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## Interventions and Management

**1. J Bone Joint Surg Am. 2015 Mar 18;97(6):507-11. doi: 10.2106/JBJS.N.01104.**

**Smaller body size increases the percentage of blood volume lost during posterior spinal arthrodesis.**

Jain A1, Sponseller PD1, Newton PO2, Shah SA3, Cahill PJ4, Njoku DB1, Betz RR5, Samdani AF4, Bastrom TP2, Marks MC2; Harms Study Group.

BACKGROUND: Our goal was to analyze the relationship between patient size and the proportion of blood volume lost during spinal arthrodesis in patients with a diagnosis of adolescent idiopathic scoliosis, Scheuermann kyphosis, or cerebral palsy. We hypothesized that smaller patients (those with less blood volume) lose a greater proportion of circulating total blood volume during surgery. METHODS: We reviewed a large, multicenter database, identifying patients with adolescent idiopathic scoliosis (1832), Scheuermann kyphosis (106), or cerebral palsy (196) who had undergone posterior spinal arthrodesis for spinal deformity. Blood volume (estimated from body weight) was used as a measure of patient size. Our primary outcome was the proportion of total circulating blood volume lost (intraoperative blood loss/blood volume, expressed as a percentage). RESULTS: On multivariate analysis, there was a negative relationship between intraoperative blood loss/blood volume and blood volume in patients with adolescent idiopathic scoliosis (coefficient, -5.8; $p < 0.001$), Scheuermann kyphosis (coefficient, -2.5; $p < 0.001$), or cerebral palsy (coefficient, -20.3; $p < 0.001$), indicating that, despite adjustment for all other factors, smaller patients lost a greater proportion of their blood volume. In patients with adolescent idiopathic scoliosis or Scheuermann kyphosis, multivariate analysis showed that intraoperative blood loss/blood volume also increased significantly when the patient was male and with a greater number of levels fused. CONCLUSIONS: There is an inverse relationship between the proportion of blood volume lost during deformity correction surgery and size in patients with adolescent idiopathic scoliosis, cerebral palsy, or Scheuermann kyphosis.

LEVEL OF EVIDENCE: Prognostic Level IV.



PMID: 25788308 [PubMed - in process]

**2. J Bone Joint Surg Am. 2015 Mar 18;97(6):500-6. doi: 10.2106/JBJS.N.00676.**

**Long-term results and outcome predictors in one-stage hip reconstruction in children with cerebral palsy.**

Rutz E1, Vavken P2, Camathias C1, Haase C1, Jünemann S1, Brunner R1.

BACKGROUND: One-stage hip reconstruction is the gold standard for treatment of hip displacement in children with cerebral palsy. The aims of this study were (1) to report the subjective clinical, objective clinical, and radiographic outcomes; and (2) to investigate outcome predictors, including the influence of the following risk factors: femoral head shape, migration percentage, direction of migration, and age at surgery. METHODS: We reviewed 168 hip reconstructions (eighty-two right, eighty-six left) in 121 patients (101 male, twenty female) at a mean follow-up of 7.3 ± 4.6 years (range, four to eighteen years). Surgical outcomes were assessed on the basis of the pain intensity and frequency (measured on 10-point visual analog scales) as well as GMFCS (Gross Motor Function Classification System) and MCPHCS (Melbourne Cerebral Palsy Hip Classification System) scores and postoperative migration percentage. The effects of femoral head shape, preoperative migration percentage, direction of migration, and age at surgery on surgical outcome were assessed by multivariate regression adjusting for potential confounders including sex, triradiate cartilage status, type of cerebral palsy, and surgical technique. RESULTS: Pain intensity and frequency were reduced significantly. Preoperative femoral head shape had no significant effect on the changes in pain, MCPHCS grade, and GMFCS level. The preoperative migration percentage was the most influential risk factor with respect to postoperative outcome. Age at surgery had no effect on the changes in pain score and GMFCS level. The overall surgical complication rate was 10.5%. CONCLUSIONS: Our data on 168 hip reconstructions at a mean follow-up of seven years showed significant and clinically meaningful improvements in pain intensity and frequency as well as in clinical scores and hip coverage. Analysis of potential risk factors showed only the preoperative migration percentage to have a relevant influence on outcomes.

LEVEL OF EVIDENCE: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.



PMID: 25788307 [PubMed - in process]

**3. J Pediatr Orthop. 2015 Mar 12. [Epub ahead of print]**

**Acetabular Remodeling After a Varus Derotational Osteotomy in Children With Cerebral Palsy.**

Chang FM1, Ma J, Pan Z, Ingram JD, Novais EN.

BACKGROUND: The optimal surgical intervention for hip dysplasia in cerebral palsy (CP) is controversial. The purpose of this study was to determine (1) whether an isolated varus derotation osteotomy (VDRO) for the treatment of CP hip dysplasia allows for acetabular remodeling as measured by acetabular depth ratio (ADR), (2) the predictive factors for acetabular remodeling after an isolated VDRO for the treatment of CP hip dysplasia, and (3) to establish the normal ADR in typical children for comparison. METHODS: Eighty-seven CP patients (174 hips) treated with an isolated VDRO between 2003 and 2009 were retrospectively reviewed. The average age at surgery was 4.6 years (range, 2.4 to 10.6 y) and the average follow-up period was 5.1 years (range, 1.1 to 9.9 y). Acetabular remodeling was assessed on radiographs by the ADR. Changes in preoperative and postoperative ADR were analyzed using linear mixed-effects models. Patients were divided into 2 different groups for the postoperative ADR analysis: Gross Motor Function Classification System (GMFCS) levels I, II, and III compared with GMFCS levels IV and V. The progression of ADR versus age was determined in a set of 917 normal children (1834 hips) for comparison. RESULTS: There was a statistically significant increase (improvement) in ADR postsurgically for the collective CP set ($P<0.001$) and for both GMFCS categories (I/II/III, IV/V: $P<0.001$). GMFCS level, sex, and intraoperative neck shaft angle (NSA) were determined to be significant predictors for postoperative ADR improvement. GMFCS level was the most significant predictor for an increase in ADR after surgery ($P<0.001$). Less improvement in ADR was observed in patients of GMFCS levels IV and V compared with patients of GMFCS levels I, II, and III ($P<0.001$). A lower intraoperative NSA resulted in greater postoperative increase in ADR ($P<0.05$). CONCLUSIONS: Overall, isolated VDRO allowed for acetabular remodeling in CP hip dysplasia. Acetabular remodeling was increased in patients of GMFCS levels I, II, and III compared with patients of GMFCS levels IV and V. Increased varization at the time of VDRO improved acetabular remodeling. This study recommends considering

GMFCS level and intraoperative NSA during surgical planning for CP hip dysplasia.

LEVEL OF EVIDENCE: Level IV-retrospective study.

PMID: 25785594 [PubMed - as supplied by publisher]

**4. J Pediatr Orthop B. 2015 Mar 19. [Epub ahead of print]**

**Distal femoral derotational osteotomy with external fixation for correction of excessive femoral anteversion in patients with cerebral palsy.**

Skiak E1, Karakasli A, Basci O, Satoglu IS, Ertem F, Havitcioglu H.

