STROKE & NEUROVASCULAR DISORDERS

FP88
PERINATAL STROKE RISK FACTORS: SYNDROME-CONTROLLED ANALYSIS IN THE CANADIAN CEREBRAL PALSY REGISTRY

Elizabeth Williams1, Maryam Oskoui2, Lynn Dagenais1, Michael Shevell1, Adam Kortan1
1University of Calgary, Canada; 2McGill University, Montreal, Canada

Objectives: Perinatal stroke causes most hemiparetic cerebral palsy (CP). Pathophysiology is unknown with limited case-control studies. Comparisons to related disease states may provide unique insight. The population-based Canadian CP registry (CCPR) collects imaging and >70 risk factor variables. We hypothesized that perinatal strokes carry unique risk factor profiles within CP populations.

Methods: CCPR enrolls children across 13 Canadian centers. Systematic chart reviews and parental interviews acquire >150 variables including potential risk factors. Data current to June 2013 was extracted (REDCap) and analyzed. Imaging reports for hemiparetic CP cases were classified as: (1) definitive stroke (arterial or venous), (2) probable stroke, (3) not stroke (alternate diagnosis), or (4) inconclusive. Risk factor variables were compared between definitive stroke and two disease control groups: (1) hemiparetic CP, not stroke and (2) all other CP. Univariate analysis informed multivariate logistic regression.

Results: Of 1168 children (57.6% male, median+/-2=23mos), hemiparetic was the most common CP phenotype (29%). Definitive perinatal stroke was common (158, 49%) compared to non-stroke (109, 34%) and 6.7% were arterial (33% venous). Comparing stroke to non-stroke hemiparetic CP found seven univariate associations but none persisted on multivariate analysis. Comparing stroke to other CP types demonstrated independent associations with preeclampsia (2.33, 1.11-4.95, p=0.025), prematurity (0.165, 0.093-0.295, p<0.001), maternal drug use (5.03, 2.05-12.13, 95% CI 2001) and male gender (1.47, 0.97-2.19, p=0.09).

Conclusions: CP registries are a valuable source of disease-specific etiologies including perinatal stroke. Stroke-specific risk factors may include previously (male gender) or inconsistently (preeclampsia) reported associations and novel factors (maternal drugs). Syndrome-controlled approaches may inform perinatal stroke pathogenesis.

FP89
PROFILE OF CHILDHOOD CEREBROVASCULAR OUTPATIENT CLINIC AT HOSPITAL IN THE SOUTH OF BRAZIL

Josemar Marchezan, Marcela Matos Monteiro Gonçalves, Josiane Ranzan, Leticia Machado da Rosa da Silva, Rafaela Vasconcelos Viana, Manuela Graeff da Rosa, Gabrielle Casagrande Dagostim, Michele Michelin Becker, Maria Isabel Brigatti Winckler, Lygia Ohlweiler, Rudimar dos Santos Riesgo. Hospital de Clinicas de Porto Alegre, Brazil

Introduction: Cerebrovascular disease in children has been increasingly diagnosed and studied, with advancements in technology and medical imaging. Its incidence ranges from 2 to 13 in 100,000 births/year. Arterial ischemic stroke (AIS) is the most common childhood cerebrovascular disease. This issue has been extensively studied all over the world, especially during the last decade.

Methods: Data from the Childhood Cerebrovascular Outpatient Clinic at a public hospital were retrospectively reviewed, from March/2002 until September/2013. Patients with age varying from 0 to 18 years (at the moment of the stroke) were included.

Results: The sample is comprised of 133 cases of cerebrovascular disease, divided into three categories: 1) AIS, with 107 patients; 2) Hemorrhagic stroke, with 18 patients; 3) Sinovenous thrombosis, with 8 patients. Regarding age of the stroke, 36% occurred during prenatal period. In our sample, males were more affected than females (54.1%), as well as Caucasian children (86.4%). Six patients died due to cerebrovascular disease.

Discussion/Conclusion: In our sample, AIS was the most prevalent situation, in a slightly high percentage when compared with literature, probably because this specific disease was the first to be analyzed in our Center. The other results are in concordance with previous international studies. Our data show the relevance of cerebrovascular disease in neonates, children, and adolescents. These acute neurological situations must have to be remembered and diagnosed in the paediatric population, especially in the neonatal period.

