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## Interventions and Management

### 1. Clin Ther. 2012 Mar 23. [Epub ahead of print]

#### **Glycopyrrolate for Chronic Drooling in Children.**

Eiland LS.

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**BACKGROUND:** Sialorrhea, or drooling, is seen in the pediatric population, especially in patients with cerebral palsy and other neurodevelopmental disabilities. If medication use is warranted, anticholinergic agents are the drug of choice; however, adverse effects limit their use. Glycopyrrolate, a synthetic anticholinergic that acts at peripheral muscarinic receptors, has been used off-label for excessive drooling in children with neurodevelopmental disabilities for years. Product formulations restricted the use of glycopyrrolate. However, an oral solution was approved by the US Food and Drug Administration for children ages 3 to 16 years with neurologic disorders for chronic severe drooling in 2010; it became available for use in 2011. **OBJECTIVE:** This article provides an overview of the pharmacology, clinical efficacy, and tolerability of glycopyrrolate when used for sialorrhea in children. **METHODS:** To evaluate the efficacy and safety profile of glycopyrrolate for the treatment of sialorrhea in children, a comprehensive search was performed of the MEDLINE database (1966-February 25, 2012) and International Pharmaceutical Abstracts as well as references from additional review articles identified. Searches were conducted using the terms glycopyrrolate, sialorrhea, drooling, secretion, and pediatrics. The terms drug-induced and Parkinson disease-associated sialorrhea were excluded from the search. The pharmaceutical manufacturer of the oral solution was contacted for medical and study information. **RESULTS:** Oral bioavailability of glycopyrrolate varies widely, with a median of 3.3%. Mean C(max) in children was determined to be 0.37 µg/mL, and mean T(max) was 3.1 hours. The clearance in children ranges from 0.6 to 1.43 L/kg/h. The t(½) ranges from 22 to 130 minutes and 19 to 99 minutes in infants and children, respectively. Six studies describing the use of glycopyrrolate for drooling in children were identified. A double-blind, crossover trial of 27 patients (age range, 4-19 years) demonstrated a reduced mean drooling score (modified Teacher's Drooling Scale [1 = never drools to 9 = clothing, hands, and objects frequently become wet]) for glycopyrrolate (mean highest tolerated dose, 0.11 mg/kg) compared with placebo of 1.85 versus 6.33 (P < 0.001). In a parallel study of 36 patients (age range, 3-16 years), 14 of 20 patients randomized to receive glycopyrrolate solution showed improvement in the mean modified Teacher's Drooling Scale score compared with only 3 patients receiving placebo (-3.5 vs -0.1, respectively). Glycopyrrolate was initiated at 0.02 mg/kg per dose orally TID (Max dose: 3 mg) and titrated over a 4-week period. Adverse effects identified in studies include dry mouth (9%-41%), constipation (9%-39%), and behavioral changes (18%-36%). **CONCLUSIONS:** Glycopyrrolate is effective in decreasing sialorrhea in children with cerebral palsy or other neurodevelopmental disabilities. Adverse effects did occur, more frequently at higher doses, and should be monitored.

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## 2. BMC Pediatr. 2012 Mar 26;12(1):38. [Epub ahead of print]

### **Splint: The efficacy of orthotic management in rest to prevent equinus in children with cerebral palsy, a randomised controlled trial.**

Maas JC, Dallmeijer AJ, Huijij PA, Brunstrom-Hernandez JE, Kampen PJ van, Jaspers RT, Becher JG.

**BACKGROUND:** Range of motion deficits of the lower extremity occur in about the half of the children with spastic cerebral palsy (CP). Over time, these impairments can cause joint deformities and deviations in the children's gait pattern, leading to limitations in mobility. Preventing a loss of range of motion is important in order to reduce secondary activity limitations and joint deformities. Sustained muscle stretch, imposed by orthotic management in rest, might be an effective method of preventing a decrease in range of motion. However, no controlled study has been performed. **METHODS:** A single blind randomised controlled trial will be performed in 66 children with spastic CP, divided over three groups with each 22 participants. Two groups will be treated for 1 year with orthoses to prevent a decrease in range of motion in the ankle (either with static or dynamic knee-ankle-foot-orthoses) and a third group will be included as a control group and will receive usual care (physical therapy, manual stretching). Measurements will be performed at baseline and at 3, 6, 9 and 12 months after treatment allocation. The primary outcome measure will be ankle dorsiflexion at full knee extension, measured with a custom designed hand held dynamometer. Secondary outcome measures will be i) ankle and knee flexion during gait and ii) gross motor function. Furthermore, to gain more insight in the working mechanism of the orthotic management in rest, morphological parameters like achilles tendon length, muscle belly length, muscle fascicle length, muscle physiological cross sectional area length and fascicle pennation angle will be measured in a subgroup of 18 participants using a 3D imaging technique. **DISCUSSION:** This randomised controlled trial will provide more insight into the efficacy of orthotic management in rest and the working mechanisms behind this treatment. The results of this study could lead to improved treatments. Trial Registration Number Netherlands Trial Register NTR2091.