Patients with cerebral palsy (CP) disorder often develop rotational hip deformity. Increasing deformities impair already diminished walking abilities; femoral osteotomies are often performed to maintain and improve walking abilities. Fixation of osteotomies with condylar plates has been used successfully, but does not often enable immediate postoperative full weight-bearing. To avoid considerable postoperative rehabilitation deficit and additional bone loss because of inactivity, a postoperative treatment with full weight-bearing, is therefore, desirable. Self-tapping Schanz screws with a unilateral external fixator crossing the knee joint providing stronger anchoring in osteopenic bone might fulfill these demands. A retrospective study was carried out on 27 ambulatory CP patients, mean age 17.5 years (range 9-22 years); 11 patients with bilateral severe intoeing deformities underwent a supracondylar femoral osteotomy between September 2008 and April 2012. All patients were allowed to bear their full weight postoperatively. The aim of this study was to describe the technique, the results of this technique, to evaluate the time required for bone healing, and the type of complications associated with a distal derotational femoral osteotomy fixed with a uniaxial external fixator crossing the knee joint. A total of 27 patients were studied [mean weight 48.8 kg (range 29.8-75 kg)]. The mean preoperative rotation included internal rotation of 69° and external rotation of 17°. All patients were evaluated clinically and radiographically for a minimum of 1 year after surgery. There was a significant decrease in the mean medial rotation from 69° to 32° (P=0.00034). The lateral rotation increased significantly from preoperative 17° to postoperative 45° (P=0.0011). The femoral anteversion decreased significantly from a mean of 55° preoperatively to a mean 17° postoperatively (P=0.030). All patients, except one, achieved solid fusion uneventfully. One patient was a 16-year-old female who had sustained a knee flexion contracture of 30° because of a delay in the physiotherapy program. One 13-year-old female patient with a bilateral osteotomy had a nondisplaced fracture in her right femur after a direct trauma 2 weeks after removal of an external fixator, and was treated by a cast. Another 17-year-old male patient developed a nonunion because of loosening of two pins and achieved solid union after revision by dynamic compression plate plating. Besides four cases with superficial pin-tract infection, no other complications were documented. Minimally invasive supracondylar femoral derotational osteotomy fixed with a unilateral external fixators crossing the knee joint is a reliable procedure in CP patients. Most patients can be treated with early postoperative full weight-bearing. However, removal of the knee joint crossing fixator should be performed as early as possible to achieve a full range of motion.

PMID: 25794115 [PubMed - as supplied by publisher]

**5. J Child Orthop. 2015 Mar 19. [Epub ahead of print]**

**A functional electrical stimulation system improves knee control in crouch gait.**

Khamis S1, Martikaro R, Wientroub S, Hemo Y, Hayek S.

BACKGROUND: Crouch gait is a major sagittal plane deviation in children diagnosed with cerebral palsy (CP). It is defined as a combination of excessive ankle dorsiflexion and knee and hip flexion throughout the stance phase. To the best of our knowledge, functional electrical stimulation (FES) has not been used to decrease the severity of crouch gait in CP subjects and assist in achieving lower limb extension. PURPOSE: To evaluate the short- and long -term effects of FES to the quadriceps muscles in preventing crouch gait and achieving ankle plantar flexion, knee and hip extension at the stance phase. METHODS: An 18-year-old boy diagnosed with CP diplegia [Gross Motor Function Classification System (GMFCS) level II] was evaluated. The NESS L300® Plus neuroprosthesis system provided electrical stimulation of the quadriceps muscle. A three-dimensional gait analysis was performed using an eight-camera system measuring gait kinematics and spatiotemporal parameters while the subject walked shod only,

with ground reaction ankle foot orthotics (GRAFOs) and using an FES device. RESULTS: Walking with the FES device showed an increase in the patient's knee extension at midstance and increased knee maximal extension at the stance phase. In addition, the patient was able to ascend and descend stairs with a "step-through" pattern immediately after adjusting the FES device. CONCLUSIONS: This report suggests that FES to the quadriceps muscles may affect knee extension at stance and decrease crouch gait, depending on the adequate passive range of motion of the hip, knee extension, and plantar flexion. Further studies are needed in order to validate these results.

PMID: 25786388 [PubMed - as supplied by publisher]

**6. J UOEH. 2015;37(1):11-5. doi: 10.7888/juoeh.37.11.**

**Stress fracture of the navicular bone in a patient with cerebral palsy: a case report.**

Yoshikawa M1, Nakanishi Y, Kawamura Y, Matsuo K, Saeki M, Wada F.

A 14-year-old girl with cerebral palsy (spastic diplegia) underwent examination due to a chief complaint of right foot pain, and was diagnosed with a stress fracture of the central one third of the navicular bone. The fracture was considered to have developed due to repeated loading on the navicular bone as a result of an equinus gait. Therefore, she underwent osteosynthesis and Achilles tendon lengthening to correct the equinus deformity. Following our review of the current literature, we did not identify any reports of stress fracture of the navicular bone in cerebral palsy. We believe that in cases where cerebral palsy patients with paralytic equinus complain of foot pain, the possibility of stress fracture of the navicular bone should be considered.

PMID: 25787097 [PubMed - in process] Free full text

**7. Joint Bone Spine. 2015 Mar 13. pii: S1297-319X(15)00024-X. doi: 10.1016/j.jbspin.2014.10.019. [Epub ahead of print]**

**A swollen thigh and knee pain in a cerebral palsy child - Scurvy.**

Agarwal A1, Shaharyar A2, Kumar A2, Bhat MS2.

PMID: 25776446 [PubMed - as supplied by publisher]

**8. PM R. 2015 Mar 11. pii: S1934-1482(15)00127-6. doi: 10.1016/j.pmrj.2015.03.005. [Epub ahead of print]**

**The efficacy of ankle-foot orthoses on improving the gait of children with diplegic cerebral palsy: a multiple outcome analysis.**

Ries AJ1, Novacheck TF2, Schwartz MH2.