NEUROLOGICAL INVOLVEMENT IN CHILDREN WITH E. COLI O104:H4-INDUCED HAEMOLYTIC URAEMIC SYNDROME

Angela Bauer1, Sebastian Loos1, Dirk Horstmann1, Frank Donnentag1, Lars Pape1, Dieter Haffner2, Thurid Ahlenstiel1, Markus Kemper1, Carla Wehmann2, Ulrike Lobel1, Johanna Lemke1, Georg Hillebrand1, Annette Miel1, Jun OH1, Hans Hartmann1. 1Department of Paediatrics, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany; 2Department of Paediatric Kidney, Liver, and Metabolic Diseases, Hannover Medical School, Hannover, Germany; 3Institute of Diagnostic and Interventional Neuroradiology, Hannover Medical School, Hannover, Germany; 4Department of Child and Adolescent Psychiatry and Psychotherapy, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany; 5Department of Diagnostic and Interventional Neuroradiology, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

Objectives: This study analyses the neurological involvement and the mid-term outcome in paediatric patients with haemolytic uraemic syndrome during the German epidemic 2011 caused by E. coli O104:H4.

Design, Setting, Patients: Data regarding clinical signs, magnetic resonance imaging (MRI) and electroencephalography (EEG) findings during the acute disease were analysed in 50 patients aged 1.5–17.5 years (median 11.9). Follow-up visits were performed after 3 and 6 months.

Results: In 25 children underwent neuropsychological testing (WISC IV) after 6 to 9 months of follow-up.

Results: Neurological involvement was observed in 14/50 (28%) patients, including stupor or coma in 11/50 (22%), seizures in 11/50 (22%), visual disturbances in 4/50 (8%), hemiparesis in 2/50 (4%), and myocloni in 3/50 (6%). One patient died and one developed residual hemiparesis. EEG was more frequently abnormal in patients with neurological involvement (12/14 vs. 13/36, p=0.03). Cranial MRI was obtained in 11 patients with neurological involvement with abnormal findings in 5. After 3 and 6 months, 28/42 (67%) and 17/39 (44%) of the patients complained about on-going reduced performance. Neuropsychological testing showed a slightly lower global intelligence quotient in patients with neurological involvement (113.4±2.8 vs. 119.4±1.8, p=0.07), mainly due to a reduced processing speed index.

Conclusions: Neurological involvement was frequent in paediatric patients with haemolytic uraemic syndrome caused by E. coli O104:H4, but there was a high incidence of pathological EEG-findings even in patients without clinical signs of neurological involvement in the acute phase. Major neurological sequelae were rare and neuropsychological outcome favorable after 6 months.

IS D-DIMER MEASUREMENT USEFUL IN PEDIATRIC CEREBRAL SINOVENOUS THROMBOSIS?

Ana Marisa Lagman-Bartolome1, Leonardo R. Brandao1, Ann-Marie Pontigon1, Gabrielle DeliBreve1, Daune MacGregor1, Rand Asklani2, Ivanna You3, Mahendranath Mohari4. 1Division of Neurology, Dept. of Pediatrics, 2Division of Hematology/Oncology, Dept. of Pediatrics, The Hospital for Sick Children, Toronto, Canada

Introduction: Pediatric CSVT diagnosis is dependent on neuroimaging (MRV/CTV). Biomarkers to suspect, quantify and prognosticate CSVT are lacking. D-dimer (DD) assay is useful in adults for diagnosis/prognosis.

Objectives: To determine frequency of elevated DD and its correlation with clot burden and outcome in paediatric CSVT.

Methodology: Children (29-days-18-years) with CSVT and DD assay from Sept’99-Dec’09 were identified. Patients with DD performed <7 before and <14 days after CSVT diagnosis were included. Clinical data, D-dimer (abnormal level: any value > institutional age-specific normative value, ng/mL) and neuroimaging data (high clot burden (>1 sinus with thrombus), haemorrhage, CSVT-propagation, recanalization) were analyzed. Groups were compared by Fisher’s exact/Chi-Square test. Logistic regression was used for outcome prediction.

Results: Ninety-three CSVT patients were identified. Sixty had DD. Forty-six (21 males) were included [mean age: 8-yr, median time (in relation to CSVT-diagnosis) of DD-assay: 4.6-2.2 days]. DD was elevated in 32/46 (70%). No significant differences (with respect to age, gender, clinical/radiological features, risk factors, treatment) were found between those with and without elevated DD, except strong trends...
with respect to high clot burden [97% with, 79% without elevated DD, (p=0.069)] and CSVT-propagation [25% with, 0% without elevated DD, (p=0.0845)]. Logistic regression analysis revealed 55% (p=0.1384, OR 1.55, 95% CI 0.841-2.860) and 61% (p=0.1088, OR 1.61, 95% CI 0.928-3.147) increased likelihood of clot propagation and poor neurological outcome respectively per 100 unit DD increase.

