AVC de l'enfant Centre national de référence

Thursday, 09 August 2018

Hello everyone,

Le centre AVC de l'enfant is delighted to bring you this free bulletin of published research into stroke in children, as indexed in the NCBI PubMed (Medline) database.

Kind regards,
Le centre AVC de l'enfant

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Management & Cure:

Impact of a modified anti-thrombotic guideline on stroke in children supported with a pediatric ventricular assist device.

Rosenthal DN, Lancaster CA, McElhinney DB, Chen S, Stein M, Lin A, Doan L, Murray JM, Gowan MA, Maeda K, Reinhartz O, Almond CS.

J Heart Lung Transplant. 2017 Nov;36(11):1250-1257.

BACKGROUND: Stroke is the most feared complication associated with the Berlin Heart EXCOR pediatric ventricular assist device (VAD), the most commonly used VAD in children, and affects 1 in 3 children. We sought to determine whether a modified anti-thrombotic guideline, involving more intense platelet inhibition and less reliance on platelet function testing, is associated with a lower incidence of stroke.

METHODS: All children supported with the EXCOR at Stanford from 2009 to 2014 were divided into 2 cohorts based on the primary anti-thrombotic guideline used to prevent pump thrombosis: (1) the Edmonton Anti-thrombotic Guideline (EG) cohort, which included children implanted before September 2012 when dual anti-platelet therapy was used with doses titrated to Thromboelastrography/PlateletMapping (TEG/PM); and (2) the Stanford Modified Anti-thrombotic Guideline (SG) cohort, which included children implanted on or after September 2012 when triple anti-platelet therapy was used routinely and where doses were uptitrated to high, weight-based dosing targets, with low-dose steroids administered as needed for inflammation.

RESULTS: At baseline, the EG (N = 16) and SG (N = 11) cohorts were similar. The incidence rate of stroke in the SG cohort was 84% lower than in the EG cohort (0.8 vs 4.9 events per 1,000 days

of support, p = 0.031), and 86% lower than in the previous Investigational Device Exemption trial (p = 0.006). The bleeding rate was also lower in the SG cohort (p = 0.015). Target doses of aspirin, clopidogrel and dipyridamole were higher (all p < 0.003), with less dosing variability in the SG cohort than in the EG cohort. There was no difference in adenosine diphosphate inhibition by TEG/PM, but arachidonic acid inhibition was higher in the SG cohort (median 75% vs 39%, p = 0.008).

CONCLUSIONS: Stroke was significantly less common in pediatric patients supported with the Berlin Heart EXCOR VAD using a triple anti-platelet regimen uptitrated to high, weight-based dosing targets as compared with the dual anti-platelet regimen titrated to PM, and without a higher risk of bleeding. Larger studies are needed to confirm these findings.

Ischaemic stroke in children with cardiopathy: An epidemiological study. [Article in English, Spanish]

Vázquez-López M, Castro-de Castro P, Barredo-Valderrama E, Miranda-Herrero MC, Gil-Villanueva N, Alcaraz-Romero AJ, Jiménez-de Domingo A, Pascual-Pascual SI.

Neurologia. 2017 Nov - Dec;32(9):602-609.

INTRODUCTION: Ischaemic stroke is rare during childhood. Congenital and acquired heart diseases are one of the most important risk factors for arterial ischaemic stroke (AIS) in children.

PATIENTS AND METHODS: We conducted a retrospective study of all children with AIS and heart disease diagnosed between 2000 and 2014.

RESULTS: We included 74 children with heart disease who were eligible for inclusion. 60% were boys with a mean stroke age of 11 months. 20% of the patients died during the study period. 90% of the patients had a congenital heart disease, while cyanotic heart disease was identified in 60%. Hypoplastic left heart syndrome was the most frequent heart disease. In 70% of patients AIS was directly associated with heart surgery, catheterisation or ventricular assist devices. Most patients with AIS were in the hospital. Seizures and motor deficit were the most frequent symptoms. Most patient diagnoses were confirmed by brain CT. The AIS consisted of multiple infarcts in 33% of the cases, affected both hemispheres in 27%, and involved the anterior and posterior cerebral circulation in 10%.

CONCLUSIONS: Arterial ischaemic strokes were mainly associated with complex congenital heart diseases, and heart procedures and surgery (catheterisation). AIS presented when patients were in-hospital and most of the patients were diagnosed in the first 24hours.

