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PRESENTATION ABSTRACTS

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EXTREMELY LOW GESTATIONAL AGE NEWBORN - ELGAN

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Advances in obstetrics and neonatal intensive care medicine in the last decades have lead to an increased survival of neonates with extremely low gestational age. Thus, survival rates in neonates with 24 weeks of gestation are up to 75%; even survival of neonates with gestational age of 22 0/7 weeks or birth weights below 300gramms has been reported. However, this increased survival rates are accompanied with increased rates of neurosensory disabilities that raises ethical questions.

Consensus papers and treatment guidelines are still (discussed) controversial between societies of different countries. According the guideline of the Austrian Society of Pediatrics only comfort care should be performed in neonates <22 0/7 weeks of gestation. In neonates from 22 0/7 to 23 6/7 weeks of gestation resuscitation and intensive care should be provided if neonates are vital. In neonates from 24 0/7 to 25 6/7 resuscitation and intensive care should be performed, unless there are poor perinatal prognostic factors. The treatment should always be in accordance with the parents.

If decision to life support has been taken, there are controversial discussions concerning the way of treatment. Recent studies have shown that less invasive respiratory support with nasal CPAP (in combination with short intubation and surfactant application) is feasible in low gestational age neonates (<28 6/7) and helps to avoid mechanical ventilation. But, if this is applicable for extremely low gestational age neonates (<26 0/7) is still discussed controversial. Furthermore, lower arterial oxygen saturation levels in these neonates seems to be accompanied with a lower ROP rate but with higher mortality rate.

If the neonates survive, significant predictors of long term neurosensory disabilities are beside the gestational age the morbidities (e.g., bronchopulmonary dysplasia, intracranial lesions, ROP) during postnatal intensive care.

Thus, extremely low gestational age neonates at the limit of viability remain a challenge concerning ethics, treatment and prognosis.

MORTALITY, SHORT TERM AND NEURO-DEVELOPMENTAL OUTCOME OF EXTREMELY LOW GESTATIONAL AGE NEONATES AT THE NICU GRAZ

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Background

Survival rate in extremely low gestational age neonates has increased during the last decades. But decreasing mortality causes an increasing short- and long-term morbidity. At the Division of Neonatology of the Department of Pediatrics in Graz extremely low gestational age neonates are treated according a strict protocol since 2006.

Aim

In a retrospective observational study mortality, short term outcome and neuro-developmental outcome in extremely low gestational age neonates (23 0/7 to 26 6/7 weeks), who were treated in the period from 2006 to 2010, were analysed.

Patients and Methods

138 extremely low gestational age neonates, who were born in the period from January 2006 to December 2010 were included into the analysis. Mortality, short term morbidities and neurodevelopment outcome at the age of two years were analysed.

Results

Out of all 138 preterm births during this five year period 34 (24,6%) were stillbirths and 104 (75,3%) live births. 12 (11,5%) live born neonates died immediately after birth, whereby due to gestational age below 23 6/7 and poor prognosis only comfort care was performed.

Survival rate of live born neonates with decision to therapy was 74% (n = 68), (3 neonates with 23 weeks of gestation, 20 with 24 weeks, 17 with 25 weeks and 28 with 26 weeks.

Short-term morbidity was: 87% IRDS, 31% BPD, 17% IVH grade I-II, 16% IVH grade III-IV, 10% PVL, 19% ROP, 20% seizures and 9% NEC.

At the age of two years of 39 children, who were born 2006-2008 and survived, 36% had significant developmental disabilities, 31% slight impairment and 33% had age-appropriate development.

Conclusion

Of the live born neonates at the NICU Graz 74% survived and of these 36% had significant developmental disabilities. Efforts have to be undertaken to improve especially long term neuro-developmental outcome.

OUTCOME OF INFANTS WITH VLGA (22-29 WKS) BORN IN MH LJUBLJANA, SLOVENIA – COMPARISON WITH VON DATABASE

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Objective

To investigate whether short term outcome in very low gestational age infants differs between Ljubljana Maternity Hospital and Vermont Oxford Database.

Patients and methods

Infants with gestational age (GA) from 22 to 29 weeks born at the Ljubljana Maternity Hospital, a tertiary referral centre for premature infants in Slovenia, during the 4-year period 2008-2011 were included in the comparison. Perinatal and early follow-up data were collected on pre-prepared VON form. eNICQ software was used for data submission. Numerical data were analyzed by independent-samples t-test if normally distributed or by Mann-Whitney U test if skewed. Categorical data were expressed as proportions and analyzed by chi-square.

Results

A total of 418 infants with gestational age 22-29 weeks were born during selected period and they were compared to 155 112 infants in VON database. No differences were detected in mortality, mortality excluding early deaths, and survival, however the survival without major morbidities was higher in Ljubljana (55.4 % vs 38.8 %, $p<0.001$). Use of prenatal steroids did not differ, frequency of C-sections was lower in Ljubljana (42.8 % vs 66.2 %, $p<0.001$), but the rate of multiples was higher (33.2 % vs 26.2 %, $p=0.001$). No differences in birth weight, head circumference and birth weight were detected. The frequency of 1-minute Apgar score < 4 was higher in VON, however there was no difference between Ljubljana and VON in the frequency of 5-minute Apgar score < 4 . Infants in Ljubljana were less likely mask ventilated in the delivery room (46 % vs 69 %, $p<0.001$) or intubated (13.3 vs 66.2 %, $p<0.001$), and there was a significant higher rate of infants who did not require any resuscitation measure after birth (52.5 % vs 6.7 %, $p < 0.001$). The rate of infants with temperature at admission $< 37^{\circ}\text{C}$ was significantly higher in Ljubljana (74 % vs 26 %, $p<0.001$). There was no difference in the rate of respiratory distress syndrome, however the use of CPAP before ventilation was higher (59 % vs 31 %, $p < 0.001$). The rates of intubated infants after leaving delivery room (62.6 % vs 81.9 %, $p<0.001$) and the need for surfactant treatment (54.7 % vs 78.4 %) were lower in Ljubljana. Use of late corticosteroid treatment did not differ. There was a significantly lower incidence of BPD in Ljubljana (26.7 % vs 42.5 %, $p<0.001$). No difference in early sepsis was noted, but there was slightly lower incidence of late onset sepsis in Ljubljana (8.8 % vs 12.5 %, $p=0.01$). Ljubljana and VON population did not differ with respect to severe IVH and PVL. The incidence of any ROP was substantially lower in Ljubljana (6 % vs 42.7 %, $p< 0.001$), where - despite the same examination rate - no case of severe ROP was diagnosed (VON 9.4 %). There was also no difference in the incidence of NEC.

Conclusion

The comparison of short term outcomes of infants with GA 22-29 wks between Ljubljana and VON showed lower rate of delivery room interventions, followed by more frequent usage of CPAP and lower intubation rate. No short term outcome variable showed worse outcome, however there was significantly lower incidence of ROP and BPD in Ljubljana, which at the end led to higher survival without major preterm morbidities when compared to VON.

SURVIVAL CHANCES AND MORBIDITIES OF EXTREMELY PRETERM NEONATES

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Background

Perinatal care has improved the prognosis and chances of survival of extremely preterm neonates over time. The risk for mortality was reduced in the last years.

Among surviving infants developed intraventricular hemorrhage (IVH) is 10%, necrotizing enterocolitis (NEC) 5-6 %, patent ductus arteriosus (PDA) is more than 60%, and 30% developed retinopathy of prematurity (ROP). More than 80% needed mechanical ventilation, 25-30% developed severe bronchopulmonary dysplasia (BPD) in european countries.

Objectives

To identify the risk factors of the mortality and morbidities of extremely preterm infants (less than 1000 g at birth or <28 weeks' gestation). To investigate survival chances in 2 periods in the past 6 years of premature infants, in birthweight group < 500 g.

Results

Risk factor for mortality was BPD. The incidence was 30% in patients < 500 g, 50% in patients 500-749 g and 18% in 750-1000 g. NEC (with or without bowel resection) 30% in preterm infants 500-749 g and 15% in 750-1000 g. IVH incidence 30% in preterm infants < 500 g, 64% in 500-749 g and 55% in 750-1000 g.

The survival rate has improved between 2009 and 2011 from 26,3% to 55,2 % in the group of patients < 500 g. (The number of patients was 6 in 2011).

The preterm infants 500-749 g have a survival rate about 70% in the 3 years period.

Between 750-1000 g the survival chance was 78-72-78% in the investigated period.

The survival rate in the preterm infants < 28 weeks of gestation was 75% in 2009, 71% in 2010 and 80% in 2011.

The survival chance improved in the last 6 years by 100% in the investigated group of preterm infants with < 500 g birthweight.

Conclusions

The outcome of fetuses born < 28 weeks of gestational age is improving over time.