**Interpretation:** D-dimer level is elevated in most children with CSVT and seems to correlate with CSVT burden, propagation and poor clinical outcome. Larger prospective study is warranted.

**FP92**

**ROLE OF PROTHROMBOTIC RISK FACTORS (THROMBOPHILIA) IN NEONATAL ARTERIAL ISCHEMIC STROKE**


**Introduction:** Newborns constitute a large proportion of childhood arterial ischemic stroke (AIS). Relevance of prothrombotic risk factors in neonatal arterial ischemic stroke (NAIS) is unknown.

**Objectives:** To study the impact of prothrombotic risk factors on NAIS.

**Methods:** A single-centre retrospective analysis (July/1999-August/2009) of NAIS cases was conducted. Prothrombotic testing included protein-C(PC), protein-S(PS), antithrombin, anti-cardiolipin-antibodies(ACLA), lupus-anticoagulant, lipoprotein-(a), homocysteine, factor-VIII, factor-IX, factor-XI and Factor-V Leiden, prothrombin G20210A (PTG) and MTHFR gene mutations. Data on non-inherited coexisting risk factors [congenital heart disease (CHD), vasculopathy, head/neck disorders, systemic disease] and anti-thrombotic therapy (ATT) (Aspirin/antiaggregants) were collected. Stroke recurrence was defined as new ischemic lesion(s) on follow-up neuromaging. Neurologic outcome was assessed by the validated Pediatric Stroke Outcome Measure (any neurodefect considered abnormal). Measures of association (Fisher's Exact) between risk factors, ATT and outcomes were studied.

**Results:** Seventy-six out of 88 NAIS cases (52 males) had prothrombotic testing. Of these 91(2%) had at least one prothrombotic risk factor (PC, ACLA, heterogeneous PTG (2 each) and ACLA-Factor-VIII, lipoprotein-(a), MTHFR- elevated homocysteine (1 each)), and 62(85%) had at least 1 non-prothrombotic risk factor [majority: CHD (81%)]. ATT was administered in 37/88(43%). Stroke recurred in 8/88(13%). Presence of prothrombotic risk factor predicted stroke recurrence [OR 6.295%CI: 1.18-32.56]; p=0.0485] and trend towards poor outcome (median f/u: 2-yr±1) [OR 6.9795%CI: 0.82-59.34]; p=0.069]. Neither presence of non-inherited risk factors nor ATT predicted outcome.

**Conclusion:** Prothrombotic abnormalities were encountered in a relatively small proportion of newborns with AIS, but they were associated with unfavourable outcome. A larger prospective multicentre study is needed to corroborate these findings.

**FP93**

**ROBOTIC QUANTIFICATION OF PROPROICEPTIVE DYSFUNCTION IN CHILDREN WITH PERINATAL STROKE**

Andrea Kuczynski, Sean Dukelow, Janice Yajure, Jamie Roe, Steve Scott, Adam Kirtom. University of Calgary, Alberta Children's Hospital, Canada

**Background:** Perinatal stroke causes most hemiplegic cerebral palsy. Sensory dysfunction is an understudied contributor to disability in part due to limited objective measurement tools. Robotic technology can quantify complex sensory function in adult stroke but has not been applied to children. We hypothesized that proprioceptive dysfunction is measurable in children with perinatal stroke and correlates with stroke type and level of disability.

**Methods:** Children from the Perinatal Stroke Project had MRI confirmed unilateral perinatal stroke (arterial stroke or periventricular venous infarction) and upper extremity functional deficit. A bilateral exoskeletal robot (KINARM) tested planar upper limb movements in an augmented reality environment. Primary outcomes were two-dimensional variability, shift, and contraction/expansion scores of a position-matching task. Clinical measures of sensory function (touch, proprioception, graphesthesias, stereognosis) were scored. Matched controls (age/gender) were tested.

**Results:** Eight perinatal stroke children (median 15±7.2 years, 4 female) (3 PVI, 5 arterial) were compared to 9 healthy controls. Stroke children demonstrated marked impairment in position matching including variability (6.04±1.4 vs 3.93±0.6cm, p= 0.004) and shift (5.16±1.9 vs 1.91±1.1cm, p<0.001). Contraction/expansion ratios also appeared abnormal (0.56±0.27 vs 0.31±0.22, p=0.09). Deficits were greater in arterial lesions compared to PVI. Clinical sensory scores were lower in cases but correlated poorly with robotic measures and motor function. Assessments were well tolerated with no adverse events.