Neonatal Arterial Ischemic Stroke: Risk Related to Family History, Maternal Diseases, and Genetic Thrombophilia.

Arnaez J, Arca G, Martín-Ancel A, Agut T, Garcia-Alix A.

Clin Appl Thromb Hemost. 2018 Jan;24(1):79-84.

The objective of this study was to evaluate the heritability of neonatal arterial ischemic stroke (NAIS) in relation to family history of thromboembolic event, maternal diseases, and thrombophilia in both parents (F5G1691A, F2G20210A, and MTHFRC677 T mutations). Forty-two consecutive infants ≥36 weeks of gestation <28 days of life with acute symptomatic NAIS and their parents, as well as 129 controls, were prospectively recruited. Information on maternal data (age, body mass index, oral contraception, migraine, epilepsy, hypertension, and immune disease) and a 3-generation pedigree regarding myocardial infarction, pulmonary embolism, cerebrovascular event, and deep vein thrombosis were obtained. Thrombophilia and maternal diseases did not differ between cases and controls, except for the use of oral contraceptives (more frequent in mothers of controls). No differences were found regarding each studied antecedent of thromboembolic event in the families. The NAIS group showed a higher presence of positive family history among second-degree maternal relatives than did the control infants (odds ratio 4.10; 95% confidence interval 1.29-12.99). Our study does not support the hypothesis that common genetic thrombophilia or familial predisposition to thromboembolic events is associated with the occurrence of idiopathic NAIS.

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Intervention & Rehabilitation:

Feasibility trial of an early therapy in perinatal stroke (eTIPS).

Basu AP, Pearse J, Watson R, Dulson P, Baggaley J, Wright B,
Howel D, Vale L, Mitra D, Embleton N, Rapley T.

BMC Neurol. 2018 Jul 23;18(1):102

BACKGROUND: Perinatal stroke (PS) affects up to 1/2300 infants and frequently leads to unilateral cerebral palsy (UCP). Preterm-born infants affected by unilateral haemorrhagic parenchymal infarction (HPI) are also at risk of UCP. To date no standardised early therapy approach exists, yet early intervention could be highly effective, by positively influencing processes of activity-dependent plasticity within the developing nervous system including the corticospinal tract. Our aim was to test feasibility and acceptability of an "early Therapy In Perinatal Stroke" (eTIPS) intervention, aiming ultimately to improve motor outcome.
METHODS: Design: Feasibility trial, North-East England, August 2015-September 2017. Participants were infants with PS or HPI, their carers and therapists. The intervention consisted of a parent-delivered lateralised therapy approach starting from term equivalent age and continuing until 6 months corrected age. The outcome measures were feasibility (recruitment and retention rates) and acceptability of the intervention (parental questionnaires including the Warwick-Edinburgh Mental Wellbeing Scale (WEBWMS), qualitative observations and in-depth interviews with parents and therapists). We also reviewed clinical imaging data and undertook assessments of motor function, including the Hand Assessment for Infants (HAI). Assessments were also piloted in typically developing (TD) infants, to provide further information on their ease of use and acceptability.
RESULTS: Over a period of 18 months we screened 20 infants referred as PS/HPI: 14 met the inclusion criteria and 13 took part. At 6 months, 11 (85%) of those enrolled had completed the final assessment. Parents valued the intervention and found it acceptable and workable. There were no adverse events related to the intervention. We recruited 14 TD infants, one of whom died prior to undertaking any assessments and one of whom was subsequently found to have a condition affecting neurodevelopmental progress: thus, data for 12 TD infants was analysed to 6 months. The HAI was well tolerated by infants and highly valued by parents. Completion rates for the WEBWMS were high and did not suggest any adverse effect of engagement in eTIPS on parental mental wellbeing.
CONCLUSION: The eTIPS intervention was feasible to deliver and acceptable to families. We plan to investigate efficacy in a multicentre randomised controlled trial.

The Feasibility of Functional Electrical Stimulation to Improve Upper Extremity Function in a Two-year-old Child with Perinatal Stroke: A Case Report.

Musselman KE, Manns P, Dawe J, Delgado R, Yang JF.

Phys Occup Ther Pediatr. 2018 Feb;38(1):97-112.

