Abstracts

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Methods The pathophysiology of necrotizing enterocolitis (NEC) includes massive production of endogenous cytokines with exaggerated activation of inflammatory pathways. Colchicine has been used as an anti-inflammatory agent. The aim of this study was to investigate the possible beneficial effects of colchicine in a neonatal rat model of NEC.

Results Rats were randomly divided into 3 groups: control group; saline-treated NEC group; colchicine-treated NEC group. NEC was induced by hyperosmolar enteral formula feeding and exposure to hypoxia/exoxygenation after cold stress. Intestinal samples were harvested for biochemical and histopathological analysis.

Conclusion The grade of intestinal injury of pups in the saline-treated NEC group was found to be significantly higher than in the control or the colchicine-treated groups (p<0.001, p=0.003; respectively). Median level of intestinal malondialdehyde was significantly higher in the saline-treated NEC group compared to the control group (p=0.006) and the colchicine-treated group (p=0.015). Significantly higher activities of intestinal superoxide dismutase and glutathione peroxidase activities were observed in the colchicine-treated NEC group compared to the saline-treated group (p=0.033 and p=0.050; respectively). Tissue levels of tumor necrosis factor-α and interleukin β were significantly higher in the saline-treated NEC group compared to rats in the colchicine-treated group (p<0.001, p=0.003; respectively). A comparison of saline-treated and colchicine-treated NEC pups revealed that treatment with colchicine was associated with significantly lower tissue levels of TNF-α and IL-1β (p<0.01, both).

Conclusion We observed that, in this model of NEC, colchicine has favorable effects on histological and biochemical changes.

188 ANALGESIA AND SEDATION IN CRITICALLY ILL CHILDREN: LOCAL RELIGION OR EVIDENCE BASED?

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Over the last decade increasingly RCT’s have been published about optimal dosing of opioids and benzodiazepines in critically ill children of different age groups.

In this way progress is made about optimal dosing as well as combination of therapies against the background of the use of novel ways of trial design.

To this effect the application of population pharmacokinetics-pharmacodynamics (NON-MEM) using sparse data have guided the design of trials preceded by in vitro simulation and prediction of dose effect responses.

Both in the premature infant as well as in the so-called surgical newborn, dosages have been adjusted based on solid observational and experimental data sets for which the results should be evaluated. Apart from short term pharmacodynamic parameters such as validated pain scores, and eventually pharmacokinetic data analysis potentially equally important is the evaluation of long term consequences both of neonatal pain and the use of opioids. Experimental data have revealed increased neuro apoptosis in the developing brain. The data of a number of RCT’s conducted by our group will be combined with prospective longitudinal data recently acquired combining quantitative sensory testing (QST) under conditions of fMRI.

In this way the question whether neonatal pain and/or opioid use results in altered pain response and long term negative sequela can be answered.

187 SYSTEMATIC REVIEW OF RANDOMIZED CONTROL TRIALS TO REVIEW THE ROLE OF PREBIOTICS IN PREVENTION OF NECROTIZING ENTEROCOLITIS IN PRETERM NEWBORNS

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Background and aims Necrotizing enterocolitis (NEC) is an important cause of mortality and serious morbidity in preterm infants. Prebiotics are specific oligosaccharides which have been shown to promote proliferation of beneficial bacteria in gut. This study was designed to investigate the possible beneficial effects of prebiotics in a neonatal rat model of NEC.

Methods Rats were randomly divided into 3 groups: control group; saline-treated NEC group; colchicine-treated NEC group. NEC was induced by hyperosmolar enteral formula feeding and exposure to hypoxia/exoxygenation after cold stress. Intestinal samples were harvested for biochemical and histopathological analysis.

Results The grade of intestinal injury of pups in the saline-treated NEC group was found to be significantly higher than in the control or the colchicine-treated groups (p<0.01, p=0.003; respectively). Median level of intestinal malondialdehyde was significantly higher in the saline-treated NEC group compared to the control group (p=0.006) and the colchicine-treated group (p=0.015). Significantly higher activities of intestinal superoxide dismutase and glutathione peroxidase activities were observed in the colchicine-treated NEC group compared to the saline-treated group (p=0.033 and p=0.050; respectively). Tissue levels of tumor necrosis factor-α and interleukin β were significantly higher in the saline-treated NEC group compared to rats in the colchicine-treated group (p<0.001, p=0.003; respectively). A comparison of saline-treated and colchicine-treated NEC pups revealed that treatment with colchicine was associated with significantly lower tissue levels of TNF-α and IL-1β (p<0.01, both).

Conclusion We observed that, in this model of NEC, colchicine has favorable effects on histological and biochemical changes.
Conclusions The mean number of painful procedures per NICU patient per day declined and analgesic treatment changed to a more tailored or individualized approach. Non-pharmacological pain- or stress reducing strategies like NICCAP and sucrose were fully embedded in our pain management. As further reduction of the number of painful procedures is unlikely we should explore newer pharmacological agents and apply non-pharmacological interventions more frequently.

