

293

THE MYOCARDIAL PERFORMANCE DURING AND AFTER 72-HOURS OF THERAPEUTIC HYPOTHERMIA FOR PERINATAL ASPHYXIA IN TERM NEONATES

doi:10.1136/archdischild-2012-302724.0293

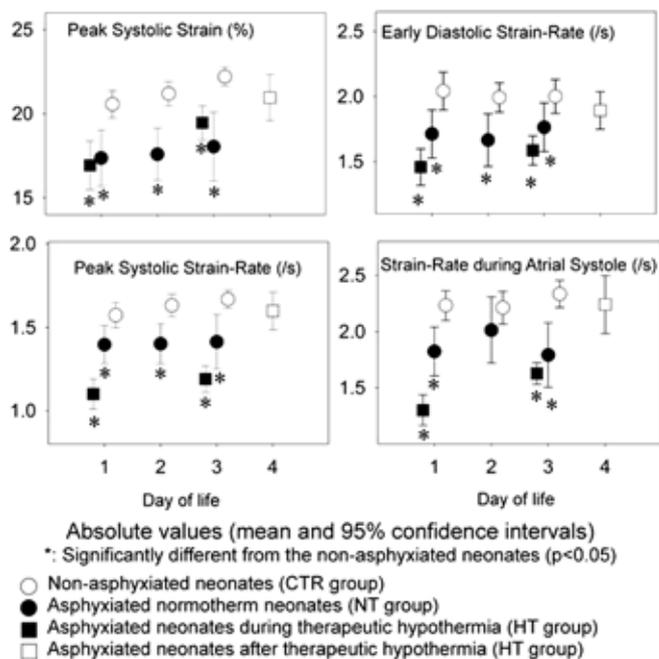
¹E Nestaas, ^{2,3}J Skranes, ^{4,5}A Støylen, ^{2,3}D Fugelseth. ¹Department of Paediatrics, Vestfold Hospital Trust, Tønsberg; ²Department of Neonatal Intensive Care, Oslo University Hospital, Ullevål; ³Faculty of Medicine, University of Oslo, Oslo; ⁴Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology; ⁵Department of Cardiology, St. Olavs Hospital, Trondheim, Norway

Background and Aims Therapeutic hypothermia after perinatal asphyxia reduces brain damage. The impact on the heart is poorly investigated. This study compare myocardial performance (MP) by ultrasound (Strain and Strain-Rate by tissue Doppler) in cooled asphyxiated term neonates (HT), asphyxiated term neonates treated with normothermia (NT) and non-asphyxiated term neonates (CTR).

Methods MP were compared in 44 HT during and after cooling, 20 NT and 48 CTR.

Results The HT-group was more severely asphyxiated than the NT-group (pH 7.07 (7.02, 7.12) (mean (95%CI)) vs. 7.21 (7.14, 7.30), Base-Excess -16.11mmol/L (-17.8, -14.3) vs. -9.3 (-13.0, -5.6) (p<0.05)).

Myocardial performance (MP) indices on day 1-4 of life



Abstract 293 Figure 1

On day 1–3, the MP was similar in the NT-group and HT-group during cooling, lower than in the CTR-group (p<0.05). The MP within each group was similar, except the CTR-group and HT-group Peak Systolic Strain and HT-group Strain-Rate during the Atrial Systole (p<0.05).

After rewarming, the MP improved in the HT-group (day 4), approaching the MP in the CTR-group on day 3.

Conclusions Although the HT-group was more severely asphyxiated than the NT-group, the myocardial performance was similarly depressed on day 1–3. The myocardial performance in the HT-group improved after rewarming (day 4), approaching the level in the CTR-group on day 3. Therapeutic hypothermia did not decrease the myocardial performance during treatment and might have had a positive impact after treatment.

294

SUCCESSFUL IMPLEMENTATION OF HYPOTHERMIA TREATMENT IN SWEDEN - OUTCOME AT 24 MONTHS OF AGE IN HYPOTHERMIA-TREATED INFANTS WITH HIE

doi:10.1136/archdischild-2012-302724.0294

K Robertson Grossmann, J Ragnö, B Vollmer, M Blennow, B Hallberg. *Neonatology, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden*

Background Hypoxic-ischemic encephalopathy (HIE) is associated with a high risk for subsequent neurological sequelae. This study evaluates the implementation of HT in Sweden. Are national guidelines adhered to? Are outcome results comparable to those from previous controlled trials?

Methods Between 2007–2009, HT was available at 8 Swedish hospitals. Outcome data regarding all 187 infants who received HT during this period was collected and scored (normal/"motor delay"/cerebral palsy (CP)/dead). Local guidelines for clinical follow-up differing from the national guidelines were also reviewed.

