ID: 9
TITLE: CEREBRAL OXYGENATION OVER THE FIRST 72H OF LIFE IN VERY LOW BIRTHWEIGHT INFANTS WITH AND WITHOUT INTRAVENTRICULAR HEMORRHAGE OR PERIVENTRICULAR LEUKOMALACIA
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CONTENT:

Intraventricular hemorrhage (IVH) in very low birth weight infants (VLBWI) happen in most of the patients within the first three days of life. The current concepts of the pathogenesis of both, IVH and periventricular leukomalacia (PVL) includes a period of cerebral ischemia. However, currently there is no established tool to recognize and eventually treat brain ischemia in a timely fashion to avert brain damage such as IVH/PVL. Cerebral tissue oxygenation (cStO2) as measured by near-infrared spectroscopy possibly indicates cerebral hypoperfusion. The objective of this study was to compare cStO2 during the first 72h of life in VLBWI with and without IVH/PVL.

In a prospective cohort study cStO2 was measured in prospectively managed inborn VLBWI along with arterial oxygenation (SpO2) and pulse rate from the first minutes of life during delivery room resuscitation and with extended monitoring during the subsequent 72h in the NICU. All parameters were recorded simultaneously every 2 seconds. cStO2 was recorded bitemporally by absolute oximetry (ForeSight®, Casmed). Cranial ultrasound was performed on day of life 4 and thereafter repeatedly until discharge. cStO2 was compared between infants with and without IVH/PVL first by calculating the mean cStO2 difference for every hour and second by computation of the area under a threshold, which was defined as the dynamic 10th percentile of all VLBWI considered otherwise as “healthy”.

Between 10/2010 and 05/2014, 166 VLBWI were studied, four of which had to be excluded because of death before 72h. IVH/PVL developed in 24/162. Infants in the IVH/PVL (no IVH/PVL) group were 67% (44%) male, had a mean gestational age of 25.9 (27.3) weeks +/- 15 (20) days and a mean birth weight of 721 (872) +/- 319 (308) grams. 71% (93%) were delivered by cesarian section, 38% (63%) had received a complete course of antenatal steroids.

Infants with IVH/PVL showed a lower cStO2. The hourly mean difference was 2.41% with a 95% confidence interval of 2.00 – 2.86. The largest difference was observed during the first 3 hours of life (Figure). Area under the threshold was not significantly different: Infants with IVH/PVL spent 6.8 (interquartile range 0.7-80.1) %hours under the threshold, infants without IVH/PVL did so for 4.4 (0.7-20.0) %hours.

VLBWI with IVH or PVL had significantly lower values of cStO2 during the first 72h of life. The magnitude of this difference varies over the time and appears to be largest in first hours of life. We speculate that even short but severe episodes of impaired cerebral perfusion may be sufficient to cause IVH.
Cerebral tissue oxygenation (cStO2) of VLBWI with and without IVH/PVL during the first 72h of life

COI: None declared
ID: 116

TITLE: SERUM NEUROFILAMENT LIGHT CHAIN LEVELS ARE AN INDEPENDENT PREDICTOR OF NEURODEVELOPMENTAL OUTCOME IN PRETERM INFANTS

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CONTENT:

Serum neurofilament light chain (sNfL) has recently emerged as a promising biomarker reflecting structural neuro-axonal damage in different neurological diseases. Our study aimed at assessing whether sNfL can predict the functional outcome in preterm infants who suffered from neonatal hemorrhagic brain injury.

In this prospective observational study, we used an ultrasensitive single-molecule array assay to measure serum and cerebrospinal fluid (CSF) concentrations of NfL in preterm infants diagnosed with periventricular/intraventricular hemorrhage (PIVH). We determined the temporal profile of serum and CSF NfL levels from first diagnosis of PIVH until term equivalent age, their association with cerebral imaging markers, and with clinical and functional outcome until 2 years of age assessed by Bayley Scales of Infant Development. We fitted univariable and multivariable logistic regression models to determine risk factors for low motor and cognitive development. Longitudinal mixed effects models modelled NfL levels using cubic spline smoothers to track the trajectory over time.