BACKGROUND: Ankle-foot orthosis (AFO) prescriptions are common for patients diagnosed with cerebral palsy (CP). Typical treatment objectives are to improve ankle-foot function and enhance general gait quality. OBJECTIVE: Determine the effectiveness of AFOs for improving the gait of children with diplegic CP. DESIGN: Retrospective analysis. SETTING: Primary clinical care facility. PARTICIPANTS: Data for 601 visits from 378 individuals (age at visit: 9.8±3.8 (mean±SD) years) who wore either a solid (SAFO), hinged (HAFO), or posterior leaf spring (PLS) AFO design was used. Individuals had a diagnosis of diplegic CP, wore the same AFO design bilaterally, and had three dimensional gait analysis data collected while walking both barefoot and with AFOs during a single session. METHODS: Differences between walking with AFOs and walking barefoot were used as outcome measures. Statistical analysis consisted of paired t-tests and multivariate ANOVAs to determine significance, main effects, and interactions of AFO design, ambulation type (walking with/without assistive devices), and barefoot level on each outcome. Minimal clinically important differences (MCID) from the literature determined clinical significance. OUTCOME MEASURES: Gait Deviation Index (GDI), ankle Gait Variable Score (GVS), knee GVS, nondimensional (ND) speed, and ND step length. RESULTS: Only step length exhibited clinically meaningful improvements for the average AFO user. Changes in step length, speed, and GDI all were statistically significant ($p < .001$). Barefoot outcome levels were the most consistent influence on outcome changes. AFO design was shown

to effect changes in speed and ankle function while ambulation type was shown to affect GDI change. CONCLUSIONS: Current AFO prescription methodologies for children with CP result in consistent gait improvements for step length only. This study emphasizes the need to develop more effective AFO prescription algorithms in an effort to improve the efficacy of AFOs on general gait quality via optimizing patient selection or AFO design.



PMID: 25771349 [PubMed - as supplied by publisher]

**9. Brain Dev. 2015 Mar 10. pii: S0387-7604(15)00023-6. doi: 10.1016/j.braindev.2015.01.007. [Epub ahead of print]**

**Relationship between stature and tibial length for children with moderate-to-severe cerebral palsy.**

Kihara K1, Kawasaki Y2, Yagi M2, Takada S3.

OBJECTIVE: To derive the equation for estimating stature, based on tibial length, for children with moderate-to-severe cerebral palsy (CP) and lower limb joint contracture or scoliosis. METHODS: The participants (3-12-years-old) included 50 children with moderate-to-severe CP (mean age, 8.3±2.4years) and 38 typically developed (TD) children (mean age, 7.5±2.6years). Thirty-four (68%) of the children with CP had a gross motor function classification system level of V. Furthermore, 40 (80%) had definite lower limb joint contracture or scoliosis. The stature and the tibial length measurements of all participants were determined. Regression equations to estimate stature, based on tibial lengths, were determined for both TD children and children with CP. Moreover, regression equations defining the relationship between tibial length and age were compared between the two groups of children, using multiple regression analysis. RESULTS: The regression equations for estimating stature, based on tibial length, were stature=tibial length×3.25+34.45 [cm], R2=0.91 (TD children), and stature=tibial length×3.42+31.82 [cm], R2=0.81 (CP children). In children with CP, tibial lengths were significantly shorter than those in similarly aged TD children. CONCLUSION: The stature of children with moderate-to-severe CP can be estimated from their tibial lengths, regardless of the presence of joint contracture or scoliosis. The tibial length may be a proxy for estimating stature during the growth assessment of children with moderate-to-severe CP.



PMID: 25769408 [PubMed - as supplied by publisher]

**10. Stereotact Funct Neurosurg. 2015 Feb 27;93(2):133-139. [Epub ahead of print]**

**Chronic Spinal Cord Stimulation in the Treatment of Cerebral and Spinal Spasticity.**

Dekopov AV1, Shabalov VA, Tomsky AA, Hit MV, Salova EM.

OBJECTIVES: The aim of this investigation is to assess the effectiveness of spinal cord stimulation (SCS) in different groups of patients with spasticity of different origin. MATERIALS AND METHODS: A retrospective study of the use of the method of SCS in 71 patients. The patient population was divided into two groups: 52 cerebral palsy (CP) cases and 19 patients diagnosed with spasticity caused by spinal injury. The mean age was 7.14 ± 4.06 and 35.68 ± 12.42 years, respectively. The CP group included 41 cases of paraparesis and 11 cases tetraparesis. One quadripolar electrode was implanted into the posterior epidural space at Th10-Th12 level and an implantable pulse generator (Itrel3, Medtronic) was placed in a standard fashion. We performed 3-5 stimulation sessions per day; each lasted 30 min. The stimulation parameters were as follows: rate 100-130 Hz, pulse width 120-300 ms, amplitude 1.5-4 V. The follow-up ranged from 2 to 9 years. RESULTS: Decrease in muscle tone was observed in all cases in the group of patients with spinal spasticity: from 3.71 ± 0.61 on the Ashworth scale before the operation to 2.26 ± 0.56 after the operation ($p < 0.001$). In the group of cerebral spasticity a significant decrease in muscle tone was observed only in patients with spastic lower paraparesis: from 3.36 ± 0.41 before the operation to 1.97 ± 0.91 after the operation ($p < 0.005$). In patients with spastic tetraparesis we did not observe any significant change in muscle tone. In 8 cases we discontinued the therapy several years after the procedure due to improvement in spasticity: in the CP group in 7 cases and in 1 spinal spasticity case, where SCS systems were explanted.

CONCLUSION: Chronic SCS may be a method of choice for patients with moderate spinal and cerebral spasticity with predominant spastic lower paraparesis. In patients with spastic tetraparesis SCS therapy did not prove to be effective. We encountered improvement of the spasticity and no need for further SCS therapy in a small group of patients (11%). This phenomenon requires further investigation.



PMID: 25765082 [PubMed - as supplied by publisher]

**11. J Child Neurol. 2015 Mar 19. pii: 0883073815575369. [Epub ahead of print]**

**Multiday Transcranial Direct Current Stimulation Causes Clinically Insignificant Changes in Childhood Dystonia: A Pilot Study.**

Bhanpuri NH1, Bertucco M1, Young SJ1, Lee AA1, Sanger TD2.

Abnormal motor cortex activity is common in dystonia. Cathodal transcranial direct current stimulation may alter cortical activity by decreasing excitability while anodal stimulation may increase motor learning. Previous results showed that a single session of cathodal transcranial direct current stimulation can improve symptoms in childhood dystonia. Here we performed a 5-day, sham-controlled, double-blind, crossover study, where we measured tracking and muscle overflow in a myocontrol-based task. We applied cathodal and anodal transcranial direct current stimulation (2 mA, 9 minutes per day). For cathodal transcranial direct current stimulation (7 participants), 3 subjects showed improvements whereas 2 showed worsening in overflow or tracking error. The effect size was small (about 1% of maximum voluntary contraction) and not clinically meaningful. For anodal transcranial direct current stimulation (6 participants), none showed improvement, whereas 5 showed worsening. Thus, multiday cathodal transcranial direct current stimulation reduced symptoms in some children but not to a clinically meaningful extent, whereas anodal transcranial direct current stimulation worsened symptoms. Our results do not support transcranial direct current stimulation as clinically viable for treating childhood dystonia.



PMID: 25792428 [PubMed - as supplied by publisher]

**12. Stem Cells Int. 2015;2015:905874. doi: 10.1155/2015/905874. Epub 2015 Feb 18.**

**A clinical study of autologous bone marrow mononuclear cells for cerebral palsy patients: a new frontier**.

Sharma A1, Sane H2, Gokulchandran N1, Kulkarni P2, Gandhi S3, Sundaram J3, Paranjape A3, Shetty A3, Bhagwanani K2, Biju H3, Badhe P1.