AIMS: To evaluate the effectiveness and feasibility (i.e. tolerability, adherence) of functional electrical stimulation (FES) for the upper extremity (UE) in a two-year-old child with perinatal stroke.

METHODS: Forty hours of FES over eight weeks was prescribed. FES to the hemiplegic triceps, extensor carpi radialis longus and brevis, extensor carpi ulnaris and extensor digitorum was timed with reaching during play. Assessments were performed before, during, and two months post-intervention. UE function (Melbourne Assessment 2 (MA2), Assisting Hand Assessment (AHA)) and

spasticity (Modified Tardieu with electrogoniometry and electromyography) were measured. The mother completed a semi-structured interview post-intervention. Descriptive statistics were used for adherence and UE measures. A repeated-measures ANOVA compared Modified Tardieu parameters (e.g. catch angle) over time. Conventional content analysis was used for the interview data.

RESULTS: The child completed 39.2/40 hours. Immediately post-intervention, improvements were observed on MA2's Range of Motion subscale and catch angle (Modified Tardieu, $p < 0.001$). Two months post-intervention, improvements were observed on MA2's Accuracy and Fluency subscales. No change in AHA score occurred. Three themes emerged from the interview: (1) Ingredients for program success; (2) Information about the FES device; and (3) The child's response.

CONCLUSIONS: UE FES was feasible in a two-year-old child with hemiplegia.

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Outcomes:

Neurodevelopment After Perinatal Arterial Ischemic Stroke.

Wagenaar N, Martinez-Biarge M, van der Aa NE, van Haastert IC, Groenendaal F, Benders MJNL, Cowan FM, de Vries LS.

Pediatrics. 2018 Aug 2. [Epub ahead of print]

BACKGROUND AND OBJECTIVES: Perinatal arterial ischemic stroke (PAIS) leads to cerebral palsy in ~30% of affected children and has other neurologic sequelae. Authors of most outcome studies focus on middle cerebral artery (MCA) stroke without differentiating between site and extent of affected tissue. Our aim with this study was to report outcomes after different PAIS subtypes.

METHODS: Between 1990 and 2015, 188 term infants from 2 centers (London [n = 79] and Utrecht [n = 109]) had PAIS on their neonatal MRI. Scans were reevaluated to classify stroke territory and determine specific tissue involvement. At 18 to 93 (median 41.7) months, adverse neurodevelopmental outcomes were recorded as 1 or more of cerebral palsy, cognitive deficit, language delay, epilepsy, behavioral problems, or visual field defect.

RESULTS: The MCA territory was most often involved (90%), with posterior or anterior cerebral artery territory strokes occurring in 9% and 1%, respectively. Three infants died, and 24 had scans unavailable for reevaluation or were lost to follow-up. Of 161 infants seen, 54% had an adverse outcome. Outcomes were the same between centers. Main branch MCA stroke resulted in 100% adverse outcome, whereas other stroke subtypes had adverse outcomes in only 29% to 57%. The most important outcome predictors were involvement of the corticospinal tracts and basal ganglia.

CONCLUSIONS: Although neurodevelopmental outcome was adverse in at least 1 domain with main branch MCA stroke, in other PAIS subtypes outcome was favorable in 43% to 71% of children. Site and tissue involvement is most important in determining the outcome in PAIS.

Bihemispheric alterations in myelination in children following unilateral perinatal stroke.

Yu S, Carlson HL, Mineyko A, Brooks BL, Kuczynski A, Hodge J, Dukelow S, Kirton A.

Neuroimage Clin. 2018 Jun 27;20:7-15.

Background: Stroke is a leading cause of perinatal brain injury with variable outcomes including cerebral palsy and epilepsy. The biological processes that underlie these heterogeneous outcomes are poorly understood. Alterations in developmental myelination are recognized as a major determinant of outcome in preterm brain injury but have not been explored in perinatal stroke. We aimed to characterize myelination in hemiparetic children after arterial perinatal stroke, hypothesizing that ipsilesional myelination would be impaired, the degree of which would correlate with poor outcome.

