

Monday 18 April 2011

This free weekly bulletin lists the latest research on cerebral palsy (CP), as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "cerebral palsy".

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Interventions

1. **World Neurosurg. 2011 Jan;75(1):138-144.**

Clinical Outcomes After Selective Dorsal Rhizotomy in an Adult Population.

Reynolds MR, Ray WZ, Strom RG, Blackburn SL, Lee A, Park TS.

OBJECT: Selective dorsal rhizotomy (SDR) is a highly effective and well-established surgical tool for correction of lower-extremity spasticity in children with spastic diplegia caused by cerebral palsy (CP). Although the literature demonstrates considerable immediate and long-term functional benefits in children treated with SDR, the effects of SDR on adults with spastic diplegia have not been thoroughly investigated. The purpose of this retrospective study was to examine the objective and subjective clinical outcomes of SDR on an adult population. **METHODS:** We reviewed the charts of 21 consecutive adult patients who underwent SDR for treatment of CP-related spastic diplegia between the years of 1989 and 2007. All patients were treated by a single surgeon (T.S.P.) and underwent formal pre- and postoperative physical therapy assessments to examine joint range of motion (ROM), gross motor function measure (GMFM), and muscle tone. The majority of patients (15/21) exhibited preoperative ambulatory independence without an assistive device. Postoperative assessments were performed at 4 months, but most patients (11/21) had longer follow-up periods (mean, 17.6 ± 30.2 months). All patients were assessed with a telephone survey to estimate pre- and postoperative function with the Katz and Lawton Activities of Daily Living (ADL) Scale. **RESULTS:** After SDR surgery, patients experienced significant improvements in lower-extremity passive joint ROM (namely, decreases in hamstring and gastrocnemius tightness) as well as in GMFM crawling and kneeling scores. In addition, spasticity in all measured lower-extremity muscle groups was decreased as compared with preoperative levels. On the basis of our patient self-assessments conducted via telephone, each patient demonstrated subjective improvements in ambulatory ability, spasticity, coordination, joint ROM, pain, overall quality of life, and independence. Also, the Lawton total instrumental ADL scale scores were subjectively improved from preoperative levels. We documented no complications, including postoperative sensory deficits, in any of our patients. **CONCLUSIONS:** Our experience suggests that SDR can be an effective treatment for CP-related spastic diplegia in ambulatory adults who are unresponsive to medical therapy and should be considered as a therapeutic option in carefully selected patients. Although our study represents the largest series of adult patients with spastic diplegia to date treated with SDR, the data collected will need to be validated in a larger, prospective clinical trial.

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2. Z Orthop Unfall. 2011 Apr 12. [Epub ahead of print]

Locking Plates for Osteosyntheses of Corrective Osteotomies in Paediatric Orthopaedic and Neuroorthopaedic Patients. [Article in German]

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BACKGROUND: Modern locking plates are widely used for the treatment of adult orthopaedic and trauma patients. Sporadic descriptions of their advantages now exist for paediatric trauma patients. Publications concerning their implantation in paediatric orthopaedic and neuroorthopaedic patients are still scarce even though it is well known that the compliance of children and adolescents is limited and that rapid mobilisation is essential for patients with disorders of neurological origin or bone metabolism to avoid developmental setbacks and perioperative fractures. **PATIENTS AND METHODS:** The principle of the locking plate system also described as internal fixateur is based on the thread bolting of the screwheads within the plate. This results in high initial stability and thus high initial loading capacity. Furthermore, it is possible to preserve soft tissue and periosteum which leads to less impaired biological bone healing. Between February 2008 and March 2010 locking plates were used for osteosynthesis in our department in 16 paediatric patients with 20 corrective osteotomies. All patients suffered from either neurological disorders or diseases with alteration of the bone metabolism. The outcome was analysed concerning safety, complications, practicability, mobilisation, consolidation of the osteotomy, loss of correction, as well as complications with the removal of the implants. **RESULTS:** Seven of the treated patients suffered from neurological disorders such as cerebral palsy or spina bifida, 9 patients had diseases with local or systemic alteration of their bone metabolism such as vitamin D deficiency and phosphate diabetes. The average age of the patients at the time of surgery was 11.18 (5-18) years. Implant-associated complications were not seen in this patient group, especially no implant failures. Mobilisation was achieved without cast treatment with at least partial weight-bearing within the first postoperative week in most cases. Loss of correction or problems with implant removal did not occur. 18 of the 20 osteotomy sites were completely healed at the 12 week follow-up. **CONCLUSION:** Locking plates are a safe and effective treatment device not only for adult trauma patients but also for the treatment of children and adolescents. When stabilisation of corrective osteotomies is performed with locking plates especially young patients benefit from this technique since mobilisation can be started earlier as compared to the use of non-angle stable plates or wires and cast immobilisation becomes unnecessary. The surgeon needs to know the range of products to pick the best implant regarding the growing skeleton's special anatomy. When choosing implants for patients with reduced bone density or impaired motor abilities as in cerebral palsy, spina bifida, and other systemic disorders, locking plates have to be taken into account to facilitate mobilisation and to avoid setbacks in motor development as well as pressure ulcers from casts. Clinical studies have to evaluate if early mobilisation combined with shorter inpatient treatment and less time and cost consuming postoperative physiotherapy or rehabilitation justify the use of the more expensive locking plates for the treatment of otherwise healthy patients.