EXTREMELY PRETERM DELIVERY. THE OBSTETRICIAN'S PERSPECTIVE

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Preterm delivery remains the biggest unsolved obstetrical problem. The risk of neonatal death and handicap is especially increased in preterm birth at < 28 weeks, defined as extremely preterm birth. Although the perinatal mortality rate due to prematurity has decreased dramatically over the past decades in high-income countries, this reduction has resulted from improvements in neonatal care for premature babies, and has occurred in spite of the unchanged or even increasing incidence of premature delivery. Most common interventions recommended to prevent prematurity have been proven to have little or no benefit. Bed rest, once universally advocated, is now largely historical, and cerclage, antibiotics or tocolytics may be beneficial only in specific circumstances. There is experimental support from animal and in vitro studies, and also empirical evidence from large randomized placebo-controlled clinical trials, that treatment with progestins (natural progesterone and 17- α -hydroxyprogesterone-acetate) may reduce the risk of preterm delivery. Slovenian guidelines for progestin treatment in the prevention of preterm delivery will be presented in the lecture. Once preterm labour is established, the goal of treatment is merely to delay delivery in order to allow for the transfer of the pregnant patient to the most appropriate hospital, for administration of group B streptococcus antibiotic prophylaxis, and for administration of corticosteroids. None of the currently available tocolytics can prolong pregnancy sufficiently to allow further intrauterine growth and maturation of the foetus. The role and controversies surrounding magnesium sulphate for neuroprotection of premature babies will also be discussed, whereas the mode of delivery of extremely preterm babies will be the topic of our invited lecture.

PRETERM DELIVERIES IN THE YEARS 2006 AND 2011.COMPARISON OF FETAL OUTCOME, MATERNAL OUTCOME AND DELIVERY MODE ACCORDING TO ROBSON'S TEN GROUPS CLASSIFICATION SYSTEM

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Objective

Even though maternal and fetal monitoring methods during pregnancy and labor are developing, the incidence of preterm deliveries on the one hand and of Cesarean Sections on the other is rising throughout the developed world over the last years. Objective of this study was to determine the main contributors to this rise by comparing data from 2006 and 2011 according to the Robson's Ten Group Classification System (TGCS) in the last 5 years concerning the change of management

Methods

Registered data from 10 obstetric departments in Styria, Austria were examined according to "Robson's 10 groups classification System" (TGCS) for deliveries for the years 2006 and 2011. This system divides deliveries in ten groups according to parity, past obstetric history, fetal presentation, gestational age and mode of onset of labor. Maternal and fetal outcome in Group 10 (preterm Deliveries group) was separately analyzed.

Results

	2006 Nr. of CS / deliveries: 2318/8448 (27,44%)				2011 Nr. of CS / deliveries: 2646/8458 (31,28%)			
Group	CS / group	% of Group of Total	CS rate in Group	Contribution of each group to total of 2006	CS / Group	% of Group of Total	CS rate in Group	Contribution of each group to total of 2011
1 Nulliparous women with a single vertex pregnancy, at ≥ 37 weeks gestation in spontaneous labour	452/2634	31,18%	17,16%	19,50%	431/2428	28,71%	17,75%	16,29%
2 Nulliparous women with a single vertex pregnancy, at ≥ 37 weeks gestation, who had	422/1001	11,85%	42,16%	18,21%	480/1117	13,21%	42,97%	18,14%

labour induced or who had CS before labour								
3 Multiparous women, without a uterine scar, with a single vertex pregnancy at ≥37 weeks gestation in spontaneous labour	122/2622	31,04%	4,65%	5,26%	97 / 2216	26,20%	4,38%	3,67%
4 Multiparous women, without a uterine scar, with a single vertex pregnancy at ≥37 weeks gestation, who had labour induced or who had CS before labour	174/673	7,97%	25,85%	7,51%	146 / 649	7,67%	22,50%	5,52%
5 Multiparous women, with at least one previous uterine scar with a single vertex pregnancy at ≥37 weeks gestation	457/617	<u>7,30%</u>	<u>74,07%</u>	19,72%	689 / 934	<u>11,04%</u>	<u>73,77%</u>	26,04%
6 All nulliparous women with a single breech pregnancy	281/285	3,37%	98,60%	12,12%	258 / 260	3,07%	99,23%	9,75%

7 All multiparous women with a single breech pregnancy, including women with a uterine scar	135/144	1,70%	93,75%	5,82%	138 / 145	1,71%	95,17%	5,22%
8 All women with multiple pregnancies, including women with a uterine scar	116/139	1,65%	83,45%	5,00%	138 / 150	1,77%	92,00%	5,22%
9 All women with a single pregnancy with a transverse or otherwise abnormal presentation, including women with a uterine scar	24/24	0,28%	100,00%	1,04%	26 / 26	0,31%	100,00%	0,98%
10 All women with a single vertex pregnancy at < 37 weeks gestation, including women with a uterine scar	135/309	<u>3,66%</u>	<u>43,69%</u>	5,82%	243 / 533	<u>6,30%</u>	<u>45,59%</u>	9,18%
	<u>Early preterm deliveries <34 g.w. 89/146</u>	<u>1,73%</u>	<u>60,9%</u>	3,84%	<u>Early preterm deliveries <34 g.w. 155/195</u>	<u>2,3%</u>	<u>79,49%</u>	5,86%

Cesarean delivery rate in our collective raised from 27,44% to 31,28%, coinciding with the international trend. Premature delivery rate (Group 10) doubled, although the Cesarean rate within this group stayed almost constant. Early preterm deliveries (subgroup of group 10) decreased by 10,6% (from 47,2% to 36,6%). Fetal outcome concerning birth weight of early preterm deliveries remained nearly constant.

Conclusion

Management of the optimization of the ideal delivery timing and management of preterm deliveries changed in the last 5 years influenced by a number of international studies (i.e.

TRUFFLE-Study). In our collective this lead to a higher number of preterm deliveries on the one hand but a lower number of early-preterm deliveries on the other. This means we bring a higher proportions of pregnancies to higher gestational ages.

MANAGEMENT OF EARLY PRETERM CASES IN A SECONDARY HOSPITAL: THE SAN BASSIANO EXPERIENCE

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Objective

The aim of this study was to analyze indications and outcomes of cases in which patients affected by severe complications of pregnancy in early preterm period (before 32 weeks) were hospitalized in our Second level Hospital, were unable to accomplish the In-utero transfer protocol to a referral III level and were delivered in our Hospital.

Material and methods

Between 2007 and 2011, seventy seven women (3 of whom carried twin pregnancies) were hospitalized at our hospital for several pathologies that included PPROM, IUGR, preeclampsia, chronic hypertension, anemia, oligo-anidramnios, polydramnios, HELLP syndrome and preterm labour. All the patients underwent laboratory tests, cardiotocography and ultrasound evaluation.

All women with suspected preterm labour underwent the fibronectin test if the cervix was \leq of 25 mm at cervicometry (all positive cases with uterine contractions underwent endovenous Tractocile). In all patients in which there was a potential risk of preterm delivery, 12 mg of betamethasone were administered immediately and a second dose 24h later.

According to our regional guidelines for preterm labour all pregnant women with threatened delivery at a gestational age less than 32 weeks should be transferred, if possible, to a referral hospital (maternities with NICU). In many cases transfer was not feasible (because of clinical contraindications) and the patients were delivered in our hospital in which there is a neonatal pathology unit (not a NICU).

Results

38 patient (49%) between 23 and 32 week were successfully transferred to other hospitals in Vicenza, Padova, Treviso, Camposampiero and Verona. Twenty eight of these patients delivered in the first 15 hours after the transfer. One of these patients with a HELLP syndrome was delivered upon arrival to the referral centre and then transferred in Intensive care unit because of post-partum eclampsia for a week, but after 3 weeks she didn't report sequelae.

Between 2007 and 2011 39 women delivered at our hospital between 23 and 32 weeks, 12 with caesarean section (3 for twin pregnancy) and 27 with spontaneous labour for a total of 42 fetuses. Four fetuses were born between 23 and 24 week, 8 fetuses were born between 25 and 28 week, 30 fetuses were born between 29 and 32 weeks. Available data on outcomes will be presented.

Conclusion

This study shows that in spite of the presence of well organized in-utero transfer means and procedures, a secondary level hospital (no NICU) must have the knowledge and the possibilities to treat early preterm cases since about half of cases cannot be transferred and the women deliver their babies there.

CAESAREAN OR VAGINAL DELIVERY FOR VERY PRETERM AND EXTREMELY PRETERM NEONATES: SLOVENIAN EXPERIENCE

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Background and objective: Despite several attempts of randomized controlled trials and many observational studies the optimal mode of delivery for very preterm and extremely preterm neonates remains controversial. Our objective was to evaluate whether mode of delivery is a predictor of neonatal death and/or 3-4 intraventricular haemorrhage in very preterm singletons and twins born in Slovenia. We further investigated the association between delivery mode and outcomes for cephalic and breech singletons separately.

Methods: A national registry-based survey of all singleton and twin pregnancies delivered at >32 weeks between 2002 and 2011 was performed. Neonates with lethal congenital anomalies, stillbirths, higher order multiples and transverse lie singletons were excluded. We evaluated the effect of delivery mode and confounding variables on neonatal mortality and/or severe intraventricular haemorrhage using multivariable logistic regression analysis.