Cerebral palsy is a nonprogressive heterogeneous group of neurological disorders with a growing rate of prevalence. Recently, cellular therapy is emerging as a potential novel treatment strategy for cerebral palsy. The various mechanisms by which cellular therapy works include neuroprotection, immunomodulation, neurorestoration, and neurogenesis. We conducted an open label, nonrandomized study on 40 cases of cerebral palsy with an aim of evaluating the benefit of cellular therapy in combination with rehabilitation. These cases were administered autologous bone marrow mononuclear cells intrathecally. The follow-up was carried out at 1 week, 3 months, and 6 months after the intervention. Adverse events of the treatment were also monitored in this duration. Overall, at six months, 95% of patients showed improvements. The study population was further divided into diplegic, quadriplegic, and miscellaneous group of cerebral palsy. On statistical analysis, a significant association was established between the symptomatic improvements and cell therapy in diplegic and quadriplegic cerebral palsy. PET-CT scan done in 6 patients showed metabolic improvements in areas of the brain correlating to clinical improvements. The results of this study demonstrate that cellular therapy may accelerate the development, reduce disability, and improve the quality of life of patients with cerebral palsy.

PMID: 25788947 [PubMed] PMCID: PMC4348592 Free PMC Article

**13. Cytotherapy. 2015 Mar 17. pii: S1465-3249(15)00074-2. doi: 10.1016/j.jcyt.2015.02.010. [Epub ahead of print]**

**Human allogeneic AB0/Rh-identical umbilical cord blood cells in the treatment of juvenile patients with cerebral palsy.**

Romanov YA1, Tarakanov OP2, Radaev SM2, Dugina TN2, Ryaskina SS2, Darevskaya AN2, Morozova YV2, Khachatryan WA3, Lebedev KE3, Zotova NS4, Burkova AS4, Sukhikh GT4, Smirnov VN5.

BACKGROUND AIMS: The term "cerebral palsy" (CP) encompasses many syndromes that emerge from brain damage at early stages of ontogenesis and manifest as the inability to retain a normal body position or perform controlled movements. Existing methods of CP treatment, including various rehabilitation strategies and surgical and pharmacological interventions, are mostly palliative, and there is no specific therapy focused on restoring injured brain function. METHODS: During a post-registration clinical investigation, the safety and efficacy of intravenous infusion of allogeneic human leukocyte antigen (HLA)-unmatched umbilical cord blood (UCB) cells were studied in 80 pediatric patients with cerebral palsy and associated neurological complications. Patients received up to 6 intravenous infusions of AB0/Rh-identical, red blood cell-depleted UCB cells at an average dose of 250 × 106 viable cells per infusion. RESULTS: Patients were followed for 3-36 months, and multiple cell infusions did not cause any adverse effects. In contrast, in most patients who received four or more UCB cell infusions, positive dynamics related to significant improvements in neurological status and/or cognitive functions were observed. CONCLUSIONS: The results confirm that multiple intravenous infusions of allogeneic AB0/Rh-identical UCB cells may be a safe and effective procedure and could be included in treatment and rehabilitation programs for juvenile patients with cerebral palsy.



PMID: 25791070 [PubMed - as supplied by publisher]

**14. BMC Anesthesiol. 2015 Mar 15;15:34. doi: 10.1186/s12871-015-0006-z. eCollection 2015.**

**Required propofol dose for anesthesia and time to emerge are affected by the use of antiepileptics: prospective cohort study.**

Ouchi K1, Sugiyama K1.

BACKGROUND: We investigated the impact of the type of neurological disorder on the required propofol dose for anesthesia and the time to emerge from anesthesia during dental treatment in patients with autism (AU), cerebral palsy (CP), and intellectual disability (ID), some of whom also had epilepsy. METHODS: We studied 224 patients with a neurological disorder who underwent dental treatment under intravenous general anesthesia. Patients were categorized according to neurological disorder (AU, CP, and ID; and with or without an antiepileptic). The propofol dose required for anesthesia, time to emerge, and modeled propofol blood concentration at emergence were evaluated. RESULTS: In patients not given an antiepileptic, we found no significant differences in the propofol dose, modeled propofol blood concentration at emergence, or time to emerge among patients with AU, CP, and ID ($P > 0.05$). When using an antiepileptic, the dose of propofol (5.7 ± 1.51 mg/kg/h) was significantly lower than without an antiepileptic (6.8 ± 1.27 mg/kg/h) ($P < 0.0001$). The modeled propofol blood concentration at emergence in patients given an antiepileptic (0.5 ± 0.03 μg/ml) was significantly lower than without an antiepileptic (0.7 ± 0.02 μg/ml) ($P < 0.0001$). The time to emerge in patients given an antiepileptic (29.5 ± 12.5 min) was significantly longer than without an antiepileptic (21.6 min ± 10.0 min) ($P < 0.0001$). CONCLUSION: The propofol dose required for anesthesia and the time to emerge from anesthesia are not affected by the type of neurological disorder, but are affected by antiepileptic use.

TRIAL REGISTRATION: University Hospital Medical Information Network Clinical Trials Registry (UMIN000014179), Date of registration 4 June 2014.

PMID: 25788855 [PubMed - in process] PMCID: PMC4364571 Free PMC Article

**15. Cochrane Database Syst Rev. 2015 Mar 13;3:CD010750. [Epub ahead of print]**

**Pharmacological interventions for pain in children and adolescents with life-limiting conditions.**

Beecham E1, Candy B, Howard R, McCulloch R, Laddie J, Rees H, Vickerstaff V, Bluebond-Langner M, Jones L.