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3. Acta Orthop Traumatol Turc. 2011 January-February;45(1):1-5. doi: 10.3944/AOTT.2011.2472.

Preoperative hematological assessment of pediatric patients with cerebral palsy.

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OBJECTIVES: Nutritional deficiencies and use of antiepileptic drugs can lead to alterations in the hematological status of children with cerebral palsy (CP), which may increase the risk of intraoperative or postoperative hematological complications. In this retrospective study, we evaluated the preoperative routine blood tests of CP patients with different levels of walking ability, who were scheduled to undergo orthopedic procedures. **METHODS:** Hemoglobin level, hematocrit, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width, white blood cell count, platelet count, prothrombin

time, activated partial thromboplastin time, and plasma fibrinogen concentration were compared between 62 consecutive CP patients [28 girls, 34 boys; mean age 8.8 years (range 2-16 years)] and 130 consecutive orthopedic patients as control [64 girls, 66 boys; mean age 9.2 years (range 2-16 years)] who did not have any skeletal, cranial, thoracic, abdominal or major soft tissue injuries, or any other infectious, metabolic, hematological or malignant tumor disorders. RESULTS: CP and control groups were similar with regard to the above-mentioned hematological parameters. In the CP group, no difference was found between Gross Motor Function Classification System for Cerebral Palsy (GMFCS) level I/II patients and GMFCS level III/IV patients in terms of these hematological parameters. CONCLUSION: Preoperative blood tests results of pediatric CP patients, walking with or without any supportive devices and undergoing orthopedic interventions, are similar to those of other orthopedic patients. Advanced preoperative hematological tests can only be recommended for CP patients with abnormal blood test results.

PMID: 21478656 [PubMed - as supplied by publisher]Free Article

4. Am J Occup Ther. 2011 Mar-Apr;65(2):211-6.

Center-of-pressure movements during equine-assisted activities.

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We compared anteroposterior and mediolateral range of motion and velocity of the center of pressure (COP) on the horse's back between riders without disabilities and riders with cerebral palsy. An electronic pressure mat was used to track COP movements beneath the saddle in 4 riders without disabilities and 4 riders with cerebral palsy. Comparisons between rider groups were made using the Mann-Whitney test ($p < .05$). The two rider groups differed significantly in anteroposterior range of COP motion, mediolateral range of COP motion, and mediolateral COP velocity. Anteroposterior COP velocity did not differ between groups. The results suggest that measurements of COP range of motion and velocity are potentially useful for monitoring changes in balance as an indicator of core stability during equine-assisted activities.

PMID: 21476369 [PubMed - in process]

5. Dev Med Child Neurol. 2011 May;53(5):443-8. doi: 10.1111/j.1469-8749.2010.03904.x.

Intrathecal baclofen and motor function in cerebral palsy.