The study included 48 infants born with less than 32 weeks of gestation. At the time point of PIVH diagnosis, sNfL median levels were 271.9 pg/mL (IQR 155.1–396.1), and strongly decreased until term equivalent age to 15.7 pg/mL (IQR 11.1–32.3). CSF values of NfL were 113-fold higher (IQR 40–211) than corresponding serum values. Additional cerebral infarction (n=23) but not post-haemorrhagic hydrocephalus with permanent external ventricular drainage (n=29) or other diseases independently determined sNfL levels. In multivariate logistic regression models, the only significant predictor of poor motor outcome at 1 and 2 years or death was sNfL level.

This study shows that early sNfL is an independent prognostic biomarker for motor functional outcome in preterm infants after PIVH.

COI: None declared
ID: 191

TITLE: PLATELET COUNT INFLUENCES THE COURSE OF RETINOPATHY OF PREMATURITY

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CONTENT:

Thrombocytes may regulate the activity of vascular endothelial growth factor (VEGF), limiting neovascularization in retinopathy of prematurity (ROP). The aim of this study was to investigate the role of platelet count, thrombocytopenia (platelet count below 100G/L) and infections in the pathogenesis of ROP.

The retrospective study compared 76 patients who developed ROP requiring treatment (mean gestational age: 25±1.72 weeks, weight: 830±206g) and a control group – 87 patients with ROP that resolved spontaneously (mean gestational age: 28±2.07 weeks, weight: 1125±352g). Laser retinal photocoagulation (n = 47), injection of VEGF inhibitor (n=5) or both (n=24) were used as treatment methods. 52 patients treated once and 24 patients required re-treatment. Peripheral blood platelet counts (at birth, before 31 weeks of postmenstrual age, before the diagnosis of ROP, before qualification for treatment and retreatment, before the treatment and retreatment), number of platelets transfusions and occurrence of early-onset (intrauterine) or late-onset (>7 days after birth) infections were abstracted.

A statistically significant difference was found in the occurrence of thrombocytopenia (p=0.015) and median platelet counts (p=0.008; cases: median 325G/L, controls: median 401G/L) before the diagnosis of ROP and the presence of late-onset infection (p=0.007). There was no significant association with platelets transfusions (p=0.402) or early-onset infections (p=0.087). The ROC curve analysis showed that the value of platelets above 232G/L may promote spontaneous resolution of ROP. Among cases statistically significant difference between patients once treated and patients that required re-treatment was found in platelet counts before the diagnosis of ROP (p=0.017; median 371G/L; 242G/L); platelet counts before first intervention (p=0.013; median 345G/L; 262G/L) and the number of transfusions (p=0.042).

The results of this study confirm the association between ROP development and its severity with platelet count. Higher platelet count before the diagnosis may induce a spontaneous resolution of ROP. Late-onset infections seem to be more significant in ROP development than intrauterine infections.

COI: None declared
ID: 283

TITLE: THE CHOPIN STUDY: A MULTICENTER STUDY ON CEREBELLAR HEMORRHAGE AND OUTCOME IN PRETERM INFANTS

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CONTENT:

Cerebellar hemorrhage (CBH) is a frequent complication of preterm birth and may play an important and under-recognized role in neurodevelopmental outcome. Association between CBH size, location and neurodevelopmental outcome is still unknown. The main objective of this study was to investigate neurodevelopmental outcome at two years of age in a large number of infants with different patterns of CBH.

Of preterm infants (≤ 34 weeks) with known CBH, perinatal factors, neuro-imaging findings and follow-up at 2 years of age were retrospectively collected. MRI scans were reassessed to determine the size, number and location of CBH. CBH was divided into three groups: punctate (≤ 4 mm), limited (> 4 mm but < 1/3 of the cerebellar hemisphere) or massive (≥1/3 of the cerebellar hemisphere). Associations between pattern of CBH, perinatal factors and (composite) neurodevelopmental outcome were assessed.