BACKGROUND: Pain is one of the most common symptoms in children and young people (CYP) with life-limiting conditions (LLCs) which include a wide range of diagnoses including cancer. The current literature indicates that pain is not well managed, however the evidence base to guide clinicians is limited. There is a clear need for evidence from a systematic review to inform prescribing. OBJECTIVES: To evaluate the evidence on the effectiveness of different pharmacological interventions used for pain in CYP with LLCs. SEARCH METHODS: The following electronic databases were searched up to December 2014: CENTRAL (in the Cochrane Library), MEDLINE, EMBASE, PsycINFO and CINAHL. In addition, we searched conference proceedings and reference lists of included studies. For completeness, we also contacted experts in the field. No language restrictions were applied. SELECTION CRITERIA:Randomised controlled trials (RCTs), quasi-randomised studies and other studies that included a clearly defined comparator group were included. The studies investigated pharmacological treatents for pain associated with LLCs in CYP. The treatment included those specifically developed to treat pain and those that acted as an adjuvant, where the treatment was not primarily developed to treat pain but has pain relieving properties. The LLC was identified by its inclusion in the Richard Hain Directory of LLCs. DATA COLLECTION AND ANALYSIS: Citations were screened by five review authors. Data were extracted by one review author and checked by a second. Two review authors assessed the risk of bias of included studies. A sufficient number of studies using homogeneous outcomes was not identified so a meta-analysis was not possible. MAIN RESULTS: We identified 24,704 citations from our database search. Nine trials with 379 participants fulfilled our inclusion criteria. Participants had cerebral palsy (CP) in five of the studies and osteogenesis imperfecta (OI) in the other four. Participants across the trials ranged in age from 2 to 19 years. All studies, apart from one cross-over trial, were parallel designed RCTs. Three of the trials on CP evaluated intrathecal baclofen (ITB) and two botulinum toxin A (BoNT-A). All of the OI trials evaluated the use of bisphosphonates (two alendronate and one pamidronate). No trials were identified that evaluated a commonly used analgesic in this patient group. Pain was a secondary outcome in five of the eight identified studies. Overall the quality of the trials was mixed. Only one study involved over 100 participants.For the two ITB studies for pain in CP, in the same study population but assessed at different time points in their disease, both found an effect on pain favouring the intervention compared to the control group (standard care or placebo) (mean difference (MD) 4.20, 95% confidence interval (CI) 2.15 to 6.25; MD 26.60, 95% CI 2.61 to 50.59, respectively). In these studies most of the adverse events related to the procedure or device for administration rather than the drug, such as swelling at the pump site. In one trial there were also eight serious adverse effects; these included difficulty swallowing and an epileptic seizure. The trial did not state if these occurred in the intervention group. At follow-up in both BoNT-A trials there was no evidence of a difference in pain between the trial arms among CP participants. The adverse events in the BoNT-A trials mostly involved those who received the intervention drug and involved seizures. Gastrointestinal problems were the most frequent adverse event in those who received alendronate. The trial investigating pamidronate found no evidence of a difference in pain compared to the control group. No adverse events were reported in this trial. AUTHORS' CONCLUSIONS: Published, controlled evidence on the pharmacological interventions for pain in CYP with LLCs is limited. The evidence that is currently available evaluated pain largely as a secondary outcome and the drugs used were all adjuvants and not always commonly used in general paediatric palliative care for pain. Based on current data this systematic review is unable to determine the effects of pharmacological interventions for pain for CYP with LLCs. Future trials with larger populations should examine the effects of the drugs commonly used as analgesics; with the rising prevalence of many LLCs this becomes more necessary.

PMID: 25768935 [PubMed - as supplied by publisher]

**16. Strabismus. 2015 Mar 19:1-6. [Epub ahead of print]**

**Clinical Outcomes of Botulinum Toxin Injection in Patients with Cerebral Palsy and Esotropia.**

Ameri A1, Mirmohammadsadeghi A, Makateb A, Bazvand F, Hosseini S.

PURPOSE: To assess the efficacy of botulinum toxin (Novotox) injection in patients with cerebral palsy (CP) and esotropia. PATIENTS AND METHODS: In a non-comparative, prospective interventional case series botulinum toxin injection was done in 44 patients with CP and esotropia. A single dose of botulinum toxin was injected in both medial rectus muscles of all patients and was repeate in 12 patients. Angle of deviation within 10 prism diopters

(PD) of orthotropia was defined as a successful outcome. RESULT: Forty-four patients (21 males) with the mean age of 47.56 ± 35.86 months were included in the study. The mean esotropia in all patients was 52.27 ± 18.40 PD (25-123 PD). The range of follow-up was 12-24 months. Thirty patients (68.18%) were treated successfully one year after surgery. The rates of success, consecutive exotropia, and residual esotropia were 61.4%, 13.63%, and 25% in the last follow-up, respectively. The logistic regression showed statistically significant results between success result and lower age, higher pre-injection deviation, one month post-injection deviation, and severe ptosis. Complications included subconjunctival hemorrhage and ptosis. CONCLUSION: Botulinum toxin injection is reasonably less invasive with light anesthesia, scar free, and a therapeutic alternative for the patient with esotropia and CP. Therefore, it can provide more possible surgical options in future.

PMID: 25789846 [PubMed - as supplied by publisher]

**17. BMC Pediatr. 2015 Dec;15(1):323. doi: 10.1186/s12887-015-0323-x. Epub 2015 Feb 13.**

**Scoping review of patient- and family-oriented outcomes and measures for chronic pediatric disease.**

Khangura SD1, Karaceper MD, Trakadis Y, Mitchell JJ, Chakraborty P, Tingley K, Coyle D, Grosse SD, Kronick JB, Laberge AM, Little J, Prasad C, Sikora L, Siriwardena K, Sparkes R, Speechley KN, Stockler S, Wilson BJ, Wilson K, Zayed R, Potter BK; Canadian Inherited Metabolic Diseases Research Network (CIMDRN).

BACKGROUND: Improvements in health care for children with chronic diseases must be informed by research that emphasizes outcomes of importance to patients and families. To support a program of research in the field of rare inborn errors of metabolism (IEM), we conducted a broad scoping review of primary studies that: (i) focused on chronic pediatric diseases similar to IEM in etiology or manifestations and in complexity of management; (ii) reported patient- and/or family-oriented outcomes; and (iii) measured these outcomes using self-administered tools. METHODS: We developed a comprehensive review protocol and implemented an electronic search strategy to identify relevant citations in Medline, EMBASE, DARE and Cochrane. Two reviewers applied pre-specified criteria to titles/s using a liberal accelerated approach. Articles eligible for full-text review were screened by two independent reviewers with discrepancies resolved by consensus. One researcher ed data on study characteristics, patient- and family-oriented outcomes, and self-administered measures. Data were validated by a second researcher. RESULTS: 4,118 citations were screened with 304 articles included. Across all included reports, the most-represented diseases were diabetes (35%), cerebral palsy (23%) and epilepsy (18%). We identified 43 unique patient- and family-oriented outcomes from among five emergent domains, with mental health outcomes appearing most frequently. The studies reported the use of 405 independent self-administered measures of these outcomes. CONCLUSIONS: Patient- and family-oriented research investigating chronic pediatric diseases emphasizes mental health and appears to be relatively well-developed in the diabetes literature. Future research can build on this foundation while identifying additional outcomes that are priorities for patients and families.

PMID: 25777594 [PubMed - in process] PMCID: PMC4334411 Free PMC Article

**18. Iran J Child Neurol. 2015 Winter;9(1):76-86.**

**Psychometric properties of the Persian version of cerebral palsy quality of life questionnaire for children.**

Soleimani F1, Vameghi R1, Kazemnejad A2, Akbar Fahimi N3, Nobakht Z3, Rassafiani M1.