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Aim: The aim of this retrospective analysis was to determine the impact of intrathecal baclofen (ITB) therapy on motor function in patients with cerebral palsy (CP). **Method:** We studied 37 patients (18 males, 19 females) with CP treated with ITB (mean age at implant 13y 7mo, SD 7y). Eighteen patients were affected by spastic diplegia, 12 by spastic quadriplegia, six by dystonic quadriplegia, and one by hemidystonia. Nine participants were in Gross Motor Function Classification System (GMFCS) level II, 13 in level III, seven in level IV, and eight in level V. Motor function was assessed by the Gross Motor Function Measure (GMFM) before the treatment and 12 months after the implant. **Results:** The collected data showed an increase in the total median GMFM score in the overall population ($p < 0.001$) and in every GMFM dimension ($p < 0.05$) except for dimension D (standing). The analysis by degree of impairment revealed that patients with severe impairment and those with mild to moderate impairment improved the total median GMFM score ($p < 0.001$ and $p < 0.05$ respectively). Analysis by age showed that the best improvements in GMFM scores were reached by patients younger than 18 years old ($p < 0.05$). Spasticity and dystonia, assessed by means of the Ashworth and Barry-Albright Dystonia scales, significantly decreased 12 months after the implant ($p < 0.001$ and $p < 0.05$ respectively). Finally, a subjective questionnaire administered to patients/caregivers revealed an overall improvement in participants' functional abilities. **Interpretation:** The results suggest that ITB therapy is an effective treatment for managing spasticity and dystonia, and for improving motor function in children with CP.

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6. Dev Med Child Neurol. 2011 May;53(5):391. doi: 10.1111/j.1469-8749.2011.03921.x.

Intrathecal baclofen and motor function in cerebral palsy.

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7. J Bone Miner Res. 2011 Apr 13. doi: 10.1002/jbmr.402. [Epub ahead of print]

High-frequency, low-intensity vibrations increase bone mass and muscle strength in upper limbs, improving autonomy in disabled children.

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BACKGROUND: Disuse osteoporosis in children is a progressive disease, which can affect quality of life. High-frequency, low-magnitude vibrations (HFLMV) act as anabolic signals for bone and muscle. **METHODS:** A prospective, randomized double-blind and placebo controlled clinical trial to assess the efficacy and safety of regional HFLMV in disabled children was performed. Sixty-five children, 6 to 9 year-old, were randomized into three groups: placebo, 60 Hz and 90 Hz. In the two active groups, a 0.3 g mechanical vibration was delivered to the radii and femora for 5 minutes each day. Following the 6 months, the main outcome was bone mineral density (BMD) at the ultradistal radius (UDR), 33% radii (33%R) and femoral necks (FN). Secondary outcomes were area and BMC at the UDR, 33%R, and FN; grip force of the upper and lower limbs; motor function; and PedsQL evaluation. An intention-to-treat analysis was used. **RESULTS:** Fifty-seven children (88%) completed the protocol. A significant increase was observed in the 60 Hz group relative to the other groups in BMD-UDR ($p = 0.011$), grip force of the upper limbs ($p = 0.035$), and "Daily activities item" ($p = 0.035$). A mixed model to evaluate the response to intervention showed a stronger effect of 60 Hz, on patients with cerebral palsy, on UDR, and that between-subject variability significantly affected the response. There were no reported side effects of the intervention. **DISCUSSION:** This work provides evidence that regional HFLMV is an effective and safe strategy to improve bone mass, muscle strength, and possibly independence in children with motor disabilities. © 2011 American Society for Bone and Mineral Research.

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8. J Physiol. 2011 Mar 21. [Epub ahead of print]

Hamstring Contractures in Children With Spastic Cerebral Palsy Result from a Stiffer ECM and Increased In Vivo Sarcomere Length.

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Cerebral Palsy (CP) results from an upper motor neuron (UMN) lesion in the developing brain. Secondary to the UMN lesion, which causes spasticity, is a pathologic response by muscle - namely, contracture. However, the elements within muscle that increase passive mechanical stiffness, and therefore result in contracture, are unknown. Using hamstring muscle biopsies from pediatric patients with CP ($n=17$) and control ($n=14$) patients we investigated

passive mechanical properties at the protein, cellular, tissue, and architectural levels to identify the elements responsible for contracture. Titin isoform, the major load bearing protein within muscle cells, was unaltered in CP. Correspondingly, the passive mechanics of individual muscle fibers were not altered. However, CP muscle bundles, which include fibers in their constituent ECM, were stiffer than control bundles. This corresponded to an increase in collagen content of CP muscles measured by hydroxyproline assay and observed using immunohistochemistry. In-vivo sarcomere length of CP muscle measured during surgery was significantly longer than that predicted for control muscle. The combination of increased tissue stiffness and increased sarcomere length interact to increase stiffness greatly of the contracture tissue in-vivo. These findings provide evidence that contracture formation is not the result of stiffening at the cellular level, but stiffening of the ECM with increased collagen and an increase of in vivo sarcomere length leading to higher passive stresses.

