

## **Appendix 1: Modified Hering-Kohl protocol for general materno-fetal anesthesia during complex percutaneous minimally-invasive fetoscopic interventions.**

### **Anesthesia management protocol**

#### **Preoperative**

On the day of admission blood count and blood group were assessed and four packed red blood cell units were cross-matched. Patients were required to fast six hours (for solids) and two hours (for clear liquids) prior to the procedure. Gastroesophageal acid aspiration prophylaxis was enhanced using 150 mg ranitidine (Ranitic®) orally one hour before induction of anesthesia. Sedatives were not given in order to avoid immobilization of the fetus before a convenient fetal position was observed. We used 600 mg clindamycin (Sobelin®) and 120 mg gentamicin (Refobacin®) for intravenous (i.v.) antibiotic prophylaxis and a 6.75 mg atosiban (Tractocile®) i.v. bolus for tocolysis immediately before induction. Temperature control was accomplished using a warming blanket (3M® Bair Hugger, Neuss, Germany) and the HOTLINE® fluid warming system (Smiths Medical International Ltd, Watford, Herts, UK). In our experience left-uterine displacement was rarely needed at this stage of pregnancy and therefore patients are postured as the surgeon prefers. Deep vein thrombosis stockings were applied to reduce the risk for thrombosis and prevent venous stasis.

#### **Induction of anesthesia**

Anesthesia was induced using the rapid sequence technique with i.v. fentanyl (Fentanyl ratiopharm®, 2 - 5 µg/kg), thiopental (Trapanal®, 5 mg/kg) and rocuronium (Esmeron®, 1.0 mg/kg). After endotracheal intubation with a cuffed tube (Mallinckrodt™, Dublin, Ireland) and confirmed placement, a 14 F oro-gastric tube (Dahlhausen®, Cologne, Germany) was placed. We used a three-lumen, 7.5 F central

venous catheter (Arrow<sup>®</sup>, Teleflex Medical, Kernen, Germany) which was usually inserted in the right internal jugular vein. We guided the placement by checking the increase in P wave size of the electrocardiogram and used this as a criterion for confirmation of proper positioning. This saved the expectant mother and fetus from X-ray exposure. The first lumen was used for continuous measurement of central venous pressure and to administer calibration fluid for the pulse contour analysis system (Pulse Contour Cardiac Output<sup>®</sup>, PiCCO<sup>®</sup>, Pulsion Medical Systems, Feldkirchen, Germany). The second lumen was used for catecholamine infusion, and the third lumen for fluid administration. Hereafter a 4 F thermistor tipped artery catheter (PulsioCath PV2014L22-A, Pulsion Medical Systems, Munich, Germany) was inserted in a femoral artery for pulse contour analysis and arterial pressure measurements. To estimate cardiac output (CO) and extravascular lung water index (EVLWI), the transpulmonary thermodilution method of the PiCCO<sup>®</sup> system was used.<sup>1,2</sup> With this technique, a bolus of cold saline is infused through the central venous catheter. A thermistor at the tip of femoral arterial line measures the saline thermodilution curve, resulting in calculations for the CO and EVLWI. The first arterial and mixed venous blood gas analysis including hemoglobin and pH were determined (Nova biomedical Critical Care Xpress, Waltham, USA) immediately after anesthetic induction. Blood gas analysis is repeated throughout the procedure.

### **Maintenance of anesthesia**

Maintenance of anesthesia was achieved using desflurane (Suprane<sup>®</sup>, MAC 0.5 to 0.7 [~3.0 – 4.2 Vol%]), repeated i.v. doses of cis-atracurium (Nimbex<sup>®</sup>, 0.02 - 0.05 mg/kg) and a continuous remifentanil infusion (Ultiva<sup>®</sup>, 0.05 – 0.1  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). Medications were adjusted to maternal and fetal hypnotic and analgesic requirements. Adequacy