OBJECTIVE: Cerebral palsy (CP) is the most common cause of chronic disability that restricts participation in daily life for children. Thereby, it is comprised of quality of life. Quality of life (QOL) measures have been a vital part of health outcome appraisals for individuals with CP and to obtain empirical evidence for the effectiveness of a range of interventions. The CP QOL-Child is a condition-specific QOL questionnaire designed for children with CP to assess well-being rather than ill-being. MATERIALS & METHODS: Forward and backward translations of the CP QOL-Child were performed for: (1) the primary caregiver form (for parents of children with CP aged 4-12 years); and (2) the child self-report form (for children with cerebral palsy aged 9-12 years). Psychometric properties assessment included reliability, internal consistency, and item discrimination, construct validity with Gross Motor Function Classification System (GMFCS) and Manual Ability Classification System (MACS) was done. SPSS was used to analyze the results of this study. RESULTS: A sample of 200 primary caregivers forchildren with CP (mean = 7.7 years) and 40 children (mean = 10.2 years) completed. Internal consistency ranged from 0.61-0.87 for the primary caregivers form, and 0.64-0.86 for the child self-report form. Reliability ranged from 0.47-0.84. Item

discrimination analysis revealed that a majority of the items (80%) have high discriminating power. Confirmatory factor analysis demonstrated a distinguishable domain structure as in the original English version. Moderate associations were found between lower QOL and more severe motor disability(GMFCS; r = .18-.32; p < .05 and MACS; r= .13 - .40; p < .05). The highest correlation between the primary caregiver and child forms on QOL was in the domain of functioning and consistent with the English version. ONCLUSION: Content validity, item discriminant validity, internal consistency, and test-retest reliability of the Persian version of the CP QOL- Child were all acceptable. Further study of concurrent validity of this version is needed.

PMID: 25767543 [PubMed] PMCID: PMC4322503 [Available on 2015-04-01]

**19. Implement Sci. 2015 Dec;10(1):202. doi: 10.1186/s13012-014-0202-0. Epub 2015 Feb 6.**

**Improving allied health professionals' research implementation behaviours for children with cerebral palsy: protocol for a before-after study.**

Imms C1, Novak I, Kerr C, Shields N, Randall M, Harvey A, Graham HK, Reddihough D.

BACKGROUND: Cerebral palsy is a permanent disorder of posture and movement caused by disturbances in the developing brain. It affects approximately 1 in every 500 children in developed countries and is the most common form of childhood physical disability. People with cerebral palsy may also have problems with speech, vision and hearing, intellectual difficulties and epilepsy. Health and therapy services are frequently required throughout life, and this care should be effective and evidence informed; however, accessing and adopting new research findings into day-to-day clinical practice is often delayed. METHODS/DESIGN: This 3-year study employs a before and after design to evaluate if a multi-strategy intervention can improve research implementation among allied health professionals (AHPs) who work with children and young people with cerebral palsy and to establish if children's health outcomes can be improved by routine clinical assessment. The intervention comprises (1) knowledge brokering with AHPs, (2) access to an online research evidence library, (3) provision of negotiated evidence-based training and education, and (4) routine use of evidence-based measures with children and young people aged 3-18 years with cerebral palsy. The study is being implemented in four organisations, with a fifth organisation acting as a comparison site, across four Australian states. Effectiveness will be assessed using questionnaires completed by AHPs at baseline, 6, 12 and 24 months, and by monitoring the extent of use of evidence-based measures. Children's health outcomes will be evaluated by longitudinal analyses. DISCUSSION: Government, policy makers and service providers all seek evidence-based information to support decision-making about how to distribute scarce resources, and families are seeking information to support intervention choices. This study will provide knowledge about what constitutes an efficient, evidence-informed service and which allied health interventions are implemented for children with cerebral palsy.

TRIAL REGISTRATION: Trial is not a controlled healthcare intervention and is not registered.

PMID: 25776773 [PubMed - in process] PMCID: PMC4328993 Free PMC Article

# Prevention and Cure

**20. Int J Clin Exp Med. 2015 Jan 15;8(1):1101-7. eCollection 2015.**

**99mTc-ECD brain perfusion SPECT imaging for the assessment of brain perfusion in cerebral palsy (CP) patients with evaluation of the effect of hyperbaric oxygen therapy.**

Asl MT1, Yousefi F2, Nemati R2, Assadi M3.

OBJECTIVE: The present study was carried out to evaluate cerebral perfusion in different types of cerebral palsy (CP) patients. For those patients who underwent hyperbaric oxygen therapy, brain perfusion before and after the therapy was compared. METHODS: A total of 11 CP patients were enrolled in this study, of which 4 patients underwent oxygen therapy. Before oxygen therapy and at the end of 40 sessions of oxygen treatment, 99mTc-ECD brain perfusion single photon emission computed tomography (SPECT) was performed, and the results were compared. RESULTS: A total of 11 CP patients, 7 females and 4 males with an age range of 5-27 years

participated in the study. In brain SPECT studies, all the patients showed perfusion impairments. The region most significantly involved was the frontal lobe (54.54%), followed by the temporal lobe (27.27%), the occipital lobe (18.18%), the visual cortex (18.18%), the basal ganglia (9.09%), the parietal lobe (9.09%), and the cerebellum (9.09%). Frontal-lobe hypoperfusion was seen in all types of cerebral palsy. Two out of 4 patients (2 males and 2 females) who underwent oxygen therapy revealed certain degree of brain perfusion improvement. CONCLUSION: This study demonstrated decreased cerebral perfusion in different types of CP patients. The study also showed that hyperbaric oxygen therapy improved cerebral perfusion in a few CP patients. However, it could keep the physiological discussion open and strenghten a link with other areas of neurology in which this approach may have some value.

PMID: 25785099 [PubMed] PMCID: PMC4358554 Free PMC Article

**21. Arch Dis Child. 2015 Mar 17. pii: archdischild-2014-307695. doi: 10.1136/archdischild-2014-307695. [Epub ahead of print]**

**Predicting severe motor impairment in preterm children at age 5 years.**

Synnes A1, Anderson PJ2, Grunau RE1, Dewey D3, Moddemann D4, Tin W5, Davis PG6, Doyle LW2, Foster G7, Khairy M8, Nwaesei C9, Schmidt B10; CAP Trial Investigator group.

OBJECTIVE: To determine whether the ability to predict severe motor impairment at age 5 years improves between birth and 18 months. DESIGN: Ancillary study of the Caffeine for Apnea of Prematurity Trial. SETTING AND PATIENTS: International cohort of very low birth weight children who were assessed sequentially from birth to 5 years. OUTCOME MEASURES: Severe motor impairment was defined as a score <5th percentile on the Movement Assessment Battery of Children (MABC), or inability to complete the MABC because of cerebral palsy. Multivariable logistic regression cumulative risk models used four sets of predictor variables: early neonatal risk factors, risk factors at 36 weeks' postmenstrual age, risk factors at a corrected age of 18 months, and sociodemographic variables. A receiver operating characteristic curve (ROC) was generated for each model, and the four ROC curves were compared to determine if the addition of the new set of predictors significantly increased the area under the curve (AUC). RESULTS: Of 1469 children, 291 (19.8%) had a severe motor impairment at 5 years. The AUC increased from 0.650 soon after birth, to 0.718 ($p<0.001$) at 36 weeks' postmenstrual age, and to 0.797 at 18 months ($p<0.001$). Sociodemographic variables did not significantly improve the AUC (AUC=0.806; $p=0.07$). CONCLUSIONS: Prediction of severe motor impairment at 5 years of age using a cumulative risk model improves significantly from birth to 18 months of age in children with birth weights between 500 g and 1250 g.

TRIAL REGISTRATION NUMBER: ClinicalTrials.gov number NCT00182312.