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9. *Pediatr Neurol.* 2011 May;44(5):357-63.

Effective results with botulinum toxin in cerebral palsy.

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This study evaluated the improvement in clinical measures and quality of life (QOL) among patients with cerebral palsy treated with botulinum toxin type A. Fifty-seven parents of cerebral palsy patients who used botulinum toxin during the time of the study were enrolled. The QOL questionnaires included the following: Child Caregiver Questionnaire, Pediatrics Outcomes Data Collection Instrument, and clinical evaluations. The questionnaires were administered before the first use of botulinum toxin and approximately 1 year later, a mean interval of 13.8 months. Treatment resulted in clinical improvement in tone, upper limb function, and Gross Motor Function Classification System score. Better outcomes were observed in patients younger than 6.5 years. QOL questionnaires revealed a tendency toward improvement in the comfort dimension of the Child Caregiver Questionnaire as well as in the upper extremities and physical functions, transfers and basic mobility, and global function and symptom of the Pediatrics Outcomes: Data Collection Instrument. The QOL measures correlated with clinical evaluations. Patients with low cognitive ability and refractory epilepsy had the worst results. Children and adolescents have reduced spasticity and experience good results in the clinical measurements and in QOL after treatment with botulinum toxin.

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10. *Phys Occup Ther Pediatr.* 2011 Apr 13. [Epub ahead of print]

Exploring Issues of Participation Among Adolescents with Cerebral Palsy: What's Important to Them?

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The purpose of this cross-sectional study was to determine what participation issues are important to adolescents with cerebral palsy (CP). Two hundred and three adolescents with CP (mean age 16.0 ± 1.8 years) were assessed using the Canadian Occupational Performance Measure (COPM). This was done through semistructured interviews by trained physical and occupational therapists. Adolescents responded either directly ($n = 144$) or through a parent or a caregiver ($n = 59$) if they were unable to communicate. Issues were extracted from completed questionnaires and coded under three COPM categories (self-care, productivity, and leisure) and 16 subcategories. There was no association between the total number of issues identified and gender ($p = .99$), age ($p = .88$), type of respondent (adolescents versus parent) ($p = .27$), Gross Motor Function Classification System (GMFCS) level ($p = .93$), or 66-item Gross Motor Function Measure (GMFM-66) score ($p = .45$). The issues identified most frequently were related to active leisure (identified by 57% of participants), mobility (55%), school (48%), and socialization (44%). Interventions aimed at improving participation among adolescents with physical disabilities, such as CP, should be directed

towards these four key areas. Health care professionals should also recognize and consider the interaction of person and environment when addressing issues related to participation.

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11. *Mov Disord*. 2011 Apr 12. doi: 10.1002/mds.23723. [Epub ahead of print]

Dystonia due to cerebral palsy responds to deep brain stimulation of the globus pallidus internus.

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BACKGROUND: Cerebral palsy is the most common cause of pediatric-onset dystonia. Deep brain stimulation is gaining acceptance for treating dystonias in children. There is minimal reported experience regarding the efficacy of deep brain stimulation in cerebral palsy. **METHODS:** Fourteen patients, including 8 younger than 16 years, received bilateral implants (13 patients) or a unilateral implant (1 patient) of the internal globus pallidus and were observed in a noncontrolled, nonblinded study for at least 6 months. Motor function was assessed using the Burke-Fahn-Marsden Dystonia Movement and Disability scales and the Barry Albright Dystonia Scale. **RESULTS:** By 6 months, significant improvement was observed in the Burke-Fahn-Marsden Dystonia Movement scale ($P = .004$), the Burke-Fahn-Marsden Dystonia Disability scale ($P = .027$), and the Barry Albright Dystonia Scale ($P = .029$) for the whole cohort ($n = 14$) and in the patients treated before skeletal maturity (group 1; $n = 8$): Burke-Fahn-Marsden Dystonia Movement scale, $P = .012$; Burke-Fahn-Marsden Dystonia Disability scale, $P = .020$; and Barry Albright Dystonia Scale, $P = .027$. **CONCLUSIONS:** Deep brain stimulation may offer an effective treatment option for cerebral palsy-related dystonia, especially in those treated before skeletal maturity.