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## 3. Arch Dis Child. 2012 Apr;97(4):364-71.

### **Neuromuscular electrical stimulation for children with cerebral palsy: a review.**

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The aim of this review paper is to consider the application of neuromuscular electrical stimulation (NMES) to improve gait or upper limb function in children with cerebral palsy (CP). Although most NMES research has been directed at adults with neurological conditions, there is a growing body of evidence supporting its use in children with CP. In line with a recent meta-analysis, the use of electrical stimulation to minimise impairment and activity limitations during gait is cautiously advocated. A detailed commentary on one of the most common lower limb NMES applications, tibialis anterior stimulation (either with or without gastrocnemius stimulation) is given. Although there is a lack of randomised controlled trials and a predominance of mainly small studies, this review further concludes that the balance of available evidence is in favour of upper limb exercise NMES offering benefits such as increased muscle strength, range of motion and function in children with CP. The use of dynamic splinting with NMES has been shown to be more effective than either treatment on its own in improving function and posture. There is at present little published work to support the application of botulinum toxin type A to temporarily reduce muscle tone as an adjunct intervention to NMES in this population, although the presence of parallel applications to manage similar symptoms in other muscular disorders is noted.

[PMID: 22447997](#) [PubMed - in process]

**4. Dev Med Child Neurol. 2012 Mar 27. doi: 10.1111/j.1469-8749.2012.04261.x. [Epub ahead of print]****Feasibility and reliability of measuring strength, sprint power, and aerobic capacity in athletes and non-athletes with cerebral palsy.**

DE Groot S, Janssen TW, Evers M, VAN DER LUIJT P, Nienhuys KN, Dallmeijer AJ.

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**Aim:** The aim of this study was to analyse the feasibility and reliability of the tests used to determine muscle strength, sprint power, and aerobic capacity in athletes and non-athletes with cerebral palsy (CP). **Methods:** Twenty individuals with spastic CP (four females, 16 males; age range 18-49y; Gross Motor Function Classification System level I, n=15; II, n=5; unilateral CP, n=10; bilateral CP, n=10; athletes, n=12; non-athletes, n=8) participated in the study. Isometric and isokinetic knee flexor and extensor strength, sprint power, and aerobic capacity were determined, using, respectively an isokinetic dynamometer, a Wingate cycling test, and a graded maximal bicycle exercise test, on three occasions. Intraclass correlation coefficients (ICC), standard error of measurements, and smallest detectable differences (SDD) were calculated. **Results:** The feasibility of the isometric strength test, Wingate test, and graded exercise test was good; the isokinetic strength test was difficult to perform for five participants. The strength parameters showed moderate to good ICCs (isometric, 0.74-0.94; isokinetic, 0.88-0.93) but high SDDs (isometric, 25-45%; isokinetic, 30-45%). Sprint power (ICC 0.98; SDD 24%) and aerobic capacity (ICC 0.98-0.99; SDD 16-21%) showed good ICCs and moderate SDDs. **Interpretation:** All tests, except for the isokinetic strength test, seemed to be feasible for almost all participants. All tests are suitable for evaluating changes in a group; however, only large improvements (16-45%) can be detected when monitoring individual changes.

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**5. Indian J Orthop. 2012 Mar;46(2):221-8.****Supracondylar femoral extension osteotomy and patellar tendon advancement in the management of persistent crouch gait in cerebral palsy.**

Das SP, Pradhan S, Ganesh S, Sahu PK, Mohanty RN, Das SK.

Department of Physical Medicine and Rehabilitation, Swami Vivekanand National Institute of Rehabilitation, Training and Research, Olatpur, Bairoi, Cuttack, Orissa, India.

**BACKGROUND:** Severe crouch gait in adolescent cerebral palsy is a difficult problem to manage. The patients develop loading of patellofemoral joint, leading to pain, gait deviation, excessive energy expenditure and progressive loss of function. Patella alta and avulsion of patella are the other complications. Different treatment options have been described in the literature to deal with this difficult problem. We evaluated outcome of supracondylar femoral extension osteotomy (SCFEO) and patellar tendon advancement (PTA) in the treatment of crouch gait in patients with cerebral palsy. **MATERIALS AND METHODS:** Fourteen adolescents with crouch gait were operated by SCFEO and PTA. All subjects were evaluated pre and postoperatively. Clinical, radiographic, observational gait analysis and functional measures were included to assess the changes in knee function. **RESULTS:** Cases were followed up to 3 years. The patients walked with increased knee extension and improvement in quadriceps muscle strength. Knee pain was decreased and improvements in functional mobility and radiologic improvement were found. **CONCLUSION:** SCFEO and PTA for adolescent crouch gait is effective in improving knee extensor strength, reducing knee pain and improving function.