PMID: 25784749 [PubMed - as supplied by publisher]

**22. Cochrane Database Syst Rev. 2015 Mar 19;3:CD000104. [Epub ahead of print]**

**Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants.**

Cools F1, Offringa M, Askie LM.

BACKGROUND: Respiratory failure due to lung immaturity is a major cause of mortality in preterm infants. Although the use of intermittent positive pressure ventilation (IPPV) in neonates with respiratory failure saves lives, its use is associated with lung injury and chronic lung disease. A newer form of ventilation called high frequency oscillatory ventilation has been shown in experimental studies to result in less lung injury. OBJECTIVES: The objective of this review was to determine the effect of the elective use of high frequency oscillatory ventilation (HFOV) as compared to conventional ventilation (CV) on the incidence of chronic lung disease (CLD), mortality and other complications associated with prematurity and assisted ventilation in preterm infants who were mechanically ventilated for respiratory distress syndrome (RDS). SEARCH METHODS: Searches were made of the Oxford Database of Perinatal Trials, MEDLINE, EMBASE, previous reviews including cross references, s, conference and

symposia proceedings; and from expert informants and handsearching of journals by The Cochrane Collaboration, mainly in the English language. The search was updated in January 2009 and again in November 2014. SELECTION CRITERIA: Randomised controlled trials comparing HFOV and CV in preterm or low birth weight infants with pulmonary dysfunction, mainly due to RDS, who required assisted ventilation. Randomisation and commencement of treatment needed to be as soon as possible after the start of CV and usually in the first 12 hours of life. DATA COLLECTION AND ANALYSIS: The methodological quality of each trial was independently reviewed by the review authors. The standard effect measures were relative risk (RR) and risk difference (RD). From 1/RD the number needed to benefit (NNTB) to produce one outcome was calculated. For all measures of effect, 95% confidence intervals (CIs) were used. For interpretation of subgroup analyses, a P value for subgroup differences as well as the I2 statistic for between-subgroup heterogeneity were calculated. Meta-analysis was performed using both a fixed-effect and a random-effects model. Where heterogeneity was over 50%, the random-effects model RR was also reported. MAIN RESULTS: Nineteen eligible studies involving 4096 infants were included. Meta-analysis comparing HFOV with CV revealed no evidence of effect on mortality at 28 to 30 days of age or at approximately term equivalent age. These results were consistent across studies and in subgroup analyses. The risk of CLD in survivors at term equivalent gestational age was significantly reduced with the use of HFOV but this effect was inconsistent across studies, even after the meta-analysis was restricted to studies that applied a high lung volume strategy with HFOV. Subgroup analysis by HFOV strategy showed a similar effect in trials with a more strict lung volume recruitment strategy, targeting a very low fraction of inspired oxygen (FiO2), and trials with a less strict lung volume recruitment strategy and with a somewhat higher or unspecified target FiO2. Subgroup analyses by age at randomisation, routine surfactant use or not, type of high frequency ventilator (oscillator versus flow interrupter), inspiratory to expiratory (I:E) ratio of high frequency ventilator (1:1 versus 1:2) and CV strategy (lung protective or not) could not sufficiently explain the heterogeneity. Pulmonary air leaks, defined as gross air leaks or pulmonary interstitial emphysema, occurred more frequently in the HFOV group, whereas the risk of severe retinopathy of prematurity was significantly reduced. Although in some studies an increased risk of severe grade intracranial haemorrhage and periventricular leukomalacia was found, the overall meta-analysis revealed no significant differences in effect between HFOV and CV. The short-term neurological morbidity with HFOV was only found in the subgroup of two trials not using a high volume strategy with HFOV. Most trials did not find a significant difference in long-term neurodevelopmental outcome, although one recent trial showed a significant reduction in the risk of cerebral palsy and poor mental development. AUTHORS' CONCLUSIONS: There is evidence that the use of elective HFOV compared with CV results in a small reduction in the risk of CLD, but the evidence is weakened by the inconsistency of this effect across trials. Probably many factors, both related to the intervention itself as well as to the individual patient, interact in complex ways. In addition, the benefit could be counteracted by an increased risk of acute air leak. Adverse effects on short-term neurological outcomes have been observed in some studies but these effects are not significant overall. Most trials reporting long-term outcome have not identified any difference.

PMID: 25785789 [PubMed - as supplied by publisher]

**23. Dev Neurosci. 2015 Mar 17. [Epub ahead of print]**

**Human Umbilical Cord Blood Cells Ameliorate Motor Deficits in Rabbits in a Cerebral Palsy Model.**

Drobyshevsky A1, Cotten CM, Shi Z, Luo K, Jiang R, Derrick M, Tracy ET, Gentry T, Goldberg RN, Kurtzberg J, Tan S.

Cerebral palsy (CP) has a significant impact on both patients and society, but therapy is limited. Human umbilical cord blood cells (HUCBC), containing various stem and progenitor cells, have been used to treat various brain genetic conditions. In small animal experiments, HUCBC have improved outcomes after hypoxic-ischemic (HI) injury. Clinical trials using HUCBC are underway, testing feasibility, safety and efficacy for neonatal injury as well as CP. We tested HUCBC therapy in a validated rabbit model of CP after acute changes secondary to HI injury had subsided. Following uterine ischemia at 70% gestation, we infused HUCBC into newborn rabbit kits with either mild or severe neurobehavioral changes. Infusion of high-dose HUCBC (5 × 106 cells) dramatically altered the natural history of the injury, alleviating the abnormal phenotype including posture, righting reflex, locomotion, tone, and dystonia. Half the high dose showed lesser but still significant improvement. The swimming test, however, showed that joint function did not restore to naïve control function in either group. Tracing HUCBC with either MRI biomarkers or PCR for human DNA found little penetration of HUCBC in the newborn brain in the immediate newborn period, suggesting that the beneficial effects were not due to cellular integration or direct proliferative effects but rather to paracrine signaling. This is the first study to show that HUCBC improve motor performance in a dose-dependent manner, perhaps by improving compensatory repair processes. © 2015 S. Karger AG, Basel.

PMID: 25791742 [PubMed - as supplied by publisher]

**24. Dev Neurosci. 2015 Feb 27. [Epub ahead of print]**

**Serial Plasma Metabolites Following Hypoxic-Ischemic Encephalopathy in a Nonhuman Primate Model.**

Chun PT1, McPherson RJ, Marney LC, Zangeneh SZ, Parsons BA, Shojaie A, Synovec RE, Juul SE.