Data of 218 preterm infants with CBH were analyzed. Of 177 infants the composite outcome score could be obtained. Forty-eight out of 119 infants (40%) with punctate CBH, 18 out of 35 infants (51%) with limited CBH and 18 out of 23 infants (78%) with massive CBH had an abnormal composite outcome score. No significant differences were found for the composite outcome between punctate and limited CBH (p = 0.42).

The risk of an abnormal outcome increased with increasing size of CBH. Infants with limited CBH have a more favorable outcome than infants with massive CBH. It is therefore important to distinguish not only between punctate and larger CBH, but also between limited and massive CBH.

COI: None declared
ID: 285

TITLE: THE BIMP STUDY: BRAIN INJURY IN MODERATE-LATE PRETERM NEONATES – FREQUENCY AND FINDINGS AT CUS AND MRI

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CONTENT:

Moderate-late preterm (MLPT) infants, born at 32 – 36 weeks gestation, do not routinely undergo neuro-imaging. Therefore, little is known about the incidence of brain abnormalities.

Objective To describe findings on cranial ultrasound (CUS) and magnetic resonance imaging (MRI) and risk factors for brain injury in MLPT infants.

Ongoing prospective cohort study of unselected MLPT infants born at IVKC. Data were collected at three time points. CUS was performed at day 3-4 and before discharge. At term equivalent age (TEA) CUS was repeated and MRI was additionally performed. CUS and MRI were scored using a newly introduced scoring system for abnormalities in the ventricles, white matter (WM) and basal ganglia, including minor changes.

So far, data of 102 infants have been analyzed. At day 3-4, non-physiological periventricular echogenicity (PVE) was noted in 26 out of 102 (25%) infants. At TEA PVE was seen in twelve, corresponding with WM changes on MRI in four. In three additional infants with normal CUS findings, WM changes were seen on MRI. Grade 1 and 2 intraventricular hemorrhage (IVH) were seen in eleven infants, of which one was complicated by a periventricular hemorrhagic infarction. A watershed infarction was found in one infant. No subdural hemorrhages were noted. Moderate preterm infants (32+0 – 33+6 weeks gestation) and those who needed respiratory support were most likely to have abnormal imaging (respectively OR 2.61 95%CI 1.01 – 6.73; p<0.05 and OR 3.97 95%CI 1.40 – 11.28; p<0.05).

Non-physiological PVE and low grade IVH were frequently seen on early CUS. The incidence of WM changes decreased over time. Around TEA neuro-imaging abnormalities were still present in 20% of MLPT infants. Clinical follow up is needed to investigate the association between these findings that may indicate (reversible) brain injury and neurodevelopmental outcome and to consider whether routine neuro-imaging is warranted in (selected) MLPT infants.

COI: None declared
ID: 472
TITLE: LONG TERM NEUROLOGIC EFFECTS OF NEONATAL CAFFEINE TREATMENT IN A RABBIT MODEL OF PRETERM BIRTH
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CONTENT:
Caffeine is commonly administered to improve respiratory outcomes in preterm infants. However, through its action on the adenosine receptor it might affect brain development. Clinical studies show that caffeine is beneficial for neurologic outcome at 18 months, with a less pronounced effect at pubertal age. Animal studies show more conflicting results on brain-related outcomes. Herein we aimed to investigate the (pre)pubertal effects of neonatal caffeine administration in a rabbit model of preterm birth. The preterm rabbit model is very appropriate for assessment of neuro-cognitive impairments as the rabbit is a perinatal “brain developer”, similar to the human.

Rabbit does underwent cesarean section at 29 days of gestation, corresponding to 24-28 wks in humans in terms of brain development (full term 32 days). Each wet nurse fostered two of her own term vaginally born pups and 7-8 preterm pups. Pups were randomly allocated to enteral administration of either saline or caffeine for 7 or 17 days respectively. At postnatal day 70-84, neurobehavioural tests were performed to assess anxiety, motor activity, learning and memory through: Open Field test (OF), Dark-Box and Object Recognition Task (ORT). Brains were harvested for immunostaining of neurons (NeuN), synapses (Synaptophysin), myelin (MBP) and astrocytes (GFAP). Seven preterm saline, 8 preterm caffeine, 8 preterm caffeine 17d, 5 term saline (controls) and 5 term caffeine 7 d were analyzed.