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Epidemiology / Aetiology / Diagnosis & Early Treatment

12. *J Perinat Med*. 2011 Apr 14. [Epub ahead of print]

Using prophylactic, but not tocolytic, magnesium sulfate to reduce cerebral palsy related to prematurity: what dose, and what about infant mortality?

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Strategies for the prevention of cerebral palsy (CP) remain incompletely characterized. Recognizing that half of all cases are associated with preterm delivery (Australian CP Register Report, 2009), research protocols aimed at reducing its prevalence have focused on interventions in pregnancies at risk for preterm birth. Compelling data from recent clinical trials have led to an emerging consensus favoring the use of antenatal magnesium sulfate for preterm neuroprophylaxis. Unresolved, however, is the critical question regarding the "best dose". Acknowledging that any substance in high enough doses becomes toxic, the "best dose" is really the least dose that achieves efficacy, while minimizing potential toxicity among susceptible fetuses. Importantly, credible evidence from these CP prevention trials indicates that antenatal magnesium sulfate, if dosed appropriately, may also decrease infant mortality - a worthy goal in its own right. Accordingly, whether we achieve (a) reduction in CP only, (b) simultaneous reduction in CP and infant mortality, or (c) CP reduction offset by possibly increased pediatric mortality, may depend on selection of dose. In this Opinion paper, we review the findings of all major randomized trials that tested the magnesium hypothesis for prevention of CP. In addition, we discuss future research, in progress, that is hoped to refine estimates of best dose.

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13. Turk J Pediatr. 2010 Nov-Dec;52(6):630-7.

Assessment of "general movements" in high-risk infants by Precht analysis during early intervention period in the first year of life.

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This study was performed to assess the neurological status of high-risk infants by "general movements" (GMs) method and to compare it with the findings of standard clinical neurological examination and neuroimaging findings during the early rehabilitation period. Neurodevelopmental examination was performed by a neonatologist at the corrected ages of 40 weeks, and 3, 6 and 12 months. Assessment of the physiotherapist included video recording of "Precht Analysis of GMs" from the first week of life to the corrected age of 5 months. All infants underwent an early physiotherapy program, and follow-up examinations continued until 12 months. A percentage of agreement of 0.86 was found between cranial ultrasound imaging results and GMs and of 0.78 between neurological examination and GMs. Precht analysis was found to be important for detecting neurological dysfunction and differentiating normal neurological development in high-risk infants during the early intervention period. This analysis can be used complementary to other diagnostic and imaging techniques in the follow-up of preterm infants.

PMID: 21428196 [PubMed - indexed for MEDLINE]

14. J Pediatr. 2011 May;158(5):860-1.

Low Apgar score is associated with cerebral palsy in children.

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PMID: 21482248 [PubMed - in process]

15. J Pregnancy. 2011;2011:809569. Epub 2010 Dec 27.

Prenatal brain damage in preeclamptic animal model induced by gestational nitric oxide synthase inhibition.

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Cerebral palsy is a major neonatal handicap with unknown aetiology. There is evidence that prenatal brain injury is the leading cause of CP. Severe placental pathology accounts for a high percentage of cases. Several factors predispose to prenatal brain damage but when and how they act is unclear. The aim of this paper was to determine if hypoxia during pregnancy leads to damage in fetal brain and to evaluate the localization of this injury. An animal model of chronic hypoxia produced by chronic administration of a nitric oxide synthase inhibitor (L-NAME) was used to evaluate apoptotic activity in fetal brains and to localize the most sensitive areas. L-NAME reproduces a preeclamptic-like condition with increased blood pressure, proteinuria, growth restriction and intrauterine mortality. Apoptotic activity was increased in L-NAME brains and the most sensitive areas were the subventricular and pallidum zone. These results may explain the clinical features of CP. Further studies are needed.

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