**Conclusion:** Robotic quantification of proprioception is feasible in perinatal stroke. Sensitivity and quantification appear superior to clinical exam. Disordered proprioception is an under-recognized component of disability and a novel therapeutic target.
Conclusion: Malignant cerebral edema, is a severe complication of infarcts involving the middle cerebral artery territory. These patients have a more severe deficit on presentation and prolonged seizures. Large territorial infarcts, and proximal artery occlusion is seen in these patients. The early recognition of these findings could be helpful for clinicians in order to identify patients at risk.

**FP96 SHINGLES OF THE BRAIN - RECURRENT HERPES ZOSTER OPHTHALMICS CAUSING ARTERIOPATHY AND BASAL GANGLIA INFARCTION**

Nomazulu Dlamini, Luis Amarya, Ata Siddiqui, Jean-Pierre Lin, Evelina Children's Hospital, Guy's and St Thomas' Hospital, London, United Kingdom; Department of Ophthalmology, St Thomas' Hospital, London, United Kingdom

Introduction: Varicella zoster is thought to lie quiescent in the trigeminal ganglion following an episode of chicken pox. Viral reactivation occurs with retrograde infection of the first division of the trigeminal nerve and the clinical phenomenon of Herpes zoster ophthalmicus (HZO). Direct and indirect mechanisms affecting the neurovascular bundle are implicated in the aetiology of post-varicella angiopathy arterial ischaemic stroke (AIS) although pathological evidence is limited to.

Case: A five year old girl with a history of chicken pox at four weeks of age was diagnosed with HZO of the left eye (Fig 1). This remained indolent in the left eye despite treatment. Ten weeks after initial presentation, she presented with right sided choreoathetosis. MRI and MRA demonstrated left basal ganglia signal change, narrowing of the terminal left internal carotid artery (ICA), proximal anterior and middle (MCA) cerebral arteries (Fig 2). Ultrasound angiography revealed abnormal velocities of the left MCA and ICA. Protein S and C levels were transiently low. Further investigations were normal. She received a second course of HZO treatment and Dipyridimole. Choreoathetosis and MRI changes resolved however there was persistent narrowing of the vessels.

Conclusion: We propose HZO related AIS is the clinical equivalent to shingles of the brain supporting a peri-infectious, immune mediated inflammatory basis for the condition. We suggest pathology targeted treatments such as Acyclovir and corticosteroids be considered and that further research is required in this area.

**FP97 ISOLATED BILATERAL CAROTID ARTERITIS PRESENTING WITH STROKE IN CHILDHOOD**

Kevin Alfred Shapiro, Ferdinando Buonanno. University of California, San Francisco, United States; Massachusetts General Hospital, United States

Introduction: Most arterial ischemic strokes in children are attributable to acquired vasculopathies, a significant subset of which are inflammatory in nature. The cervical carotid system in particular is often involved in Takayasu arteritis (TA), a systemic vasculitis that classically affects the aortic arch and its major branches. We discuss the case of a 16 year old girl with stroke and transient ischemic symptoms due to isolated inflammatory occlusive lesions of both carotid arteries.

Case Report. Our patient presented with stuttering onset of right-sided weakness and was found to have an acute ischemic stroke in the left basal ganglia and internal capsule. Labs were notable for elevated serum inflammatory markers. Vascular imaging demonstrated severe occlusive disease of both common carotid arteries, without involvement of the aortic arch or other branches. Her disease initially progressed, but stabilized with anticoagulation, antiplatelet therapy, corticosteroids, methotrexate, and cyclophosphamide. She subsequently presented with transient left-sided symptoms correlated with decreased perfusion in the territory of the right internal carotid artery.

Discussion. The common carotid arteries are among the most frequently affected vessels in TA. In children, approximately 52% of patients have common carotid involvement (1). However, isolated involvement of aortic branch vessels occurs in only 5% of cases (2), and isolated involvement of the common carotid arteries has not been reported to our knowledge.

Conclusions. Isolated inflammation of the common carotid arteries occurs in children and may present with ischemic stroke. A combination of aggressive antithrombotic, anti-inflammatory and immune-modifying therapy appears to halt disease progression.