Birth weight was lower in the preterm (n=38) than in term pups (n=14) (37.6±1.0 vs 57.7±2.3g; p<0.0001); no difference between the treatment groups. Survival was lower in preterm saline than in term pups (33% vs 85%;p=0.03); whereas caffeine treated preterm pups did not differ from term control pups. In the OF test, preterm saline pups covered less distance compared to controls (435.5±558.8 vs 1272±842.7m;p=0.048) and were more likely to stay in the peripheral zone (92.7±10.9 vs63.0 ± 33.3 %;p=0.029). Corresponding differences were not present between preterm caffeine pups and term controls. The term caffeine group and the preterm caffeine 17d group were comparable to term control pups. In the ORT no differences were found between groups. Histologic analysis of neuron density, synaptic density or myelin did not reveal any differences between groups in any of the analyzed regions.

This is the first study reporting long-term effects of caffeine in an animal model of preterm birth. At a clinically comparable dose and duration caffeine appeared to be safe without affecting the structure of neurons, astrocytes, synapses, or myelin. Postnatal caffeine appeared to improve anxious behavior seen in preterm rabbits at prepubertal age. Future studies might explore the effects of caffeine in preterm pups with acquired brain damage.

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Neu-N stain of a caffeine treated animal. Hippocampal CA1, CA3, dentate gyrus, hypothalamus, caudate nucleus and amygdala were analyzed on each slide. There were no differences in neuron density in any of the regions.
COI: None declared
ID: 577

TITLE: THE INSULIN-LIKE GROWTH FACTOR 1 (IGF-1) SYSTEM IN THE PRETERM RABBIT PUP - A CHARACTERIZATION OF THE IGF-1 MRNA EXPRESSION IN LIVER, IGF-1 PROTEIN LEVELS IN SERUM AND BRAIN DISTRIBUTION OF IGF-1 RECEPTORS

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CONTENT:

IGF-1 is an essential regulator of fetal growth and brain development. Preterm birth in the human is followed by a rapid decrease in serum levels of IGF-1 and decreased levels of IGF-1 have been associated with development of severe morbidity. A recent clinical trial indicated that supplementation with IGF-1 prevented development of severe intraventricular hemorrhage (IVH) in extremely preterm infants. In order to better understand possible mechanisms involved in IGF-1-induced IVH prevention, we evaluated important aspects of the endogenous IGF-1 system; IGF-1 mRNA expression in the liver and associated serum protein levels and brain IGF-1 receptor (IGFR) distribution in the preterm rabbit.

Rabbit pups were delivered by cesarean section at E29 (preterm) or by vaginal delivery (term = E32), housed in a controlled environment and fed twice daily with bovine colostrum via a gastric tube. Serum concentrations of IGF-1 protein and liver expression of IGF-1 mRNA were determined at 0, 2, 6, 12, 24, 48 and 72 h of age in preterm pups. Paraffin brain sections from perfusion fixed untreated animals (preterm pups at 20 h and term pups at 5-7 h and 96 h) were prepared for immunohistochemistry against IGF1R, by labeling with primary antibodies against IGF1R, and processed for chromogen visualization and density/quantitation analysis with confocal microscopy.

Mean (SD) serum concentrations of IGF-1 decreased from 166 (33) ng/ml at birth (E29) to 28 (9) ng/ml at day 3 (P0). Hepatic expression of IGF-1 mRNA did not vary over time. The IGF1R was widely distributed in multiple brain regions in both preterm and term pups (Fig). The most abundant density of IGF1R was observed in the choroid plexus, the subfornical organ, the meninges, major fiber tracts, the cortex and subependymal germinal zones. The IGF1R, was mainly localized on outer cell membranes, on cell bodies and along nerve fibers. Quantitative analysis of IGF1R immunoreactivity showed similar IGF1R densities in preterm and term pups of corresponding ages. IGF1R density decreased with increasing postnatal age in term pups.