Methods: Retrospective, controlled cohort study. Participants were identified through the Alberta Perinatal Stroke Project (APSP), a population-based research cohort (n > 400). Inclusion criteria were: 1) MRI-confirmed, unilateral arterial perinatal stroke, 2) T1-weighted MRI after 6 months of age, 3) absence of other neurological disorders, 4) neurological outcome that included at least one of the following tests - Pediatric Stroke Outcome Measure (PSOM), Assisting Hand Assessment (AHA), Melbourne Assessment (MA), neuropsychological evaluation (NPE), and robotic sensorimotor measurements. FreeSurfer software measured hemispheric asymmetry in myelination intensity (primary outcome). A second method using ImageJ software validated the detection of myelination asymmetry. A repeated measures ANOVA was used to compare perilesional, ipsilesional remote, and contralesional homologous region myelination between stroke cases and typically developing controls. Myelination metrics were compared to clinical outcome measures (t-test, Pearson's correlation).

Results: Twenty youth with arterial stroke (mean age: 13.4 ± 4.2yo) and 27 typically developing controls (mean age: 12.5 ± 3.7yo) were studied in FreeSurfer. Participants with stroke demonstrated lower myelination in the ipsilesional hemisphere ($p < 0.0001$). Myelination in perilesional regions had lower intensity compared to ipsilesional remote areas ($p < .00001$) and contralesional homologous areas ($p < 0.00001$). Ipsilesional remote regions had decreased myelination compared to homologous regions on the contralesional hemisphere ($p = 0.016$). Contralesional myelination was decreased compared to controls ($p < 0.00001$). Myelination metrics were not strongly associated with clinical motor, robotic sensorimotor, or neuropsychological outcomes though some complex tests requiring speeded responses had moderate effect sizes.

Conclusion: Myelination of apparently uninjured brain in both the ipsilesional and contralesional hemispheres is decreased after perinatal stroke. Differences appear to radiate outward from the lesion. Further study is needed to determine clinical significance.

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Case Report:

Stroke and peripheral embolisms in a pediatric patient with giant atrial myxoma: Case report and review of current literature.

Wu Y, Fu XM, Liao XB, Zhou X.

Medicine (Baltimore). 2018 Jul;97(30):e11653.

RATIONALE: Cerebral stroke with peripheral embolism due to left atrial myxoma is very rare in children. Misdiagnosis may occur because of nonspecific symptoms in the heart.

PATIENT CONCERNS: We present a case of a 16-year-old boy who presented with ischemic stroke and embolisms in the lower extremity, caused by a giant left atrial myxoma.

DIAGNOSES: Left atrial myxoma.

INTERVENTIONS: A giant gelatinous mass was completely excised, and the histopathological findings confirmed the diagnosis of atrial myxoma.

OUTCOMES: The temperature of the right lower extremity recovered gradually, and pulse of the right dorsalis pedis artery became palpable 10 days after the surgery. The strength of the bilateral lower extremity was level 5 at discharge.

LESSONS: Our case, along with the review of the literature, highlights the fact that myxomas often initially present with multiple embolisms but with few cardiac symptoms. Transthoracic echocardiography should be performed immediately to make a definitive diagnosis.

A Case of a 4-Year-Old Female with a Primary Spinal Malignancy Presenting with Froin's Syndrome.

Hale AT, Fricker GP, Crook TW.

Pediatr Neurosurg. 2018;53(1):64-68.

We report the case of a 4-year-old female with a primary extradural intramedullary atypical teratoid/rhabdoid tumor (AT/RT) leading to a middle cerebral artery (MCA) infarct and Froin's syndrome. She presented with a 6-pound weight loss over the previous week, as well as a decreased urinary output and an altered mental status. She underwent a brain MRI that revealed a left MCA infarct, mild ventriculomegaly, and bilateral internal carotid artery, M1, and A1 stenosis. An external ventricular drain (EVD) was placed due to increased intracranial pressure. Cerebrospinal fluid (CSF) was analyzed via lumbar puncture that revealed extremely elevated protein. However, CSF sampled from the EVD was completely normal, a phenomenon called Froin's syndrome. The following day, she developed a right MCA infarct. Her grim prognosis was discussed with her family and care was eventually withdrawn. The patient underwent an autopsy which confirmed a spinal AT/RT. To our knowledge, this is the first reported case of stroke and Froin's syndrome as the initial manifestations of a primary spinal AT/RT with a late onset of spinal cord compression due to tumor obstruction.