**FP98 LONG-TERM NEUropsychological OUTCOME AFTER CHILDHOOD CEREBRAL SINOVENOUS THROMBOSIS**

Aly Aitz, Robyn Westmacott, Gabrielle delHebre, Daune Macgregor, Rand Askalan, Ivanla Yau, Mahendranath Mohanri, Division Of Neurology, Dept Of Pediatrics, The Hospital For Sick Children, Toronto, Canada, Canada

Introduction: Clinical outcome from childhood cerebral sinovenous thrombosis (CSVT), particularly in younger children, is poor. Most studies report ‘general’ neurological outcomes; few describe neuropsychological outcomes.

Aim: To study the spectrum of neuropsychological deficits following childhood CSVT.

Methods: Retrospective analysis of neuropsychological testing (NPT) performed in children with CSVT from 1995-2011. NPT included IQ (Wechsler Intelligence Scale for Children (WISC-IV)); Wechsler Preschool & Primary Scale of Intelligence (WPPSI-III), executive function (Behaviour Rating Inventory of Executive Function (BRIEF)) and attention (Test of everyday attention (Tea-Ch)). Full scale IQ (FSIQ) included verbal comprehension (VCI), perceptual reasoning (PRI), working memory (WMI) and processing speed (PSI) index.

Results: NPT (mean age: 5.4 years (neonatal CSVT), 8.5 years (non-neonatal CSVT)) was performed in 48/206 patients. Forty-one (34 males) were included; (exclusions: cavernous sinus thrombosis (5), prematurity (1), co-existing arterial stroke (1)). NPT revealed some abnormality in 87% (across one (29%)/multiple (58%) domains) compared to normative population. FSIQ was abnormal in 64% (VCI-69%, PRI-80%, WMI-71%, PSI-79%). FSIQ (p = 0.026), VCI (p = 0.608), PRI (p = 0.032), WMI (0.124) and PSI (p = 0.007) scores were lower. No differences were seen in FSIQ between groups [normates/non-normates (p = 0.827), single/multiple sinus thrombosis (p = 0.2), present/absent parenchymal lesions (p = 0.991)] except gender: Males had lower FSIQ (p = 0.006) (PRI = 0.004), WMI (p = 0.003), PS (p = 0.002), BRIEF: Metacognition (p = 0.061), executive composite (p = 0.0950) and Tea-Ch (p = 0.046) scores.

Conclusions: Many childhood CSVT survivors (males > females) have significant residual cognitive deficits detectable only by NPT on long-term follow-up. NPT is indicated for more accurate CSVT outcome assessment.

**FP99 HYPOTHERMIA IN HYPOXIC ISCHEMIC ENCEPHALOPATHY PRELIMINARY RESULTS IN NEURODEVELOPMENTAL OUTCOME**

Claudio G. Wasiburga, Guillermo Colantonio, Ana Pedraza, Luis Prudent. Pediatric Medical Director Head Pediatric Neurology Cognitive Neurology Institute- INECO Neuroscience Favaloro Foundation- INFF, Argentina; Neonatologist, SuizoArgentino, Los Arcos, Argentina; Argentina

Introduction: Perinatal asphyxial encephalopathy (PAE) is associated with high morbidity and mortality rates worldwide and is a major burden for the patient, the family, and society. The objective of the study was to evaluate neurodevelopmental outcome of newborn babies who underwent a protocol of Hypothermia in the first 72 hs of life. Taking into consideration that the incidence for PAE has not changed in the last 20 years, there is an urgent need to improve outcomes in affected infants.

Methods: To present our preliminary experience from two Institutions with 30 cases of clinical application of therapeutic corporal hypothermia for PAE. Systemic hypothermia temperature to 33.5ºC was begun and continued for 72 hours. Normalization of temperature is by 0.5ºC per hour. We included in a protocol all babies fulfilling criteria.

Results: Coding was well tolerated with no adverse reactions. Neurodevelopmental follow up of the surviving infants from 3 months to 40 months. There was considerable reduction on mortality and reduce on moderate PAE neurological disability. None developed feeding problems, oculomotor abnormalities, spasticity or seizures on follow up.

Conclusions: Induction of hypothermia to 33.5ºC central temperature for 72 hours in infants who had PAE improved neurologic outcomes in survivors. Hypothermia is beneficial on neurodevelopmental outcome in PAE babies. Our preliminary experience with this modality in a large neonatal service is consistent with the clinical findings of published trials. Decreasing motor, sensory and cognitive handicap and disability. Whether hypothermic therapy improves neurodevelopmental outcomes in long term is uncertain.