In line with what is observed in the preterm human infant, serum protein levels of IGF-1 in the preterm rabbit pup decrease rapidly following birth. The IGF1R is widely expressed in the brain following birth, with high expressions in regions and structures relevant for vessel rupture in IVH. The preterm rabbit thus presents a well-suited model for characterization and evaluation of mechanisms involved in IGF-1 induced prevention of IVH.
Figure. Insulin-like growth factor receptor immunoreactivity demonstrated in a sagittal view of a preterm rabbit brain, color-coded for illustration of the wide distribution and its densities (red= high, green= medium and blue= low). Inserted, bottom right, high levels of IGF1R in the choroid plexus (green, insert), showing double fluorescence labelling with astrocyte marker (red, GFAP) and cell nuclei (blue).

COI: DL and AH hold stock/stock options in Premalux AB, and received consulting fees from Shire. NB and GC are employees of and own stock/stock options in Shire.
ID: 600

TITLE: LOW SERUM LEVELS OF PDGF AND BDNF AT POSTNATAL DAY 1 ARE ASSOCIATED WITH DEVELOPMENT OF IVH IN EXTREMELY PRETERM INFANTS

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CONTENT:

Extremely preterm infants are at considerable risk of impaired brain maturation as well as developing the vascular-related brain injury intraventricular hemorrhage (IVH), which is associated with brain sequelae and lifelong effects on neurodevelopment. Preterm birth is also linked to alterations in hormonal axis and growth factor systems with major roles in neuro- and angiogenesis and ultimately in organ development. Multiple studies have identified early brain-targeted effects of growth factors but the association to IVH is not clear. The aim of this study was therefore to investigate the association between early serum levels of growth factors and the subsequent development of IVH.

Clinical variables were collected prospectively from a cohort consisting of 90 infants < 28 gestational weeks at birth. Blood samples were retrieved at postnatal day 1 and serum levels of brain derived neurotrophic factor (BDNF), platelet derived growth factor (PDGF), vascular endothelial factor (VEGF), Insulin-like growth factor-1 (IGF-1) and erythropoietin (EPO) were analyzed. Cerebral ultrasound was performed during the first week of life as well as on clinical indication. Univariate correlation was performed, where p < 0.2 was considered level of inclusion in logistic multivariate analysis. Matching of infants was performed by the variables Gestational age (GA) at birth, Gender, APGAR 5, Mortality, and Birth weight in descending order.

In total, 12 infants developed IVH grade III-IV (severe IVH) and 26 infants developed IVH grade I-II. Growth factor serum levels were available in 85 infants. Serum levels of PDGF and BDNF were significantly lower at postnatal day 1 in infants developing severe IVH compared to infants without IVH (p = 0.032 and p = 0.047), Figure 1. When adjusting for GA, serum levels remained lower for PDGF (p = 0.035). When matching individuals, serum levels of PDGF were significantly lower at postnatal day 1 (p = 0.030). When comparing infants developing IVH grade I-IV with the rest of the cohort, levels of BDNF were lower in infants with IVH (p = 0.008), also when adjusting for GA (p = 0.029). No significant differences were observed in serum levels of VEGF, EPO, and IGF-1.

This study shows that low levels of PDGF and BDNF early after birth are associated with the development of IVH. Both PDGF and BDNF are involved in angiogenesis through the recruitment of perivascular cells, promotion of endothelial cell survival and the induction of neoangiogenesis. These findings will be further investigated in a larger multicentre study with the aim to locate a potential predictive biomarker for IVH.
Figure 1, Serum levels of PDGF (ng/L) and BDNF (ng/L) on postnatal day 1 are lower in extremely preterm infants developing severe IVH.
Serum levels of PDGF (A) and BDNF (B) were lower postnatal day 1 in infants developing severe IVH in a cohort consisting of 90 extremely preterm infants, 95% CI.
Severe IVH = intraventricular hemorrhage grade III and IV, CI = confidence interval.