190 PREDICTING THE EFFICACY OF ORAL SUCRose IN REDUCING PAIN DURING OPHTHALMICAL EXAMINATION FOR RETINOPATHY OF PREMATURITY: A PROSPECTIVE RANDOMISED STUDY

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Background and aim Retinopathy of prematurity (ROP) is one of the major morbidity among preterm infants. Although, local anesthetics reduce pain to some extent, eye examination still remains as a painful procedure. We aimed to evaluate the effect of oral sucrose combined with local anesthetics for pain relief during ophthalmological examination.

Method A total of forty patients under 32 weeks of gestational age were included in the study. Infants were randomly assigned to receive either oral sucrose solution (Group-1: n=21) or sterile water (Group-2: n=19) combined with topical proparacaine hydrochloride two minutes before examination. Pacifier was used in all patients as non-nutritive sucking during the study. Pain score was evaluated by premature infant pain profile (PIPP) scale. Each infant was video-recorded during and after the procedure.

Results Both groups were similar in terms of gestational age, birth weight, postnatal age and actual weight. There was no significant difference between groups in behavioral state, heart rate and oxygen saturation before the examination. At spectum insertion, heart rate variability was similar in both groups whereas oxygen desaturation was apparent in Group-2 (Group-1: 1.7±10.8 and Group-2: 2.5±0.6, p=0.001) and PIPP scores were also lower in Group-1 (Group-1: 14.5±1.8 and Group-2: 17.2±1.7, p=0.001). Total time of crying was significantly shorter in Group-1 (Group-1: 59.8±12.1 and Group-2: 36.5±21.4, p=0.001).

Conclusion Procedural pain is known to have acute and even long term negative, behavioral and developmental effects in neonates. In our study, use of sucrose in addition to local anesthetics during ophthalmological examination is shown to attenuate pain.

191 MORPHINE PREMEDICATION FOR INTUBATION IN PRETERM INFANTS - A PHARMACOKINETIC AND PHARMACOGENETIC REPORT

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Background and aims Morphine is used in preterm infants, but data are scars on pharmacokinetics (PK), pharmacodynamics (PD) and pharmacogenetics (PG). We aimed to study PK and PD/PG relation of morphine in infants included in a RCT comparing morphine with short-acting analgosedation as premedication for intubation.

Methods 17 preterm infants with a median (IQR) gestational age of 26.6 (25.1–28.7) w, birth weight 924 (721–1240) g and postnatal age 136 (17.5–322) h were randomized to receive morphine (0.5 mg/kg).

Blood samples for morphine, M6G and M3G concentrations were collected before administration, 20 min, 6 and 24 h after intubation. DNA was isolated from salivary swabs to genotype 18 polymorphisms in 12 genes using Taqman assays. Pain assessment (ALPS-0 and EDIN scales) was performed and additional morphine boluses were offered accordingly. The morphine level/pain score relation and the genotype influence on time to achieve a low pain score was calculated.

Results In infants receiving no additional doses, clearance was 1.5–3.3 ml/kg/min in 5 infants of 5–34 h and 9.9 in one infant of 332 h postnatal age.

Both morphine and morphine+M6G/S correlated with mean ALPS-0 score at 6h (p=0.02 and 0.04) and 24 h (p=0.01 and 0.02). The COMT rs4680G>C (Val158Met) SNP was significantly correlated with time to reach the lowest pain score. COMT rs4680A patients experienced a faster response to opioids compared to rs4680G patients in both groups (p=0.001 and p=0.072).

Conclusions Morphine clearance is dependent on postnatal age in premature infants. Genotyping would improve individual dosing of opioids during NICU-care.

192 ANALGESIA MODULATES CORTICAL RESPONSE TO PAINFUL PROCEDURES IN EXTREMELY PRETERM NEWBORN INFANTS

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Introduction Proper pain management in the neonatal intensive care unit (NICU) is essential. The clinical pain assessment depends on objective measurement of indirect behavioural and physiological pain indicators. Cortical pain processing has been observed in preterm infants from 24 weeks gestational age but no study has focused exclusively on cortical pain response in extremely premature infants (<28 weeks gestational age).

Aims This study aimed to demonstrate cortical pain processing in extremely preterm infants. Furthermore, the study aimed to investigate the impact of analgesic drugs on cerebral haemodynamics and the relationship between behavioural and cortical pain responses.

Material and Methods A clinical study was performed in the NICU, including preterm infants ≤28 weeks gestational age or with a birth weight ≤1500 grams. Patients with severe on-going intraventricular haemorrhage or hydrocephalus were excluded. The infants were studied during routinely performed venepunctures and endotracheal tube suction. Near-infrared spectroscopy was used for the study of cortical activity, parallel to observation of systemic haemodynamics and pain assessment with the Premature Infant Pain Profile and Échelle Douleur Inconfort Nouveau-Né.

Results During the procedures significant increases in the cerebral concentration of oxygenated haemoglobin were observed bilaterally during venepuncture and unilaterally during endotracheal tube suction. Simultaneously, minor alterations in systemic haemodynamics occurred. The cerebral pain response was significantly reduced by analgesia.

Conclusions These results indicate the existence of cortical pain processing in very premature infants. Analgesia reduces this cortical response.

193 IMAGING TOOLS TO ASSESS THE DEVELOPMENT OF CORTICAL MORPHOLOGY AND CONNECTIVITY

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