Results: 1902 neonates were included: 985 singleton cephalic, 313 singleton breech, and 604 twins. 102 were delivered at 22 0/7 to 23 6/7; 523 at 24 0/7 to 27 6/7; and 1259 at 28 0/7 to 31 6/7 weeks. Caesarean delivery rate was 34%, neonatal mortality rate 6,9%, and intraventricular haemorrhage rate 3,8%. After adjustment for risk factors (plurality – singletons vs. twins, presentation of singletons – cephalic vs. breech, gestational age, corticosteroid therapy, intrauterine growth restriction, preeclampsia, and amnionitis) delivery mode had no effect on the composite outcome of neonatal mortality or intraventricular haemorrhage (OR 0,97; 95% CI 0,68-1,40), nor on intraventricular haemorrhage alone (OR 0,95; 95% CI 0,56-1,61).

Conclusions: Caesarean delivery did not enhance survival nor did lower the risk of severe intraventricular haemorrhage in very preterm and extremely preterm neonates irrespective of plurality and presentation in singletons.

EXTREME PRETERM PREGNANCY AND NEWBORN

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Prematurity plays a major role, and it maintain the leading position in perinatal morbidity and mortality. If we add the problems of the somatical/mental postnatal care of the surviving newborns, it's importance must be highlighted, because remains a significant public health issue and principal cause of neonatal death and of long-term neurodevelopmental disturbances.

Situation is also the same in Hungary, where the number of live birth per year is around 95,000 of which about 8-9% are preterm birth. Rate of prematurity in the Department of Obstetrics and Gynecology, University of Szeged is around 12-15%, because the majority of threatened preterm delivery cases in the south-east region of Hungary, are referred here on the basis of the concept of in utero transportation. Our clinic, which is a tertiary obstetrical center, is in a permanent professional contact with the Neonatal Intensive Care Unit at the Department of Pediatrics.

The incomplete organ development of a preterm, and especially of a very low birtht (less than 1500 g), or an extremely low birth weight (less than 1000 g) newborns put them in a very difficult situation which occur during the transition from intrauterine to extrauterine life. Mode of prenatal care, in time recognition and adequate therapy of the different types of maternal risk factors and the signs of threatened preterm delivery, prevention of the respiratory distress syndrome, are also measures which can help this transition.

During labour, determination of the intrauterine position of the fetus, correct evaluation of the estimated weight, the integrity of the membranes, the signs of infections, choose of the optimal mode of delivery, prevention of the different types of newborn injuries, imposes enormous medical, moral and ethical tasks for the obstetrical and neonatological team. In time presence of this late crew is also crucial for immediately start of the adequate newborn therapy.

LETHAL AND NON-LETHAL FETAL CARDIOPATHIES: PARENT COUNSELING

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Improvement of prenatal diagnostics has resulted in an early detection of severe congenital heart defects (CHD) before birth. It is a big responsibility to diagnose fetal cardiac disease and to make a relevant statement concerning the probable course and prognosis of the disease. The marked improvements in neonatal cardiac surgery and neonatal intensive care have made it possible that babies with severe cardiopathies can now be operated on successfully. The critical issue is that which CHD can be regarded as lethal today. Informing parents about the outcome of the sick fetus is a big responsibility and could be the source of important bioethical dilemmas; the short-term and long-term outcome of the fetus, the presence of other malformation(s), medical and nursing personnel, equipments of cardiac surgery and neonatal intensive care unit, the age of the parents, disease(s) of the parent(s), possibility to have more children, the situation of the family, unemployment connected to bring up a chronically ill child must all be taken into consideration. In this presentation we would like to address the different aspects of counseling by presenting some particular cases from our experience.

Case 1. Truncus arteriosus was diagnosed at 18 weeks gestation (GW). Having 2 healthy children, the fairly old parents did not want to keep the pregnancy, but abortion was not done. The baby died after cardiac surgery, the mother became depressed.

Case 2: Ventricular septal defect (VSD) and aortic arch interruption were diagnosed at 20 GW, without chromosomal aberration. The parents insisted on keeping the pregnancy. The baby was born with a lot of minor and major anomalies, which could not be diagnosed prenatally. The baby was treated in the NICU because of septicemia. Cardiac surgery was performed at 5 weeks of age, and the baby is doing well. Mental retardation is suspected.

Case 3: at 26 GW transposition of the great arteries and VSD were diagnosed. The parents would have asked for termination of pregnancy, if they had known it earlier. The baby was born and doing very well and discharged home. Cardiac surgery is planned later because the co-existing pulmonary stenosis prevents pulmonary hypertension.

Case 4: Tetralogy of Fallot and pulmonary atresia were diagnosed at 22 GW of a first pregnancy. Successful Blalock Taussig shunt was performed, and the baby was discharged home. Complete recovery can be expected after total correction of CHD.

Case 5: At 20 GW a complex CHD is detected. TGA, CAVC, univentricular heart, and Ivemark syndrome was diagnosed. At least 4-5 cardiac surgeries would be necessary to be done, the mental status is questionable. After a multidisciplinary consilium the pregnancy was terminated.

Case 6: At 17 GW severe fetal hydrops (pleural effusion, ascites and pericardial effusion) was diagnosed in a fetus with CAVC. Chromosomal and virologic investigations were advised. The fetus died in the maternal womb at 20 GW.

The principles of bioethics should be taken into consideration (autonomy, justice, charity). We should avoid incorrect information, which could have severe consequences. It causes a lot of stress for the parents and doctors as well. Decision making is the right of the parents, but before doing it, they require the most accurate and up-to-date information. Having a sick fetus causes enormous stress for the pregnant woman and her relatives. The parents should be carefully informed on the predictive value of the major and minor sonographic markers which indicate CHD, to help them in their decision on the pregnancy. All help must be provided to achieve a possible complete or nearly complete recovery. The suspected diagnosis must be repeatable. If it is necessary, we should ask for a so-called second opinion.

NEONATAL OUTCOME AFTER EXTREME PRETERM DELIVERY IN PREGNANCIES COMPLICATED BY EARLY ONSET PREECLAMPSIA, ECLAMPSIA AND HELLP-SYNDROME

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Objective

To analyze neonatal outcome after extreme preterm delivery before 27 weeks of gestation in early-onset preeclampsia, eclampsia and HELLP-Syndrome

Patients and Methods

Maternal and neonatal outcome of 21 pregnancies complicated by preeclampsia (P), eclampsia (E) or/and HELLP-Syndrome (H) (Group P/E/H) were compared to the outcome of 45 normotensive women (control group, C) delivered between 23rd and 27th week of gestation at the Department of Obstetrics and Gynaecology, Medical University Graz. Exclusion criteria were premature rupture of membrane (PROM), intrauterine infection and twin pregnancy. Statistical analysis was performed by χ^2 -Square Test and the $P < 0.05$ was accepted as significant.

Results

The P/E/H-group included 9 women with preeclampsia, 1 woman with eclampsia and 11 women with HELLP-Syndrome. Two of the pregnancies were terminated after IUFD and 4 children died several days after delivery (3°/oo). In the C group, there were 6 cases of IUFD and 11 children died several days after delivery (4°/oo), n.s.

IUGR occurred in 20 women (95%) of the P/E/H-group compared to one pregnancy (2%) in the C-group ($p < 0.001$).

All P/E/H women and 33 C women received betamethasone for lung maturation. 10 children from P/E/H (52, 6%) and 15 children from C (38, 5%), n.s. had asphyxia, 17 P/E/H (94, 5%) and 33 C (84%) IRDS, n.s., 4 P/E/H (22%) and 14 C (37, 8 %) PVL, $P < 0.05$, 7 P/E/H (39%) and 10 C IVH (28, 6 %), n.s., 5 P/E/H (27, 8%) and 4 C (10, 8 %) cerebral palsy, $P < 0.05$, and 7 P/E/H children (38, 9%) and 26 C children (72, 2 %) neonatal sepsis, $P < 0.01$ (Tab.1)

	IUGR	IUFD	neonatal death	Asphyxia	IRDS	Sepsis/infection	IVH	PVL	cerebral palsy	development delay
C-group	1 (2 %)	6 (13%)	11 (24%)	15 (38,5%)	33 (84%)	26 (72,2%)	10 (28,6%)	14 (37,8%)	4 (10,8%)	5 (5,4%)
P/E/H-group	20 (95%)*	2 (9,5%) ns	4 (19%) ns	10 (52,6%)*	17 (94,5%)	7 (38,9%)*	7 (39%) ns	4 (22%)*	5 (27,8%)*	1 (7,10%) ns

Tab. 1

Legend: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns= not significant, IUGR: intrauterine growth restriction, IUFD: intrauterine fetal death, IRDS: infant respiratory distress syndrome, IVH: intraventricular hemorrhage, PVL: periventricular leucomalacia

Conclusion

Children from P/E/H suffer more frequently from growth restriction, asphyxia and cerebral palsy than children after extreme preterm delivery for other reasons. The higher incidence of cerebral palsy could be due to the higher frequency of intrauterine asphyxia. Otherwise, the decreased incidence of sepsis is associated with less PVL in P/E/H.