COI: None declared.
ID: 662
TITLE: SEPSIS-INDUCED CHANGES IN CEREBROSPINAL FLUID PROTEINS AFFECT THE DEVELOPING HIPPOCAMPUS
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CONTENT:

Preterm infants are susceptible to sepsis, which in turn may lead to neurodevelopmental disorders. How systemic infection affects brain development and functions is poorly understood, and good biomarkers for early diagnosis and treatment for sepsis-induced brain injury are lacking. We hypothesized that systemic infection alters protein composition of cerebrospinal fluid (CSF), and that infection-exposed CSF directly affects hippocampal development. First, we characterized CSF proteome changes in septic preterm infants. We then investigated how CSF from systemically infected preterm pigs, as a model for preterm infants, affects the immature porcine hippocampus in ex vivo cultures.

Proteins in CSF from very preterm infants (<32 weeks gestation), diagnosed as sepsis (SEP, n=19, culture-proven) or sepsis-free (CON, n=10, suspected sepsis, but not confirmed) were profiled by mass spectrometry (MS)-based proteomics. Many SEP infants developed cerebral abnormalities later. In addition, CSF was collected from 5 d-old preterm piglets with or without bacteremia (CON, BAC), defined as positive bacterial culture in both bone marrow and liver. These CSF samples, reflecting mild exposure to systemic infection, were added into culture media of hippocampal slices obtained from healthy newborn preterm pigs (90% gestation, caesarean section). Following 4 h of in vitro culture, the CSF, hippocampal tissue and culture media were then collected for proteomic analysis.

The SEP infants (high risk of later cerebral abnormalities) showed a distinct CSF proteome profile compared with CON infants. The differentially expressed proteins (DEPs) included upregulation of acute immune response proteins (HP, C1QB, C9, CD14) and down-regulation of neuritogenesis and cell differentiation proteins (FN1, MEGF8, COL5A1, Fig 1). BAC pigs showed upregulation of CSF proteins related to neuroinflammation. Immature pig hippocampal slices responded differently to CSF from BAC and CON pigs, with 126 and 508 DEPs in hippocampal tissue and secretome, respectively. Proteins related to mitochondrial function (NDUF), neural migration (TUBB4A, MINP), neuron projection guidance and synaptogenesis were changed. Four proteins (APLP1, COL5A1, PCOLCE, SEZ6L) were down-regulated in both CSF from SEP infants and proteins secreted from hippocampal slice exposed to infected CSF.

Sepsis markedly affects CSF protein composition and neural circuits in developing hippocampus. The proteomics-identified DEPs may serve as potential targets to prevent later neurodevelopmental disorders in sepsis survivors. Using preterm pigs as a model for preterm infants, ex vivo hippocampal slice cultures can be used as a novel experimental tool to investigate multi-cellular responses to changes in CSF after infection.

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Fig 1. MA plot showing overview of differentially-expressed proteins in CSF from septic and control preterm infants. Each dot represents an identified protein with average protein expression level at x-axis and log 2 fold change of sepsis versus control at y-axis. Dots above 0 at y-axis were upregulated proteins in septic condition. Grey dot: not differentially expressed proteins. Red dots, differentially expressed proteins.
COI: None declared
ID: 957

**TITLE:** NOVEL MODEL OF POST-HEMORRHAGIC VENTRICULAR DILATATION AND LONG-TERM OUTCOME FOLLOWING INTRAVENTRICULAR HEMORRHAGE IN THE PRETERM RABBIT PUP

**AUTHORS:** Olga Romantsik 1, Matteo Bruschettini 1, Susanne Grönlund 1, Bo Holmqvist 2, David Ley 1

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**CONTENT:**

Intraventricular hemorrhage (IVH) is a serious complication of prematurity and is associated with cerebro-cerebellar damage, leading to post-hemorrhagic ventricular dilatation (PHVD) and long-term neurodevelopmental impairment. The preterm rabbit pup model of IVH mimics to a high degree the patho-physiological events, the brain maturation and vessel anatomy of the extremely preterm infant with IVH. However, evaluation of long-term outcome has as yet been limited by an immature systemic physiology and high mortality. We here present a unique preterm rabbit model enabling study of long-term outcome following preterm IVH up to young adolescent age.