of fetal anesthesia was judged as sufficient if there were no fetal movements and no sustained increases of the fetal heart rate after painful stimuli or sustained fetal bradycardia as detected by intermittent Doppler ultrasound interrogations. This examination was conducted before and after induction of anesthesia, before intra-amniotic access, after amnioinfusion, before insufflation and at the end of procedure. A bispectral index (BIS QUATRO, Covidien<sup>®</sup>, Neustadt (Donau), Germany) score between 40 and 50 was judged as an adequate maternal anesthetic depth. Using the train-of-four method (TOF watch<sup>®</sup>, Essex Pharma GmbH, Munich, Germany), we ensured a sufficient degree of abdominal wall relaxation needed for performing the surgical procedures. Additionally, we limited uterine insufflation pressures to a minimum, preferably lower than 20 mmHg. The i.v. fluid used was Ringers solution (~ 4 ml·kg<sup>-1</sup>·h<sup>-1</sup>) at maintenance requirements. One bolus of 500ml hydroxyethyl starch (HAES, Tetraspan<sup>®</sup>, B. Braun Melsungen, Germany, 6 % / 130 000) was allowed. Subsequent observations in cases conducted after 11/2013 (unpublished data) indicate that patients are hemodynamically stable without administration of any colloid. Therefore, we do not recommend the use of HAES<sup>®</sup> as a volume expander for this procedure anymore. Pre- and intraoperative Doppler ultrasound measurements of the placental blood flow and fetal hemodynamics were used to adapt the anesthetic management if necessary. If needed, a continuous epinephrine<sup>1</sup> infusion (Suprarenin<sup>®</sup>, starting with 0.1 µg·kg<sup>-1</sup> min<sup>-1</sup>) was allowed, to assure adequate fetal perfusion pressure as measured by Doppler ultrasound and after exclusion of hypovolemia by intrathoracic blood volume (ITBV) measurement (ITBV > 850 ml·m<sup>-2</sup>). Mechanical ventilation was provided with a standard anesthetic machine (Primus<sup>®</sup>, Draeger

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<sup>1</sup> Only for the avoidance of doubt: As for all mentioned medications, also all drugs administered for fetal benefit (e.g. epinephrine, piritramid) were solely given via the circuit of the expectant mother. Therefore, all dosages were also calculated with the BW of the expectant mother.

Incorporation, Lübeck, Germany). We used a volume controlled ventilation mode with 1 l/min fresh gas flow using 75 % O<sub>2</sub> in air to maintain a FiO<sub>2</sub> between 0.5 to 0.7. The tidal volume was adjusted to ~ 6 - 8 ml/kg ideal BW, PEEP was set to 5 cm H<sub>2</sub>O, and the inspiratory-to-expiratory time ratio to 1:2. The goal for the maternal arterial carbon dioxide tension was between 35 to 40 mmHg and was achieved by adjusting the ventilator rate. Induction of partial amniotic carbon dioxide insufflation (PACI) usually requires increasing the ventilator rate by two cycles per minute. At this time, and particularly if amniotic insufflation pressures exceed 20 mm Hg, more frequent arterial blood gas measurements are required.

### **Emergence of anesthesia**

Immediately after the end of surgery, extubation was performed in the operating room. Ensuring adequate fetal analgesia during the whole procedure was a major clinical challenge in that the fetus underwent the most painful interventions yet was unable to express pain or discomfort directly. Therefore, we initiated postoperative analgesia during the emergence of anesthesia with the use of piritramid<sup>2</sup> i.v. boluses (Dipidor®<sup>®</sup>, up to 0.1 mg / kg). Because this drug commonly results in postoperative nausea and vomiting, dimenhydrinate (Vomex A®<sup>®</sup>, 62 mg) was provided before it.

### **Postoperative Monitoring**

For postoperative monitoring and to detect and attend to potential maternal and fetal complications the expectant mother was cared for in our Operative Intensive Care Unit overnight. Here we ensured close monitoring of cardiovascular parameters including values measured by the pulse contour analysis system. Special attention was needed

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to identify the first signs of any possible pulmonary edema. Intravenous antibiotics were continued until the 3<sup>rd</sup> postoperative day with gentamicin twice and clindamycin four times daily. Atosiban (9 mg/h) was infused until the first postoperative day. Thrombosis prophylaxis was started with dalteparin subcutaneous (Fragmin P forte® 0.2 ml = 5,000 IE) on the first postoperative day. A cardiotocography was performed twice daily until hospital discharge. Tocolysis with indomethacin suppository (50 mg) was allowed once in the event of early postoperative contractions.

## References

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