 1). Animal studies

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suggest that superficial coagulation, in time, may lead to functional loss of the entire underlying cotyledon [6]. Little research has been conducted on the impact of laser energy and laser power setting (wattage) on the human placental tissue. Emery et al. described the effect of Solomon laser treatment after pathological analysis on a human placenta. They concluded that solomonization leads to devitalization of the chorionic plate with shallow devitalization of the underlying villi [7].

A worldwide expert survey showed significant variation in laser power settings between centers [8]. Furthermore, it showed that the Solomon technique is gaining popularity. We therefore consider it important to investigate the impact of laser power and laser energy on placental tissue. Laser power is defined as the output wattage of the laser device that can be set by the operator. The total amount of laser energy (joule) used during a procedure is calculated automatically by the laser device and is the result of laser power and the laser time. This study aims to identify the impact of the level of laser power and the amount of energy used in laser treatment on placental tissue and pregnancy outcome.

2. Methods

2.1. Data source

For this study, all cases from the Leiden University Medical Center included in the Solomon Trial [5] were used, as well as all cases treated in our national referral center after the Solomon study was concluded.

All subjects treated between 2008 and 2014 at the Leiden University Center during the Solomon trial were eligible for this study. Inclusion criteria for laser surgery were: monochorionic pregnancy, gestational age between 13 and 28 weeks, TTTS Quintero stage 1 with severe clinical symptoms of polyhydramnios, or TTTS Quintero stage $\geq$2. For the analyses we extracted data on laser treatment specifics (including laser power, laser time and total energy usage), clinical outcome parameters and postpartum color-dye injected placenta pictures. Details on the color-dye procedure were previously reported [9].

2.2. Inclusion and exclusion criteria

All cases with an available placenta picture after selective or Solomon laser were included. Exclusion criteria were: missing documentation on both total energy and laser power setting, missing scale on the picture, single fetal demise and re-intervention laser therapy after the initial laser procedure. Cases with single fetal demise were excluded because placental maceration hampers color-dye injection. Cases with a re-intervention laser procedure were excluded because the visible damage could not be directly linked to either one of the laser procedures. Pictures from cases with a laser-to-delivery interval under seven days were excluded from grading, because these pictures showed no or little scarring.

2.3. Scoring placental tissue damage

In the absence of a validated scoring system for placental tissue damage, we developed one (Table 1) based on validated scar scales [10,11]. The amount of damage of each grade was measured in millimeters length and expressed as percentages of the total lasered line in Solomon cases, or lasered sections in selective cases of the placenta. In pictures that had a missing scale but showed an umbilical cord clamp, the clamp was used to gauge the scale. Measurements were performed using ImageJ 1.47v software (ImageJ, National Institutes of Health, Bethesda, Maryland, USA). Placental tissue damage was defined as the summed up value of grade 2 and 3 tissue damage. These two categories most likely cover the damage that is considered to be more severe than intended with laser coagulation. Two observers (SdV and JA) assessed all pictures independently and blinded from outcome, patient and procedural parameters. Inter-observer variability was assessed calculating the intraclass correlation coefficient. In cases with an inter-observer scoring difference of >5% of the tissue damage score, the case was discussed by the observers until consensus was achieved. We used the mean value of the tissue damage scores of both observers combined for analyses.

2.4. Analysis

The influence of laser power and laser energy on placental tissue damage was analyzed. Further analyses were conducted to determine the relation of placental tissue damage, laser power and laser energy to various outcome parameters. These included gestational age (GA) at birth, laser-to-delivery interval and preterm prelabor rupture of membranes (PPROM) before 32 weeks' gestation.

2.5. Statistical analysis

Analyses were conducted using SPSS Statistics (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Analysis for risk factors, visual placental tissue damage, laser power and laser energy, influencing either the gestational age at birth, laser-to-delivery interval and PPROM under 32 weeks gestation was conducted using univariate and multivariate regression methods. Normality of all variables was asessed prior to moddeling. The potential risk factors for each of the three outcomes were studied in a univariate regression model. The multivariate regression model included all factors that showed

Fig. 1.