Biomarkers that indicate the severity of hypoxic-ischemic brain injury and response to treatment and that predict neurodevelopmental outcomes are urgently needed to improve the care of affected neonates. We hypothesize that sequentially obtained plasma metabolomes will provide indicators of brain injury and repair, allowing for the prediction of neurodevelopmental outcomes. A total of 33 Macaca nemestrina underwent 0, 15 or 18 min of in utero umbilical cord occlusion (UCO) to induce hypoxic-ischemic encephalopathy and were then delivered by hysterotomy, resuscitated and stabilized. Serial blood samples were obtained at baseline (cord blood) and at 0.1, 24, 48, and 72 h of age. Treatment groups included nonasphyxiated controls (n = 7), untreated UCO (n = 11), UCO + hypothermia (HT; n = 6), and UCO + HT + erythropoietin (n = 9). Metabolites were extracted and analyzed using comprehensive two-dimensional gas chromatography coupled with time-of-flight mass spectrometry and quantified by PARAFAC (parallel factor analysis). Using nontargeted discovery-based methods, we identified 63 metabolites as potential biomarkers. The changes in metabolite concentrations were characterized and compared between treatment groups. Further comparison determined that 8 metabolites (arachidonic acid, butanoic acid, citric acid, fumaric acid, lactate, malate, propanoic acid, and succinic acid) correlated with early and/or long-term neurodevelopmental outcomes. The combined outcomes of death or cerebral palsy correlated with citric acid, fumaric acid, lactate, and propanoic acid. This change in circulating metabolome after UCO may reflect cellular metabolism and biochemical changes in response to the severity of brain injury and have potential to predict neurodevelopmental outcomes. 

PMID: 25765047 [PubMed - as supplied by publisher]

**25. Exp Ther Med. 2015 Apr;9(4):1336-1344. Epub 2015 Jan 27.**

**Clinical study of cerebral palsy in 408 children with periventricular leukomalacia.**

Shang Q1, Ma CY1, Lv N1, Lv ZL2, Yan YB3, Wu ZR1, Li JJ1, Duan JL1, Zhu CL4.

This study aimed to investigate the high risk factors, cerebral palsy (CP) subtypes and comorbidities of periventricular leukomalacia (PVL). Based on treatment conditions at a specialist hospital, a cross-sectional clinical study and retrospective analysis of computed tomography and magnetic resonance imaging examinations was conducted to evaluate the risk factors, subtypes and comorbidities of CP in children with PVL. Among the 408 children with PVL, 8.58% were born with a weight of ≤1,500 g and 44.36% were born with a weight of ≥2,500 g. In addition, 36.76% of these children had a gestational age of ≤32 weeks and 37.75% had a gestational age of ≥37 weeks. The proportion of the children born with various high risk factors was 95.59%, including perinatal infections and hypoxia. Severe PVL was observed in preterm infants (63.41% with a gestational age of <28 weeks and 21.95% with a gestational age of 28-30 weeks) and low-birth weight infants, which were prone to quadriplegia (43.90%). The common comorbidities included visual and auditory disorders, epilepsy, mental retardation and language barriers. Visual and auditory disorders (26.96%) were the most common comorbidities. PVL was identified primarily in premature and low-birth weight infants. The degree of PVL was found to be negatively correlated with gestational age and birth weight. The degree of PVL in the full-term infants correlated with exposure to infections or hypoxia. Quadriplegia is common among the various subtypes of CP. Visual and hearing disorders are the most common comorbidities of CP; these comorbidities occurred most frequently with quadriplegia.

PMID: 25780432 [PubMed] PMCID: PMC4353777 Free PMC Article

**26. Int J Clin Exp Med. 2015 Jan 15;8(1):737-43. eCollection 2015.**

**Apolipoprotein E knockout induced inflammatory responses related to microglia in neonatal mice brain via astrocytes.**

Liu Y1, Xu X2, Dou H3, Hua Y1, Xu J1, Hui X1.

More and more evidences suggestted that ApoE plays an important role in modulating the systemic and central nervous inflammatory responses. However, there is a lack of exacted mechanism of ApoE. In this study, we aimed to investigate whether apolipoprotein E (ApoE) induced inflammatory responses and apoptosis in neonatal mice brain from ApoE deficient (ApoE(-/-)) and wildtype (WT). Compared to control group, the microglia cell from ApoE(-/-) mice showed more severe inflammation and cell death such as iNOS and IL-1β. Furthermore, anti-inflammatory such as TGF-β, IL-10 from microglia and astrocytes in ApoE(-/-) mice were decreased. On the other way, TGF-β from astrocytes can inhibit inflammation factors secretion from microglia. Our findings suggested that the anti-inflammation factor such as IL-10 mainly from microglia and TGF-β mainly from astrocyte is significant decreased after Loss of ApoE function in ApoE(-/-) mice which induced severe inflammation. Furthrtmore, anti- inflammation factor such as IL-10 and TGF-β Therefore, we conclude that apolipoprotein E knockout induced inflammatory responses related to microglia in neonatal mice brain via astrocytes.

PMID: 25785051 [PubMed] PMCID: PMC4358506 Free PMC Article

**27. PLoS One. 2015 Mar 20;10(3):e0115083. doi: 10.1371/ journal.pone.0115083.**

**Elevated Endogenous Erythropoietin Concentrations Are Associated with Increased Risk of Brain Damage in Extremely Preterm Neonates.**

Korzeniewski SJ1, Allred E2, Logan JW3, Fichorova RN4, Engelke S5, Kuban KC6, O'Shea TM7, Paneth N8, Holm M9, Dammann O10, Leviton A2; ELGAN study investigators.

BACKGROUND: We sought to determine, in very preterm infants, whether elevated perinatal erythropoietin (EPO) concentrations are associated with increased risks of indicators of brain damage, and whether this risk differs by the co-occurrence or absence of intermittent or sustained systemic inflammation (ISSI). METHODS: Protein concentrations were measured in blood collected from 786 infants born before the 28th week of gestation. EPO was measured on postnatal day 14, and 25 inflammation-related proteins were measured weekly during the first 2 postnatal weeks. We defined ISSI as a concentration in the top quartile of each of 25 inflammation-related proteins on two separate days a week apart. Hypererythropoietinemia (hyperEPO) was defined as the highest quartile for gestational age on postnatal day 14. Using logistic regression and multinomial logistic regression models, we compared risks of brain damage among neonates with hyperEPO only, ISSI only, and hyperEPO+ISSI, to those who had neither hyperEPO nor ISSI, adjusting for gestational age. RESULTS: Newborns with hyperEPO, regardless of ISSI, were more than twice as likely as those without to have very low (< 55) Mental (OR 2.3; 95% CI 1.5-3.5) and/or Psychomotor (OR 2.4; 95% CI 1.6-3.7) Development Indices (MDI, PDI), and microcephaly at age two years (OR 2.4; 95%CI 1.5-3.8). Newborns with both hyperEPO and ISSI had significantly increased risks of ventriculomegaly, hemiparetic cerebral palsy, microcephaly, and MDI and PDI < 55 (ORs ranged from 2.2-6.3), but not hypoechoic lesions or other forms of cerebral palsy, relative to newborns with neither hyperEPO nor ISSI. CONCLUSION: hyperEPO, regardless of ISSI, is associated with elevated risks of very low MDI and PDI, and microcephaly, but not with any form of cerebral palsy. Children with both hyperEPO and ISSI are at higher risk than others of very low MDI and PDI, ventriculomegaly, hemiparetic cerebral palsy, and microcephaly.

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