FETAL PHYSIOLOGY AND INTERVENTION

Abstracts 93-100

93  Tissue graft materials for skin patch during in-utero spina bifida repair in a sheep model

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OBJECTIVE: Use of off-label tissue graft materials such as acellular dermal matrix (ADM) for the in-utero repair of severe spina bifida (SB), where primary closure of the skin layer is not possible, is associated with poor neurological outcomes. Cryopreserved human umbilical cord patch (HUC) has regenerative, anti-inflammatory and anti-scarring properties, and has shown to provide watertight SB repair. We tested the hypothesis that HUC is a superior skin patch compared to ADM for reducing inflammation at repair site and preserving the spinal cord function.

STUDY DESIGN: In timed-pregnant ewes with twins, on gestational day (GD) 75, the spina bifida was created without myelotomy (functional model). On GD 95, repair was performed using HUC vs. ADM patch (randomly assigned) sutured to the skin edges. Additionally, full thickness skin closure as a conventional repair (CR) served as a positive control. The delivery was performed at GD 140, neurological assessments of the lambs were performed, blinded to treatment, using Texas Spinal Cord Injury Scale (TSCIS) for gait, proprioception, and nociception. Lambs without spina bifida were used as controls (CTL). Histological assessment (blinded) was performed using Mason's trichrome and immunofluorescence for myeloperoxidase (MPO; neutrophils), reactive astrocytes (inflammation) using co-staining for vimentin and GFAP.

RESULTS: The combined hind limbs TSCIS was significantly higher in HUC compared to ADM and CR (Figure 1A). Both ADM and CR group exhibited loss of proprioception and mild to moderate ataxia. On histology, the arachnoid layer was thickened (inflammation) by 2-3 fold in ADM and CR compared to HUC and CTL (Figure 1B). There was lower MPO positive cells in the HUC (61 [15-300]) compared to ADM (5 [0-9]), p=0.018. The astrocyte activation in the posterior column was increased in ADM and CR lambs compared to HUC (Fig. 2: p=0.03).

CONCLUSION: HUC as a skin patch is superior in preserving the spinal cord function through reduction in underlying inflammation associated with ADM and conventional repair.

94  Noninvasive instantaneous measurement of neonatal brain oxygenation with light emitting diodes to detect hypoxic-ischemic encephalopathy

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OBJECTIVE: We currently use electronic fetal heart rate monitoring as a screening test for fetal hypoxic-ischemic encephalopathy (HIE), and neonates suspected of having HIE at birth are triaged to hypothermia treatment within 6 hours of birth. We have demonstrated the transcranial, instantaneous measurement of superior sagittal sinus oxygen saturation (sO2) in an in vivo neonatal piglet model to detect HIE using functional photoacoustic (fPA) imaging with pulsed laser light generated by a Nd:YAG optical parametric oscillator. Convenience and safety will be improved if brain oxygenation can be measured with a small, inexpensive, light emitting diode (LED) as the light source.

STUDY DESIGN: Neonatal piglets, aged 3-7-days, were placed under general endotracheal anesthesia with a catheter in the superior sagittal sinus (n=5). Systemic hypoxia was produced by stepwise decreasing fractionally inspired oxygen (FiO2): 100, 21, 19, 17, 15, 14, 13, 12, 11, 10%. At each FiO2, the LED-based fPA imaging system captured a coronal cross-section of the piglet head,
followed by direct blood sampling. Near-infrared LEDs emitted pulsed light at 690 and 850 nm at 50- to 125-times lower energy level compared to that emitted by the Nd:YAG laser (0.18-0.4mJ vs. 10mJ per pulse). We used an energy density of 0.02-0.05mJ/cm², well below the American National Standards Institute safety limit in human tissue of 20mJ/cm². We compared the fPA measurement of superior sagittal sinus sO₂ against that measured directly by blood sampling.

RESULTS: fPA measurements correlated with direct measurements of sO₂ with R² = 0.68. (Fig 1b) The correlation between the slope (0.94) and y-intercept (4.14%) were very close to ideal positive correlation. The detection precision in the critical sagittal sinus sO₂ (< 30%) was confirmed with sensitivity (94.12%), specificity (85.71%), accuracy (89.47%), positive predictive value (84.21%), and negative predictive value (94.74%).

CONCLUSION: LEDs can instantaneously and noninvasively measure superior sagittal sinus sO₂ which suggests the feasibility of fetal and neonatal brain monitoring to detect HIE.

Figure 1a. Safe, real-time, functional photoacoustic (fPA) monitoring system for neonatal brain monitoring. Coronal cross-section of neonatal piglet using dual-wavelength LED sources at 690 and 850nm.

Figure 1b. Correlation of superior sagittal sinus oxygen saturation (sO₂) estimated photoacoustically with direct blood gas measurement.

**95 Early laser surgery is not associated with preterm delivery or reduced neonatal survival in TTTS**

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OBJECTIVE: To evaluate the association of laser photocoagulation of placental anastomoses (LPA) prior to 18 weeks (early LPA), very preterm delivery (PTD) and neonatal survival in patients with twin—twin transfusion syndrome (TTTS).

STUDY DESIGN: This cohort study included TTTS cases undergoing LPA between 2002 and 2018 at two institutions. Regression analysis was performed to determine the association of early LPA with the study outcomes adjusted for Quintero stage, selective fetal growth restriction (estimated fetal weight or birthweight discordance ≥25% and < 10th percentile), gestational age at delivery, maternal age ≥35 years old, BMI >35, placental location and preterm premature rupture of membranes (PROM). Survival analysis with Cox proportional hazard model were applied to examine the interval from surgery-to-delivery according to the timing of LPA, while adjusting for confounding variables.

RESULTS: 418 TTTS cases were included with early LPA in 16.3% (68/418). The overall rates of delivery at less than 28, 30 and 32 weeks were 27.2%, 39.6% and 53.4%, respectively. Dual twin survival or survival of at least one twin to 30 days were 90.9% and 67.2%, respectively. No significant differences were noted between early LPA and LPA ≥18 weeks in terms of delivery rate < 28 (19.1% vs. 23.4%; p = 0.4), 30 (38.2% vs.39.9%; p = 0.7) and 32 (44.1% vs. 55.2; p = 0.1) weeks, preterm PROM rate (29% vs. 24.2%; p = 0.4) or in the proportion of dual twin survival (63.9% vs. 67.8%; p = 0.6) or survival of at least one fetus (91.8% vs. 90.7%; p = 0.8) to 30 days of life. Early LPA was associated with longer surgery-to-delivery interval compared to LPA ≥18 weeks (median: 106 days; range: 2-164 vs. median: 69.3 days, range: 0-146; p < 0.001) while adjusting for confounding variables (Hazard ratio: 2.7, CI: 1.9-3.9; p < 0.001, Figure). Early LPA was not associated with early PTD, preterm PROM or decreased neonatal survival in the regression model.

CONCLUSION: Laser surgery prior to 18 weeks of gestation is not associated with excess preterm delivery, preterm PROM or decreased neonatal survival when compared with surgery at or after 18 weeks.

**96 Fetal neurodevelopmental recovery in donors after laser surgery for twin–twin transfusion syndrome**

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OBJECTIVE: To evaluate the association of laser photocoagulation of placental anastomoses (LPA) prior to 18 weeks (early LPA), very preterm delivery (PTD) and neonatal survival in patients with twin—twin transfusion syndrome (TTTS).