EXTRAPERITONEAL (ECS) CESAREAN SECTION: RELAUNCH OF A SURGICAL TECHNIQUE AND COMPARISON WITH THE TRADITIONAL MISGAV-LADACH METHOD

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Introduction

The idea behind the extraperitoneal approach is not to expose the peritoneal cavity to blood, amniotic fluid, vernix and mechanical irritation. The objective of this study is to compare ECS and TCS (transperitoneal caesarean section modified to Misgav Ladach) with respect to parameters of surgical morbidity.

Methods

54 patients with an indication for an elective cesarean section were invited to participate in the study. This study is designed as a prospective, randomized and single blind trial. The primary endpoint of the study is postoperative abdominal pain measured on a VAS scale ranging from 0-10. Secondary endpoints are intraoperative nausea and vomiting, postoperative shoulder pain, intestinal and urinary complications.

Results

Patients after ECS had significant less maximal postoperative pain than patients after TCS. Mean peak pain scores on postoperative days 1 and 2 were 4.16 (± 1.34) and 2.56 (± 1.42) for ECS and 5.26 (± 1.89) and 3.22 (± 1.72) for TCS, respectively ($p=0.033$). Requests for analgesics were significantly less after ECS. Among other secondary endpoints intraoperative nausea and postoperative shoulder pain were significantly reduced with ECS. No bladder injury occurred in either group. No difference was observed for estimated blood loss and neonatal outcome. Urogenital distress, urinary tract infection and bowel dysfunction did not differ at discharge from hospital and six weeks after.

Discussion

ECS is technically feasible and seems to reduce postoperative pain and surgical morbidity.

WATER LABOR AND WATER BIRTH: A REVISION OF THE CURRENT LITERATURE, THE EXISTING BIRTH POOLS' LIMITS AND A PROPOSAL FOR A NEW PROTOTYPE

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Background

The latest literature revisions concerning waterbirth bring out the undisputed benefit of water on pain tolerance during labor [1-6], indeed even the Scientific Community suggests to each facility to offer this type of childbirth [3]. There is, in fact, no scientific evidence that proves laboring-waterbirthing exposes the patient to a higher complication than traditional delivery. Nevertheless, nowadays there are only a few facilities offering this service. The reasons of this lack in water birth services may be caused by the poor midwife training and, also, by the huge technical limitations of the existing birthing pools, which do not provide an immediate response to a potential emergency. This forces the midwife to awkward and inadequate care during delivery.

Purpose

First, the following work aims to encourage water labor-water birth and to a hospital staff training. Secondly, its aim is also to popularize a new recently patented prototype of birth pools able to ensure both the birth physiology and an immediate response when obstetric care is required.

The new prototype

This type of birth pool will include a narrowing area - called "Postazione d'Assistenza" (Staff care workspace) - where the staff in charge will be positioned. A multi-functional and a multi-directional integrated delivery bed will be positioned in the centre of the birth pool, just in front of the "Postazione d'Assistenza"; thanks to its hydraulic slipping mechanism it will be able to lift itself, move closer to the "Postazione d'Assistenza", and slant itself in every position so it can be ejected from the pool in case of emergency. This delivery bed will be made of soft and waterproof material to let the patient assume a "on hands and on knees" position, so Gaskin maneuver can be performed to resolve a possible shoulder dystocia. In case of physiological labor, the patient will be able to move freely thanks to the supporting surfaces designed to let the patient take any alternative positions, known for helping fetal progression. On each side of the bed there will be two supporting surfaces just in case of emergency or to control the perineum status. The patient will sit on the bed which, in a few seconds, can be transformed into a delivery bed with a removable sterilized supporting shelf. As a result, it will be possible to safely expel the placenta, and carry out a donation of the umbilical cord, a perineal repair or any other urgent procedure (e.g. assisted delivery, or patient transfer due to cesarean section), directly in the pool without wasting any time.

Conclusion

It is necessary to promote more awareness on this subject inside hospitals. This prototype may become a precious technological innovation, a new fundamental tool that all women will benefit from in terms of practice and safety.

CHILDREN BORN AFTER IN VITRO FERTILIZATION – PROBLEM OF TWINS THROUGH THE EYES OF THE PEDIATRICIAN

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Background

Double embryo transfer (DET) in In Vitro Fertilisation (IVF) is sometimes used also in women younger than 36 years and therefor increases the rate of twin pregnancy. The most substantial problem resulting from multiple pregnancies relates to newborn immaturity subsequent to preterm birth which increases the number of infants with very low birth weight (VLBW) and the number of neonatal intensive care unit (NICU) admissions.

Objective

To evaluate if in Slovenia strict recommendation of single embryo transfer (SET) could further reduce the number of VLBW infants and the number of intensive care unit admissions.

Methods

Data were collected from National Perinatal Information System (NPIS) for period 2002-2010. Dizygotic twins after IVF procedure were compared to non-IVF dizygotic twins. Separately, analysis of twin admission to NICU Ljubljana for 2010 was performed.

Results

In the period of 2002-2010 the rate of twin births after IVF has declined from 1 % to 0.5%, which relates to the reduction of IVF twin pregnancies from 25 to 13.6%. The rate of stillbirths in IVF dizygotic twins is 1.4-times higher and the risk for very low birth weight is 4-times higher than in IVF sigletons. Among older women (≥ 36 yrs) the rate of twin pregnancies remained almost unchanged. 128 VLBW dizygotic twins were born to < 36 yrs old women. In the nine-year period it might be possible to prevent around 100 ELBW births. Separate analysis for 2010 showed also an increased rate of major morbidities or mortality in DET IVF twins admitted to NICU Ljubljana compared to non-IVF twins.

Conclusion

Strict following of recommendation for SET could further reduce the number of VLBW infants and the number of NICU admissions.

THE PERINATAL OUTCOME OF ADOLESCENT PREGNANCIES

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Introduction

Pregnancy among teenagers is a global problem and these pregnant girls are considered a high risk group. Teenage pregnancies are associated with higher rates of maternal and neonatal complications.

Materials and methods

A retrospective analysis was carried out on the data on all mothers aged below 18 years who had delivered at the Department of Obstetrics and Gynecology, University of Szeged, between 2001 and 2010. During this period, overall 23157 births were recorded, and 177 mothers were younger than 18 years. 182 neonates (0,8%) were born to these mothers. We compared the data on the adolescent mothers with those on all mothers who delivered in Hungary in that period.

Results

85% of the adolescent mothers were 17-18 years old, 15% 15 years old or younger. The main gestational age was $37,6 \pm 2,8$ weeks. The frequency of cesarean section was 34% and that of operative vaginal delivery was 2%. The main birth weight was significantly lower in the adolescent group than in the general hungarian population (2905 ± 682 versus 3340 g). The frequency of the premature deliveries (22,5% versus 8%) and intrauterine growth retardation (15,4% versus 10%) was significantly higher, congenital malformations (8,8% versus 4%) occurred more often in the study group. The number of transfers to the Neonatal Intensive Care Unit (8,8% versus 8%) was not different in the two groups. The umbilical cord blood pH was less than 7,2 in 13,2% of the neonates from the adolescent pregnancies.

Conclusions

A young maternal age is associated with a higher risk of an adverse neonatal outcome.

PERINATAL OUTCOME OF BREECH PRESENTATION BY DIFFERENT DELIVERY MODES

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Background

The worldwide occurrence of breech presentation at term is around 3-4% of all pregnancies. This incidence obviously decreases with increasing gestational age. Before the year of 2000 the chosen method of delivery was nearly even between vaginal delivery (VD) and Caesarean section (CS). At the turn of the century Term Breech Trial Collaborative Group (TBTCG) study results were published and it was verified that the CS has significantly better outcome for the newborn than VD.

Methods

In the years of 1991, 1996, 2000, 2001 and 2006, all together 10296 deliveries occurred at our department. After the exclusion of multiple and preterm deliveries, there were 246 term, breech presentations (2.4%). The mean gestational age, mean birth weight, birth trauma, 5 min. Apgar-score, umbilical cord blood pH and the need of admission to the neonatal intensive care unit (NICU) were evaluated. For statistical calculation we used χ^2 -probe, Fischer's exact test and Student t-probe.

Results

The mean birthweight was significantly higher in the CS vs. VD group (3211g vs. 2912g). Significantly more newborns were born with pH < 7.2 and 5 min. Apgar-score < 7 in the VD group than those born by CS (21% vs. 9.5% and 7% vs. 4.8%). The need of NICU treatment was higher in the VD group however the difference was not significant. The rate of CS increased from 47.2% to 97.4% from 1991 to 2006 at our department.

Conclusion

Similar to the TBTCG our results also showed better outcome for the neonates born by CS in breech delivery, which caused a quick increase in the rate of CS, in our department.