Results

Abstract 294 Table 1

Outcome	N=163/187 (24 children lost but alive)
Normal	109 (58%)
"Motor delay"	10 (5%)
Cerebral palsy	20 (11%)
Dead	24 (13%)

Outcome data was available in 87% of treated infants. 13% had died, 74% had been assessed between 15–36 months of age with a neurological exam and using scales for grading of severity of CP, such as the Gross Motor Classification System. 35% had been assessed according to national guidelines using Bayley III.

Conclusions HT has been successfully implemented; however structured, comprehensive assessments according to national guidelines are not always carried out. In particular, only about 1/3 of infants undergo a psychometric developmental assessment. The incidence of severe adverse neuromotor outcome is comparable to what was to be expected from earlier RCTs, showing that HT has a significant positive effect also outside of controlled trials.

295

ROLE OF ANAPYREXIA IN PERINATAL ASPHYXIA IN TERM NEWBORNS: AN OPEN LABELED RANDOMIZED CONTROLLED TRIAL

doi:10.1136/archdischild-2012-302724.0295

A Garg, A Saini, S Nangia. *Department of Pediatrics, Kalawati Saran Children's Hospital, Delhi, India*

Background and Aims To compare anapyrexia (a physiological decrease in body temperature in neonates in response to hypoxia) with normothermia (conventional management) with respect to immediate outcome and neuro-developmental outcome at 3 and 6 months of age in full term asphyxiated newborns.

Methods Fifty full term intramural neonates with severe birth asphyxia were randomized to Study (Anapyrexia) group and Control (Normothermia) group. Neonates in Anapyrexia group were allowed to remain at their own intrinsic temperature for a period of 72 hours. Neonates randomized to the Normothermia group had their temperature maintained between 36.5°C to 37.5°C with assistance from the servocontrolled radiant warmer. All neonates were managed according to standard management protocol of the unit. The subjects were monitored closely for any adverse effects, seizures, and development of HIE. The neurological examination was done at 6 hourly interval for the first 24 hours and then at 12 hourly interval. The surviving neonates were followed up at 3 months and 6 months of age.

Results The development of HIE stage 3 was significantly lower in Anapryxia group(8%) than in the Normothermia group(28%) ($p=0.032$; [RR]=0.285). Fifteen neonates in the anapryxia group had normal outcome versus only 9 in the normothermia group($p=0.049$, [RR]=0.5). The incidence of mortality(12% vs 16%, $p=0.264$, [RR]=0.75) complications and baseline characteristics were comparable.

Conclusions Anapryxia if allowed to persist for 72 hours after birth, alleviates the ill effects of hypoxic ischemic insult and results in improved outcome in the neonates particularly the neuro-developmental outcome at 6 months of age.

296 PHARMACOKINETICS, CLINICAL EFFICACY AND SAFETY OF LIDOCAINE IN ASPHYXIATED NEWBORNS TREATED WITH THERAPEUTIC HYPOTHERMIA

doi:10.1136/archdischild-2012-302724.0296

¹MPH van den Broek, ^{1,2}CMA Rademaker, ³ADR Huitema, ⁴HLM van Straaten, ²MC Toet, ²LS de Vries, ^{1,5}ACG Egberts, ²F Groenendaal. ¹University Medical Centre Utrecht; ²Wilhelmina Children's Hospital/UMCU, Utrecht; ³Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam; ⁴Isala Clinics, Zwolle; ⁵Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands

Background and Aims Therapeutic moderate hypothermia for neuroprotection in asphyxiated newborns can influence pharmacokinetics and pharmacodynamics. Lidocaine is administered if seizures persist despite initial therapy. Because cardiotoxicity is a potential risk of lidocaine, dose adjustment under hypothermia might be necessary to prevent toxicity. The aim was to evaluate the effect of hypothermia on lidocaine pharmacokinetics and to evaluate the efficacy and safety under hypothermia.

Methods Hypothermic data were obtained from the SHIVER-study. Term born newborns with perinatal asphyxia and encephalopathy with lidocaine therapy were included. Therapeutic hypothermia (33.5°C, for 72 hours) was applied within 6 hours after birth. Lidocaine dosing under hypothermia was reduced; initial dose 2 mg/kg in 10 minutes, followed by an infusion of 4 mg/kg/h during 6 hours. Subsequently the infusion was reduced to 2 mg/kg/h during 12 hours, and then stopped.

Data from normothermic newborns were obtained from a previously published study (van den Broek *et al.*, 2011). Pharmacokinetic modelling was performed using NONMEM.

Results 22 hypothermic newborns were included and were compared with 26 normothermic newborns. Based on a one-compartmental model with allometric relationships, lidocaine clearance was decreased by 24% under hypothermia, while relative metabolite formation was unchanged. During hypothermia no effect of lidocaine on heart frequency could be observed and the observed efficacy, i.e. decrease of seizure activity, was 78%.