Rabbit pups were delivered by cesarean section at E29 (3 days prior to term). IVH was induced by intraperitoneal injection of 50% glycerol at 3 h of age. Following initial feeding via gastric tube the preterm pups were placed and housed with wet nurse rabbit does together with part of the does offspring. Presence and distribution of IVH was detected by high-resolution ultrasound (HRU, Visual Sonics Vevo 2100) at 24 and 48h. Neurological examination was performed at 28 days and behavioral tests between 28-31 days of age. Pups were terminated at 32 days of age following in vivo perfusion fixation. Cerebral ventricular morphology was assessed with HRU ex vivo and brain sections evaluated with immunohistochemistry (IHC).

A total of 21 (IVH=8; Control=13) preterm rabbit pups completed the study protocol. Postnatal growth did not differ between IVH and control pups with a mean (SD) weight at 32 days of 564 (99) g in IVH pups and 616 (77) g in control pups, p=0.19. Ex vivo ultrasound confirmed moderate/severe PHVD in 6/8 pups with an initial IVH. There were no differences in motor performance between the groups (motor activity, righting reflex, coordination and muscle strength on a 60° slope). Object recognition test revealed decreased recognition and exploration at a 4h interval in IVH pups as compared to control pups, p<0.05. Macroscopic appearance of brains with PHVD and control is illustrated in Fig 1. Evaluation with IHC of regional cerebral/cerebellar myelination, neuronal and synaptic density will be presented.

The presented model of preterm IVH and long-term outcome enables novel opportunities for the study of long-term outcome, extending the prospective for prevention and treatment of PHVD and functional impairment following preterm IVH.

**IMAGES:**

https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=25d3f94bb7fd3a8177e2a205fbbfccc-MjAxOS0wNSM1Y2UyNyZDMyNGQ0

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TITLE: ULTRASOUND CHARACTERISTICS OF PERIVENTRICULAR HAEMORRHAGIC INFARCTION AFFECTING MORTALITY AND NEURODEVELOPMENT IN VERY PRETERM INFANTS.

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CONTENT:

Periventricular haemorrhagic infarction (PVHI) is one of the most severe forms of brain injury seen in very preterm infants and is associated with high mortality and high rates of neurodevelopmental impairment (NDI). While broadly defined as a pathological condition, severity of PVHI can be graded by assessing specific features of the lesion. Bedside ultrasound (US) imaging allows diagnosis and monitoring of PVHI as well as characterisation of its features. We aimed to assess whether sonographic PVHI characteristics according to a previously published score are associated with outcomes of affected infants at age 2 years.

This was a retrospective analysis of cranial US imaging data from infants with PVHI, born <30 weeks of gestation in Switzerland, in 2002-2014, without major malformations. The PVHI severity score defined by Bassan et al. (2006) was assigned to the US image set where the bleed was deemed most extensive. Points were added for bilaterality, extension of the bleed and presence of midline shift, creating a score from 0 to 3. The data for the outcomes ‘death’ and ‘NDI’ at a corrected age of 2 years were exported from the prospective register of the Swiss Neonatal Network. NDI was defined as: mental or motor development index < -2SD, severe cerebral palsy, blindness or deafness. We used logistic regression to estimate the association between the Bassan score versus mortality or NDI.

Among 9103 live-born infants, 359 children suffered from PVHI. US imaging data for 157 children was considered adequate for reviewing. Within this collective 74/157 (48%) children died, 57 of which after withdrawal of care. Within the survivors, 2-year follow-up data was available for 74/83 (89%) children. Moderate to severe NDI was present in 38/74 (51%) infants. Table 1 shows the distribution of outcomes according to the Bassan scores. Logistic regression analysis showed that the Bassan score was associated with increased mortality [OR (95% CI) 3.3 (1.9 ; 5.7), p<0.001] and NDI [4.1 (1.7 ; 10.1), p=0.002].

In this collective of very preterm children, the association between the PVHI severity score and mortality may be confounded by the large proportion of children who died after decision of redirection of care. Based on three US characteristics of PVHI, this score predicts neurodevelopmental outcome at 2 years of age. This information could support parental guidance and supportive intervention of affected infants.
Title
Distribution of outcomes according to the Bassan score.
Legend
GMFCS, Gross Motor Function Classification System.

COI: None declared.