IDENTIFICATION OF CAUSES OF STILLBIRTH THROUGH AUTOPSY AND PLACENTAL EXAMINATION REPORTS

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Introduction

During the past 30 years, stillbirth rates have declined in developed countries, but this tendency now seems to have stopped. Paradoxically, the numbers of antenatal visits, ultrasonographic measurements and fetal heart rate recordings are constantly increasing. Analyses of the causes of death may help ensure new clinical guidelines leading to a further decrease in stillbirth rate.

Methods and materials

We carried out a retrospective study on a sample of stillbirths diagnosed at the Department of Obstetrics and Gynecology, University of Szeged, Hungary, between 1996 and 2010. Overall, 140 stillbirths and 29,897 births occurred during the 14-year period between 1996 and 2010, representing an average stillbirth rate of 4.7 per 1000. The results of the autopsy and the histological examination of the placenta were analyzed.

Results

The postmortem examination revealed the cause of death in 81 cases (57.9%), while 56 cases (40.0%) remained unexplained. As regards the explained cases, the cause of death was insufficiency in 38 of the 81 cases (46.9%), an umbilical cord complication (an umbilical cord knot, or a constricting loop around the neck) in 21 cases (25.9%), an infection in 8 cases (9.9%), lethal congenital malformations in 5 cases (6.2%), placental abruption in 5 cases (6.2%) and hydrops fetalis in 4 cases (4.9%). A common fetal finding was IUGR, which occurred in 67 of the 140 cases (48.54%). Interestingly, IUGR did not prove to be associated with placental insufficiency.

Conclusion

Placental insufficiency as a major contributor to the stillbirth might have been prevented during the antenatal care. A more effective screening of IUGR should be introduced in the early third trimester.

TWINS ARE NOT JUST TWO SINGLETONS - RECOMMENDATIONS FOR CARE

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The incidence of multiple pregnancies is increasing steadily. At the same time the number of deliveries in most European countries is decreasing. In a country with a population of about 8 million there are 1000-1200 twin pregnancies. Of these 1000 twins the majority are dichorionic-diamniotic pregnancies. About 3-9 are the extremely rare cases of monoamniotic pregnancies, and about 200-250 are monochorionic and diamniotic; trend increasing. About 40-50 of these will develop symptoms of *twin-to-twin transfusion syndrome* (TTTS) or of *twin-polycythemia-anemia sequence* (TAPS) with about 20-30 requiring invasive intrauterine surgery in an attempt to save the lives of these fetuses. These are conditions which do not exist in dichorionic pregnancies, therefore the term „twins“ has become insufficient for all means and purposes. We can only describe these pregnancies based on the knowledge of the chorionicity. To achieve this it is imperative that we know how, and when to diagnose the chorionicity of multiples pregnancies and also know where these patients can be referred in case of a suspected complications typical of monochorionicity. Failure of early detection results in insufficient surveillance of these pregnancies and increases significantly the rate of unjustifiable fetal loss due to common complications such as TTTS or TAPS.

The talk will give an overview on the optimal early diagnostic steps necessary for the reliable diagnosis of the chorionicity and on the scale of information these patients should receive within at the beginning of their pregnancy. Diagnostic criteria and management protocols for the optimal surveillance of monochorionic pregnancies will be discussed.

THE THERAPEUTIC CHALLENGES OF TWIN-TO-TWIN TRANSFUSION SYNDROME

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Introduction

Twin-to-twin-transfusion syndrome (TTTS) is a condition which occurs only in identical twin pregnancies. The placenta contains blood vessels which connect the circulations of the twins. Depending on the number and type of the connecting vessels, the blood continuously being exchanged between both twins can be transfused disproportionately from one twin (the donor) to the other twin (recipient). The recipient twin becomes overloaded with blood with the consequence of heart failure and polyhydramnion. The transfusion causes the donor twin to have decreased blood volume, which leads to growth retardation and poor urinary output manifesting in oligohydramnion. The polyhydramnion often leads to cervical deficiency and pPROM (preterm premature rupture of membranes) and very often causes extreme prematurity. Difference in the nuchal translucency thickness between the identical twins can be one of the first sign of TTTS. Both fetal and neonatal loss rates are very high: without treatment the mortality rate is 90-100%. The neonatal morbidity rate is 10-30% resulting mostly from fetal hypoxia and immaturity. The frequency of TTTS requiring prenatal intervention is 10-15% among monochorionic twins.

Therapeutic possibilities are 1. Laser ablation of the placental anastomotic vessels. 2. umbilical cord ligation (artificial obstruction of the umbilical cord); 3. Reduction amniocentesis (removal of the excessive amniotic fluid from the sac of the recipient twin); 4. Septostomy (creation of a hole in the membrane between the babies' sacs using a needle); From these procedures laser ablation is the causal treatment of TTTS. Special instruments and skills are need for these procedures.

Materials

In the last 5 years we had 4 TTTS cases. We performed septostomy in all cases.

Results

One of them ended with spontaneous abortion in the 22th weeks of gestation. One pregnancy resulted with caesarean section in the 36 weeks of gestation and healthy babies were born. The third pregnancy was prolonged until the 36 weeks of gestation, when both fetuses died in utero due to cord-entanglement, closing the fetal circulations. The fourth pregnancy underwent two procedures of amniodrainage and finally septostomy. Due to progredient TTTS she was finally transferred to Graz for further assessment and treatment, where a rescue cord occlusion was carried out in the 21st week of pregnancy. The procedure was made more difficult by the floating of membranes, almost inevitable after septostomy. Despite technical difficulties the procedure was uneventful and the patient returned to the referring center on the 3rd day. The surviving fetus delivered significant hydrops which slowly resolved within 10 days. The pregnancy continued uneventfully.

Conclusion

Twin-to-twin transfusion syndrome is a severe complication of monochorionicity caused by random anastomosis of blood vessels between the fetuses on the placental surface. Early diagnosis requires frequent and competent ultrasound assessment from the first trimester. About 10-15% of all monochorionic diamniotic pregnancies develop TTTS requiring intervention. Among the possible management options LASER coagulation of the connecting vessels has been proven by randomized prospective studies to yield not only higher rates of

survival, but also lowest rates of neurological complications by the surviving fetuses. The procedure requires extensive training and specialized equipment.

PRESENTATION OF A COMPUTER APPLICATION FOR PARENTERAL NUTRITION PRESCRIPTION ASSISTANCE IN NEONATES

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We have developed an application that enables computer-aided prescription of parenteral nutrition (PN) in preterm newborns. The neonatologist is presented with a simple web interface written in HTML and JavaScript. To start the calculation, some basic data (ID number, name, date of birth, gestational age and weight) needs to be inputted. The program displays the specific guidelines for the nutrient intakes based on the postnatal age in days, the gestational age and the weight of the preterm baby as proposed by Tsang *et al.*, 2005. The desired volume and the amount of each individual nutrient are filled in by the neonatologist. Any deviations from the recommended values are automatically detected, thus eliminating most of the human errors involved in manually calculating the parenteral nutrition composition. The final composition of the PN mixture is calculated based on the type and quantity of enteral feeds and any additional arterial catheter infusions. The program also considers the concentrations at which the nutrients are stable in the PN solution. An alert is shown if the concentration of any nutrient is outside the stability limits.

The data is then sent to the back-end script written in Python which submits an online order to the pharmacy. A web interface for the pharmacist displays a notification when new orders arrive and allows browsing through the history of old prescriptions. The data is stored in a database, making it available for later use and further statistical analysis. The web interface setup is beneficial since no installation on the client side is necessary and only a web browser is required. Another benefit is the low maintenance overhead. When a bug is found or a new feature is asked for, all the clients get updated immediately.

The main two benefits of our computer application for PN prescription are (1) improving the accuracy of the PN calculations, which consequently improves the delivery of nutrients to the newborn and (2) saving time in the busy routine of a neonatal intensive care unit. Additional benefits are: (3) the order form is automatically sent to the pharmacy by a web interface, reducing the chance of mistakes when filling the form and reducing paper work, (4) the stability limits for the nutrients and compounds are included, (5) the composition of different formulas and maternal milk are considered, where also the values from a milk-analyzer can be included, (6) data is stored in a database making it available for later use and further statistical analysis.

Reference:

Tsang R *et al.* Nutrition of the Preterm Infant, scientific basis and practical guidelines; second edition. Digital educational publishing Inc, 2005; Cincinnati, Ohio.

QUANTITATIVE ULTRASOUND TECHNIQUES IN ASSESSMENT OF BONE DENSITY IN NEWBORNS

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Metabolic bone disease is a common and significant problem in newborns that often give rise to osteopenia, osteoporosis and fractures. Premature infants are at significant risk for reduced bone mineral content and subsequent bone disease and they likely suffer lifelong decreased bone mineral density as a result of early birth and lack of adequate mineral stores that are typically present in full-term infants. Reduced bone mineral density occur more frequently also with concurrent conditions like vitamin D deficiency, immobility due to neurological diseases or sedation and long term treatment with drugs such as diuretics or steroids.