Conclusion Hypothermia has a clinically relevant effect on lidocaine clearance. The dosing regimen needs to be adjusted under hypothermia in order to maintain efficacy and to prevent adverse events. This model is currently validated.

297 DUAL ACTION OF NO SYNTHASES ON BLOOD FLOW AND INFARCT VOLUME CONSECUTIVE TO NEONATAL FOCAL CEREBRAL ISCHEMIA

doi:10.1136/archdischild-2012-302724.0297

¹P Bonnin, ²PL Leger, ³S Renolleau, ²O Baud, ²C Charriat-Marlangue. ¹Physiologie Clinique - Explorations-Fonctionnelles, APHM, ²U676, INSERM Unit 676; ³APHP, Service de Réanimation Pédiatrique, Paris, France

Research into neonatal ischemic brain damage is impeded by the lack of a complete understanding of the initial hemodynamic mechanisms resulting in a lesion, particularly that of NO-mediated vascular mech-

anisms. In a neonatal stroke rat model, we recently show that collateral recruitment contributes to infarct size variability.

Non-specific and selective NO synthase (NOS) inhibition were evaluated on cerebral blood-flow changes and outcome in a P7 rat model of arterial occlusion (left middle cerebral artery electrocoagulation with 50 min occlusion of both common carotid arteries). Blood-flow changes were measured by using ultrasound imaging with sequential Doppler recordings in both internal carotid arteries and basilar trunk. Cortical perfusion was measured by using laser Doppler flowmetry. We showed that global NOS inhibition significantly reduced collateral support and cortical perfusion (collateral failure), and worsened the ischemic injury in both gender. Conversely, endothelial NOS inhibition increased blood-flows and aggravated volume lesion in males, whereas in females blood-flows did not change and infarct lesion was significantly reduced. These changes were associated with decreased phosphorylation of neuronal NOS at Ser⁸⁴⁷ in males and increased phosphorylation in females at 24 hours, respectively. Neuronal NOS inhibition also increased blood-flows in males but not in females, and did not significantly change infarct volumes compared to their respective PBS-treated controls.

In conclusion, both nNOS and eNOS appear to play a key role in modulating arterial blood flow during ischemia mainly in male pups with subsequent modifications in infarct lesion.

298 ANTENATAL TAURINE SUPPLEMENTATION REDUCES CEREBRAL CELL APOPTOSIS IN FETAL RATS WITH INTRAUTERINE GROWTH RESTRICTION

doi:10.1136/archdischild-2012-302724.0298

¹J Liu, ¹XF Wang, ²HY Teng, ¹N Yang, ¹XT Ren. ¹Department of Neonatology and NICU, Bayi Children's Hospital Affiliated with General Hospital of Beijing Military Command; ²Department of Pediatrics, The Second Artillery General Hospital, Beijing, China

Intrauterine growth restriction (IUGR) is closely associated with neonatal and prenatal morbidity, mortality and even with adult diseases. Term infants with IUGR have a five- to seven-fold risk of developing cerebral palsy, compared with gestational age-matched infants with normal birth weights. Our previous study showed that antenatal supplementation of taurine can improve brain ultrastructure of fetal rats with IUGR, but the mechanism remains unclear. This paper was to explore the effect of antenatal taurine supplementation on cerebral apoptosis and glial cell line-derived neurotrophic factor (GDNF)-cysteiny aspartate specific (caspase-3) in fetal rats with IUGR. Fifteen pregnant rats were randomly divided into 3 groups: control group, IUGR and IUGR+antenatal taurine supplements. Taurine was added to the diet of the taurine group at a dose of 300 mg/kg·d from 12 days after conception until natural delivery. Two fetal rats were chosen in every litter. Brain cellular apoptosis was detected using TUNEL, and the changes in protein expression of GDNF and caspase-3 using immunohistochemistry. The results showed that (1)the counts of apoptotic brain cells in the control group, IUGR group and IUGR with antenatal taurine supplementation group were (0.28±0.57)%, (15.30±5.96)%, (9.36±3.92)%, respectively. (2) The expressions of GDNF in three groups respectively were (93.56±6.73), (120.36±6.23) and (139.56±5.28) (F= 492.56). (3) The expressions of caspase-3 in three groups respectively were (7.51± 2.31), (151.33±24.41) and (37.29±11.27) (F=128.18. Antenatal taurine can significantly decrease brain apoptosis, the mechanism maybe through increasing the expression of GDNF and decreasing the expression of caspase-3. This work was supported by Natural Science Foundation of China (81170577).

299 PRE-084, A SIGMA-1 RECEPTOR LIGAND, PROTECTS AGAINST EXCITOTOXIC PERINATAL BRAIN INJURY IN NEWBORN MICE

doi:10.1136/archdischild-2012-302724.0299