Bone monitoring is essential step towards providing the nutrients and physical stimulation needed by some newborns. Quantitative ultrasound evaluates children's bone status, including bone mineral density and bone strength. It provides comprehensive information about the bone mass, microstructure and mechanical properties of the bone. It is a highly reproducible, easily applicable and radiation-free technique that can be used for monitoring bone quality. Quantitative ultrasonography assesses bone density by measuring the speed of sound (SOS) of the ultrasound wave traveling along the cortical bone. This device measures SOS at the radius and tibia and is suitable for measurement in pediatrics having been specially designed for children and neonates with age and gestational specific references. Children tibial ultrasonography has been found to correlate with bone mineral assessment by dual energy X-ray absorptiometry.

PLACENTAL THREE-DIMENSIONAL DOPPLER INVESTIGATIONS IN PREGNANCIES COMPLICATED BY GESTATIONAL AND PRE-GESTATIONAL DIABETES MELLITUS

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The aim of our study was to assess placental vascularisation by 3-dimensional (3D) Doppler indices in pregnancies complicated by gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (pre-GDM).

Placental vascularisation of 313 pregnant women were prospectively evaluated by 3D Doppler ultrasound technique at the Department of Obstetrics and Gynecology, University of Szeged between 2011.08.01.- 2012.05.31. Vascularisation index, flow index and vascularisation flow index were determined during routine fetal ultrasound screening and compared between the study group(include 56 cases of GDM and 43 cases of pre-GDM) and the control group (214 uncomplicated pregnant women).

Pregnancies complicated either by GDM or by pre-GDM showed lower placental vascularisation indices as compared with normal pregnancies. The indirect signs of uteroplacental circulation (blood flow of umbilical and uterine arteries) in GDM and pre-GDM patients did not significantly differ from normal range. 3D Doppler indices of the placental circulation seems to be characteristic in diabetic pregnancies compared to the indirect signs of uteroplacental circulation.

PRE- AND PERINATAL SIGNIFICANCE OF SINGLE UMBILICAL ARTERY

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O The two vessels cord is associated with chromosomal trisomies and a number of structural abnormalities such as spina bifida, renal and heart defects, intrauterine growth retardation, intrauterine demise and impaired school achievements. Some severe defects can only be diagnosed after birth.

M Data collection of couples with single umbilical artery was obtained from the Department of Medical Genetics Department of Obstetrics and Gynecology and from the regional obstetric hospitals and private clinics. A database was established and analyzed with statistical methods. Associated anomalies were classified according to severity and organ system occurrence.

R Seventy six couples with diagnosis of SUA attended the our Prenatal Clinic between 2005 and 2011. Fifteen of them were first trimester diagnosis, and 4 out of them proved to be three vessels (3-VC) at the control examination. In 61 cases the SUA was recognized in weeks 18-23, two of them proved to be false diagnosis. Mean age was 28,9 years, mean body weight was 69 kg. Male/female ratio was 40/30. Genetic advise for invasive diagnosis were accepted by most of the pregnant, except three, and one of them gave birth to a newborn with trisomy 21. Chromosomal aberration was revealed in two cases: a trisomy 18 and a trisomy 21. Kidney and heart defects were found in four cases. A lethal tracheal stenosis was revealed month after birth.

C Recently, the SUA is diagnosed in weeks 18-23 and the management of this cases includes genetic counseling, chromosomal study when it is indicated except in very low risk cases for chromosomal defects calculated according to ultrasound and biochemical parameters. The risk of trisomies is high (2/76) in cases of SUA and severe adverse fetal outcome should be considered.

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NEW DEVELOPMENTS IN PERINATAL MEDICINE: OBSTETRICAL ASPECTS

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Introduction

Although “new technologies” was the original topic, it appeared clear from the beginning that it was too restrictive. If we consider the topic in its wider significance, including not only new technology but also new techniques and clinical approaches, then the issue becomes more relevant although it may be too wide. For this reason we chose to deal with some of the new developments, mainly those that have or may have in the near future a great impact on Perinatal Medicine.

The “Short Cervix”

One of the hottest topics in obstetrics is ultrasound detected “Short cervix” and how to deal with it in order to reduce preterm delivery: Progesterone? Cerclage? Pessary?

In a meta-analysis of individual patient data from five placebo-controlled randomized trials of progesterone supplementation of women with asymptomatic midtrimester sonographic short cervix, progesterone supplementation was associated with a 30 to 50 percent reduction in preterm birth <28, <33, and <35 weeks and a 40 percent reduction in composite neonatal morbidity and mortality [1]. These benefits were similar at progesterone doses of 90, 100, and 200 mg daily and for women with and without a history of prior preterm birth. Beneficial effects were noted at cervical lengths <10 mm, 10 to 20 mm, and 21 to 25 mm, but only the 10 to 20 mm group reached statistical significance.

A multicenter trial randomly assigned 385 pregnant women with cervical length <25 mm at 20 to 23 weeks to use of a cervical pessary or expectant management (no pessary) [2]. The majority of these patients (89 percent) had no history of previous preterm birth and none were treated with progesterone or cerclage. The pessary group had a significantly lower rate of spontaneous preterm birth <28 and <34 weeks than the expectant management group.

Early detection of maternal risk for Preeclampsia

Preeclampsia is one of the leading causes of maternal and fetal mortality worldwide and a main cause of preterm labour. The aim for the early diagnosis is to start a preventive therapy by administration of 100 mg acetylsalicylic acid (ASS, aspirin) before 16 weeks of pregnancy (reduction of risk for severe preeclampsia: RR 0, 1; 95% KI 0, 1–0, 74) [3].

Maternal risk factors alone are insufficient to select a high risk population. Biophysical parameters like Doppler of the uterine arteries, 3D Power Doppler, 3D measure of placental volume and Power Color Doppler of placental perfusion may play a role, but these techniques alone have low predictive values. Aiming to predict preeclampsia in the I trimester, several biochemical markers have been tested: PAPP-A was first identified as a predictive marker [4]). PlGF is also in the first quarter of pregnancy decreased. Further promising targets for first trimester screening are PP-13, soluble endoglin, inhibin A, activin A, pentraxin 3, P-selectin, IGFBP-1 and 3, adiponectin, resistin, L-arginine, asymmetric dimethylarginine (ADMA), and homoarginine. From recent studies, the combination of history, biophysical parameters and biochemical markers in the 1st trimester show high predictive values for early onset preeclampsia and at a lesser degree for late onset preeclampsia [4,5].

Serum Biochemistry as Screening tool for Fetal Growth Restriction

First trimester combined screening for aneuploidy has been the focus of extensive research.

Models incorporate maternal characteristics and serum biochemical markers with nuchal translucency in order to predict adverse outcomes. The levels of some biochemical markers are altered in SGA and FGR pregnancies. A raised maternal serum alpha-fetoprotein (AFP) is associated with an increased risk of low birth weight in the absence of structural abnormality or aneuploidy. Low levels of maternal serum pregnancy-associated plasma protein A (PAPP-A) (at the lowest 5th percentile) are associated with an increased risk of an SGA infant [6]. A recent multicenter study related levels of first trimester PAPP-A and second trimester AFP to adverse pregnancy outcome. In that study, the odds ratio for delivering an SGA infant for women with a high AFP was 0.9 (95% CI 0.5–1.6) and for women with a low PAPP-A was 2.8 (95% CI 2.0–4.0). However, when a low PAPP-A at 10 to 14 weeks gestation and high AFP between 15 and 21 weeks gestation were combined, the odds ratio for delivering an SGA infant was 8.5 (95% CI 3.6–20.0). Thirty-two percent of women with this combination delivered a low birth weight neonate (less than 2,500 g) [7]. Several other placental markers are the subject of continued research including human chorionic gonadotrophin (hCG), ADAM12 (A Disintegrin and Metalloprotease), Placental protein 13 (PP13), serum soluble Fas (sFas) and placental growth factor (PIGF), amongst others. However, results show that detection rates are below levels warranted for large population screening.

Histopathological and Molecular Diagnostics and FGR

The patterns of gene expression that define hypoxic injury to trophoblasts are not well understood. However, studies using techniques such as high-density oligonucleotide microarrays, in situ hybridization, and quantitative PCR are reporting that placental villi from human pregnancies complicated by FGR demonstrate characteristic changes in “hypoxic trophoblast signature transcripts” [8]. Protein families such as cytokines, growth factors, and angiogenic peptides are suggested to play a role in the pathogenesis of FGR [9]. Proteomic techniques may provide an adjunct to the genomic approaches. These techniques are novel; however, the potential combination of fetal biophysical testing and informatics-based molecular analysis may prove useful in the future management of FGR.

Noninvasive Prenatal Diagnosis

After years of looking for fetal cells in the maternal circulation to use for genetic prenatal diagnosis, it seems that cell-free fetal DNA (cffDNA) will provide the basis for a safer, noninvasive approach to prenatal diagnosis. Since the identification of cffDNA in maternal plasma in the late 1990s, there has been much research on how cffDNA can be used as an alternative to invasive tests to provide safer, yet robust, noninvasive prenatal diagnosis (NIPD) for families at high risk of genetic disorders and for other pregnancy complications such as haemolytic disease of the newborn and fetal aneuploidy. In recent months we have seen the publication of papers describing implementation of this technology into routine obstetric practice to direct administration of anti-D for all RhD-negative mothers³ and as part of standard genetic care to determine fetal sex for women at high risk of sex-linked disorders. The clinical utility of NIPD in reducing the need for invasive testing⁴⁻⁶ and favorable costs have been clearly demonstrated.

In the most recently published study, the “NICE” study[10], the Digital ANalysis of Selected Regions (DANSR), an assay that selectively evaluates specific genomic fragments from cfDNA, was used. When combined with a novel analysis algorithm, the Fetal-fraction Optimized Risk of Trisomy Evaluation (FORTE), it provides an individualized assessment of trisomy risk. Of the 81 T21 cases, all were classified as High Risk for T21 and there was 1 false-positive result among the 2888 normal cases, for a sensitivity of 100% (95% confidence interval [CI], 95.5–100%) and a false-positive rate of 0.03% (95% CI, 0.002–0.20%). Of the 38 T18 cases, 37 were classified as High Risk and there were 2 false-positive results among the 2888 normal cases, for a sensitivity of 97.4% (95% CI, 86.5–99.9%) and a false-positive rate of 0.07% (95% CI, 0.02–0.25%). The authors conclusion was that Chromosome-

selective sequencing of cell-free DNA and application of an individualized risk algorithm is effective in the detection of fetal T21 and T18. They emphasized however, that further experience in larger populations of average-risk women is needed to clarify the role and utility of cfDNA in clinical practice.

Conclusion

Novel technologies continue to emerge in many obstetrical fields. Ultrasound and Doppler with recent 3D and 3D Power Doppler studies continue to give satisfaction in evaluating parameters that require volume and perfusion analysis. Biochemistry, histopathology and molecular biology are being introduced more and more in screening and diagnosis of complicated pregnancies. Everyday clinical practice is improved by introducing new assistance approaches and by updating and upgrading instrumentation and accessories. Although the global economical crisis represents an obstacle to innovation, every effort should be made to acquire and make use of the new tools, especially those with evidenced improved accuracy, efficiency and efficacy.

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MOBILE CARDIOTOCOGRAPHY – NANO-ELECTRONICS FOR MOBILE AMBIENT ASSISTED LIVING SYSTEMS (MAS)

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Background

At the moment continuous monitoring of the fetal heart rate is exclusively done in high-risk pregnancies during their presence in the labor ward. Limiting factors are the large number of midwives needed and the fact that the women are bounded to the CTG console for the time of monitoring. So in those cases not only medical reasons, but also patients comfort and satisfaction have to be taken into account.

Aim of the MAS – ENIAC Mobile Cardiotocography Project is the development of a miniaturized mobile-CTG-unit till 2013, which makes continuous long term monitoring of the FHR possible. In the first step usage is planned for high-risk inpatients, but also advances to an easy-to-use home tool are discussed.

Project

Goal of the project partnership “ENIAC Joint Undertaking” – including universities, public institutions and industry – is the modification of existing technologies, miniaturization and combination of new fields of research. The final product will be attributed to small size, high patient comfort and easy usability. Therefore only the FHR- and the tocography sensor will be in contact with the patient’s abdomen. The signal will be transmitted and analyzed by an automated software-algorithm, which will be integrated in a smartphone application based on operating system Android®. If the analysis of the FHR appears to be nonreassuring the smartphone automatically informs the obstetrical unit and advises the patient to contact hospital.

State of development

A first demonstrator is already developed and processing for version 2 is currently ongoing. Gathering of the FHR, which is done acoustically by a highly sensitive microphone, will be improved in the next version. Research on radiation exposure rates is finalized and in the attempt to minimize exposure levels antenna design is still under modification. Analyzing software is ready to use for non-automatic individual interpretation. A first clinical on-body testing is planned for the end of the year.

Outlook

A mobile CTG-unit can be used in many applications. In addition to an increase of the safety feeling of worried woman in low-risk pregnancies at home, especially patients with high-risk pregnancies, who are in outpatients care with close control interval would benefit from mobile home CTG monitoring. In monitoring of inpatients with high-risk pregnancies, e.g. Preeclampsia or IUGR, a change from point-to-point tracing to continuous monitoring would set place. That would cause a significant increase of knowledge about current fetal status and give the opportunity of faster reactions to pathological situations.

“TWO-STEP” DELIVERY: EFFECT ON UMBILICAL ARTERY HEMATOCRIT AND PH.

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Objectives

The timing of umbilical cord clamping has a profound effect on the amount of blood that remains in the infant's circulation at birth. However, there is no evidence to support a relationship between cord clamping time and other active management techniques of the third stage of labor.

Objective was to examine the association between head-to-body delivery by 'two-step' approach, that include waiting for the next contraction to deliver the shoulders, and early cord clamping (<1 min) and its effect on the amount of blood that remains in the infant's circulation at birth and cord artery blood gas parameters.

Materials

Prospective observational study on 50 consecutive at term, uncomplicated vaginal deliveries with singleton cephalic fetuses during January 2012 in Policlinico Abano Terme, Abano Terme, Italy.

Methods

Cord arterial blood gas parameters and hematocrit (Hct) were compared to the reference values obtained in 50 healthy, control neonates, matched for gestational age, vaginally delivered by 'one-step' approach. Data analysis was performed with SPSS for Windows statistical package (version 13)

Results

In our study population, Head-to-body interval was timed and was always inferior to 3 minutes. The groups had similar demographic and biomedical characteristics at baseline. The mean cord artery hematocrit (Hct 50.2 vs. 44.9; $p < 0.001$) levels were significantly higher in the head-to-body interval 'two-step' approach group, but there was no significant difference in the umbilical artery pH (7.30 vs. 7.29; $p = 0.45$).

Conclusions

Head-to-body delivery by 'two-step' approach increases the red cell mass in term infants and does not increase the risk of neonatal anemia. It is a safe, simple and low cost delivery procedure that should be incorporated in integrated programs that are aimed at reducing iron deficiency anemia in infants. Early cord clamping facilitates this action.

NEW TECHNOLOGIES IN FETAL IMAGING

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Two-dimensional ultrasound is the primary modality of fetal anatomy examination before birth. Its widespread use, with the undeniable progress in detecting malformations led to the emergence of a significant proportion of unclear diagnosis of abnormalities. Advanced imaging techniques allow further clarification of such a situation, where it is important that any diagnostic doubt processed with adequate advanced technique. Advanced techniques include color Doppler, three-dimensional ultrasound and magnetic resonance imaging.

Although still limited experience with their use, are increasingly crystallize a clear indication for the use of each based on the following principles. In suspected vascular anomalies, which occur independently or as part of the individual malformations additional examination with color or power Doppler is recommended. To view each part of the body of the fetus regardless of its position as the spatial representation uses three-dimensional ultrasound. Finally, nuclear resonance due to the strongly pronounced soft tissue contrast, provides the most detailed presentation of the fetal body from all imaging modalities. Its use in large malformations of the brain increased the detection efficiency of complex malformations of the brain, allowing prenatal detection of a series of ultrasonic ungraspable disfigurement that often accompany brain abnormalities.

EVALUATION OF PLACENTAL VASCULARISATION BY 3D DOPPLER INVESTIGATION

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At present ultrasound technique is one of the fundamental diagnostic tools in modern medicine. It is widespread and applied by all obstetricians in Europe.

Three-dimensional ultrasound (3D-US) technique is an important new method in the prenatal care of pathological cases. Besides imaging we can perform more developed Doppler examinations, as well.

The vascular examination of the placenta gathers ground increasingly, because placentation abnormality results in pathological pregnancy including e.g. IUGR, GDM, PIH and EPH. The indirect Doppler flow parameters of uteroplacental circulation (velocity analysis of umbilical and uterine arteries) are less sensitive in regard to pathological state of pregnant women.

The placental 3D Doppler examination is typical of 3D-US technology targeting the intraplacental blood circulation. Placental vessels and blood flow can be investigated by 3D Doppler indices to evaluate circulation. The vascularization index, which represents the blood vessels within the volume of interest. The flow index shows the average blood flow intensity. The vascularisation flow index combines the information on vessel presence (vascularity) and amount of blood cells transported (blood flow).

The 3D Doppler indices were significantly depressed in affected pregnancies compared to unaffected ones.

The 3D Doppler technique seems to be a promising new method to predict subsequent alteration related to placental circulation.

CEREBRAL AND PERIPHERAL MUSCLE NEAR INFRARED SPECTROSCOPY (NIRS) IN NEONATES

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Background

Non invasive continuous measurement of regional tissue oxygenation and hemodynamics by near infrared spectroscopy (NIRS) is of increasing interest in neonatal intensive care. Studies in neonates were mainly performed with continuous wave/spatially resolved NIRS till now, which measures relative changes of oxygenated and deoxygenated haemoglobin and regional tissue oxygenation.

Methods

Using reflection method the application of the NIRS optodes is on the same side with a defined interoptode distance. Peripheral-muscle NIRS can be combined with venous occlusions that enables the calculation different hemodynamic parameters.

Results

At the NICU Graz changes of cerebral oxygenation during episodes of apnea, tilting manoeuvres and transition after birth were analysed. Concerning peripheral muscle oxygenation changes during the first week of life, transition after birth and the influence of smoking during pregnancy, asphyxia, inflammation and associations with physiological parameters were analysed.

Conclusion

NIRS has the advantage to measure oxygenation and hemodynamics non-invasively in regions of interest (brain, peripheral-muscle...). Main problem remains reproducibility but with improving techniques and devices, with establishment of standardized measurement procedures NIRS might reach an accuracy and reproducibility to become clinically relevant in neonates.

THE BENEFIT OF COMPUTER ASSISTED PRESCRIPTION OF PARENTERAL NUTRITION IN ELGANS

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Background

Extrauterine growth restriction is still a problem in the population of ELGANS after they leave the NICUs all over the world. Subnormal growth often persists into childhood and can have potential adverse effects on later neurodevelopment.

Because of immature gut ELGANS in the first days of life mostly depend on parenteral nutrition (PN). This is often inadequate and prone to errors because prescribing it requires detailed knowledge and calculations. As a result of suboptimal prescription significant cumulative deficits occur.

To improve our nutritional practice the computer assisted prescription of PN with incorporated guidelines was introduced in our NICU in the second half of 2011. The programme has been developed in collaboration between neonatologists specialized in the field of nutrition and artificial intelligence experts.

Aim

To evaluate the effectiveness of computerized prescription of parenteral nutrition in improvement of nutrition practice in NICU.

Patients and methods

This was a retrospective, observational study with a nonprobability, convenience sampling to obtain medical records on ELGANS treated at our level III NICU. In the study group 20 ELGANS after computerization of PN prescription (July 1st, 2011 to December 31st, 2011) were enrolled. They were compared to 20 ELGANS in the control group before the computerized prescription (January 1st, 2011 to June 30th, 2011). For each enrolled infant daily parenteral and enteral intake of macronutrients, calcium and phosphate in five sequential time intervals of the first 28 days of life was calculated (day 1-3, 4-7, 2nd, 3rd, 4th week). Outcome measures were length of PN, days to regain birth weight, growth velocity (weight gain per day, head growth per week) and weight and head circumference <10th percentile on growth curves (Tanis) at 28 days of life. Numerical data were analyzed by independent-samples t-test if normally distributed or by Mann-Whitney U-test if skewed. Categorical data were expressed as proportions and analyzed by chi-square.

Results

PN intake of macronutrients and calcium in the first three days of life was significantly better in the study group: proteins 2.3 [0.4] vs 1.7 [0.4] g/kg/day ($p<0.001$); glucose 6.6 [0.18] vs 5.7 [0.9] g/kg/day ($p=0.02$); lipids 1.4 [0.5] vs 1.0 [0.4] g/kg/day ($p=0.009$), calcium 0.62 [0.18] vs 0.28 [0.12] mmol/kg/day ($p<0.001$).

The combined enteral and parenteral intake of the study group in all five sequential intervals after birth, except for lipids, exceeded the intake of the control group.

The length of PN was not significantly different between the groups 22.4 [16.3] vs 22.6 [7.6] days ($p=0.96$). The difference in days to regain birth weight was not significant as well 11.0 [2.7] vs 12.1 days [4.1] ($p=0.31$). Weight growth velocity (14.5 [3.7] vs 11.6 [0.4] g/day ($p=0.03$)) and head growth velocity (0.9 [0.3] vs 0.7 [0.4] cm/day ($p=0.03$)) were higher in the study group. The better growth resulted also in less growth retarded (<10th percentile)

ELGANs at 28 days of life (weight 2/20 vs 9/20 ($p<0.001$); head circumference 3/20 vs 13/20 ($p<0.001$)).

Conclusion

With computer assisted prescription of PN and consequently better consistency among neonatologists we improved delivery of nutrients in early life. We decreased ex utero growth retardation already on 28th day of life. New procedure is less time consuming and saves time in busy daily routine in NICU.

CEREBRAL ACTIVITY MONITORING IN NEONATES – A VALUABLE TOOL

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NICUs worldwide deal with prevalent and diverse neurologic morbidity. Over the past few decades neonatologists were faced with advances in clinical assessment and technology aiming to objectify the magnitude of brain damage and predict its consequences. This is in part a reflection of growing interest in neonatal brain disorders and neuroprotection. Besides neurologic assessment and neuroimaging, interpretation of cerebral electrical activity provides the clinician with an insight of functional repercussion of the actual brain insult. Electroencephalography (EEG) and amplitude-integrated EEG should be the standard in neurological evaluation of sick term and preterm neonates, taking into account safety and comfort of the procedure. Digital video-EEG monitoring enables long-term recording of cerebral activity in acutely compromised infant and correlation of pathological traces with behavioral changes. Along with video recording, polygraphic channels (EMG, ECG, EOG, respiration) allow recognition of frequent artifacts and physiologic disturbances associated with cerebral dysfunction. Mounting the equipment and recording can be cumbersome in intensive care settings, and neonatal EEG specialist must be available for review. For these reasons neonatologists became more familiar with aEEG, which is more simple to apply and interpret. This modification of EEG may be more suitable for prolonged monitoring and uses only 1 or 2 channels where the raw EEG signal is processed in a way it gives an estimate of global cerebral function. Normal and pathologic traces have been well described. Its main uses are evaluation of a degree of encephalopathy and seizure detection. Compared to standard EEG however, it provides less information, and in most cases should be complemented by standard EEG.

Defined as global cerebral dysfunction, neonatal encephalopathy is etiologically diverse, most frequently caused by asphyxial insult in term and intracranial hemorrhage in preterm infants. Both EEG and aEEG have an excellent prognostic value in HIE and are being used as an entry criterion for hypothermia treatment. It is important to prolong the monitoring throughout the treatment period and beyond, since evolution of cerebral activity gives the most accurate estimation of outcome, and may even help with the decision of active treatment withdrawal.

Neonatal seizures tend to be subclinical (detected only by EEG), the proportion of which increases with severity of infant's state. It is plausible that 'seizure burden' affects neurological outcome, regardless of the underlying pathology, which suggests treating occult seizures. aEEG is a valuable tool in that respect, giving also the opportunity to evaluate the effect of anticonvulsants. However, it may miss focal seizures of origin distant from the electrodes or short lasting ones. Focal brain pathology (infarct, cyst, cortical dysplasia etc.) can be detected using EEG, although electrical changes are often similar and not diagnostic in that respect. The role of EEG/aEEG in preterm babies is well established, but more research is required in defining the normative values and traces that carry poor prognosis.

Full spectrum of information contained in cerebral electrical activity give valuable clues on infant's current state, timing of injury and outcome perspectives. These can help the clinician in treatment decisions and providing more accurate information to the parents.

NONINVASIVE MEASUREMENT OF RESPIRATORY MECHANICS IN HEALTHY NEWBORNS

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Various techniques have been employed in the measurement of lung function in infants; however, limited information is available on the mechanical properties of the respiratory system in healthy neonates. We aimed at establishing resistive and elastic parameters of the respiratory system with forced oscillations superimposed on spontaneous breathing in unsedated newborns.

Fifty-two term newborns with spontaneous vaginal delivery (SVD, n=19) and Caesarian section (C, n=23) were studied in the first 3 days after birth. Small-amplitude pseudorandom forced oscillations in the 8-to-48-Hz frequency range were superimposed on spontaneous breathing via a bacterial filter and a face mask. Respiratory impedance (Z_{rs}) was measured with the wave-tube technique, and a pneumotachograph was used for monitoring the breathing pattern. The dead space of the equipment was flushed with air at 2 l/min. Z_{rs} was recorded in successive 30-s intervals until the breathing pattern became regular reflecting accommodation to the face mask. The average study time in a newborn was ~10 min. In 5 newborns no steady state breathing was reached and technical problems arose in 2 more cases; their data were discarded. Data epochs with the lowest Z_{rs} values were averaged in each subject and the mean data were evaluated by calculating the average resistance (R) and fitting an elastance (E) – inertance (I) model.

Newborns with high Z_{rs} values associated with obvious nasal congestion and noisy breathing (n=5) were excluded from the analysis. In the remaining population, the mean±SD values of R, E, I and resonant frequency were 36 ± 11 hPa.s/l, 1267 ± 346 hPa/l, 0.054 ± 0.021 hPa.s²/l and 25 ± 4 Hz, respectively. The intraindividual within-measurement and day-to-day variations in Z_{rs} were considerable (20-150%) in the majority of newborns. There were no differences in body weight and Z_{rs} parameters between the SVD and C groups, and no statistically significant correlation was found between BW and the Z_{rs} parameters.

The high success rate indicates that the noninvasive measurement of respiratory mechanics can be accomplished in healthy newborns in the first day of the life. The interindividual differences in the Z_{rs} parameters were unrelated to that in BW, which most likely resulted from within-subject changes due to instabilities in the sleep level, breathing pattern and lung volume. Since the average Z_{rs} values were apparently stable with the resumption of quiet sleep, these latter factors need to be investigated in further studies.