[PMID: 22448063](#) [PubMed - in process] [PMCID: PMC3308666](#)

**6. Dev Med Child Neurol. 2012 Mar 27. doi: 10.1111/j.1469-8749.2012.04286.x. [Epub ahead of print]****Expanding the measures of physical capacity in cerebral palsy.**

Thorpe D.

DAHS, Division of Physical Therapy, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

[PMID: 22448650](#) [PubMed - as supplied by publisher]**7. Dev Med Child Neurol. 2012 Mar;54(3):201-2. doi: 10.1111/j.1469-8749.2011.04206.x. Epub 2012 Jan 23.****To do or not to do the other hip?**

Narayanan UG.

Comment on

Dev Med Child Neurol. 2012 Mar;54(3):231-9.

[PMID: 22268615](#) [PubMed - indexed for MEDLINE]**8. Pediatr Radiol. 2012 Mar 25. [Epub ahead of print]****Evaluation of carotid intima-media thickness, a marker of subclinical atherosclerosis, in children with cerebral palsy.**

Cece H, Yetisgin A, Abuhandan M, Yildiz S, Calik M, Karakas O, Karakas E, Iscan A.

Department of Radiology, Faculty of Medicine, Harran University School of Medicine, Sanliurfa, 63040, Turkey, hasan\_cece@yahoo.com.

**BACKGROUND:** Respiratory and cardiovascular diseases are the most common causes of death in children with cerebral palsy. **OBJECTIVE:** To evaluate sonographic carotid intima-media thickness, an early marker of atherosclerosis, in children with cerebral palsy and in healthy controls. **MATERIALS AND METHODS:** One hundred children with cerebral palsy (65 boys), mean age 6.2 (SD, 2.1) years, and 35 age-matched and sex-matched healthy controls were included. Common carotid artery intima-media thickness was measured sonographically. Differences between patients and controls were evaluated with an independent samples t-test. **RESULTS:** Age, sex distribution and levels of serum lipids were comparable between patients and controls. Average, right and left carotid artery intima-media were thicker in patients compared with controls (mean  $\pm$  SD,  $0.61 \pm 0.13$  mm vs  $0.40 \pm 0.03$  mm;  $0.61 \pm 0.14$  mm vs  $0.40 \pm 0.03$  mm;  $0.61 \pm 0.13$  mm vs  $0.40 \pm 0.03$  mm, respectively; all  $P < 0.001$ ). **CONCLUSION:** Carotid intima-media is sonographically thicker in children with cerebral palsy compared with healthy controls, which may express an increased risk of atherosclerotic diseases.

[PMID: 22450433](#) [PubMed - as supplied by publisher]**9. Qual Life Res. 2012 Mar 25. [Epub ahead of print]****Feasibility, reliability and validity of the Thai version of the Pediatric Quality of Life Inventory 3.0 cerebral palsy module.**

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**BACKGROUND:** Quality of Life (QOL) and Health-related Quality of Life (HRQOL) are now considered as

necessary outcome measures for children with cerebral palsy (CP). Various reliable and valid condition-specific HRQOL tools are available for these children. One of these is Pediatric Quality of Life Inventory (PedsQL) 3.0 CP module which has been widely used and was translated to many languages. As no Thai version is available, the authors have completed this translation. **PURPOSE:** This study then aimed to investigate psychometric properties of the newly translated Thai PedsQL 3.0 CP module and to establish parent confidence in their ratings in the translated tool. **METHODS:** Translation of the PedsQL 3.0 CP module was performed based on linguistic translation guidelines. Then, the psychometric properties of the Thai version were established. PedsQL 3.0 CP module was completed by children with CP and their parents or caregivers twice with 2-4 weeks. **RESULTS:** Respondents were 97 parents or caregivers and 54 children. Minimal missing data were found. Acceptable internal consistency was supported except for Movement and Balance Scale (self-report). Intraclass correlation coefficients for parent proxy and self-report were good to excellent (0.684-0.950). **CONCLUSIONS:** The feasibility, reliability and validity of the translated tool were supported.

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## Prevention and Cure

**10. Acta Paediatr. 2012 Mar 27. doi: 10.1111/j.1651-2227.2012.02678.x. [Epub ahead of print]**

**Compared Outcomes of Very Preterm Infants born in 2000 and 2005.**

Guerrot AM, Chadie A, Torre S, Rondeau S, Cardoso GP, Abily-Donval L, Marret S; the Perinatal Network of Haute-Normandie.

Department of Neonatal Medicine, Rouen University Hospital and EA 4309 Neovasc, Institute of Biomedical Research and Innovation, School of Medicine, Rouen University, Rouen, France.

**Aim:** To compare neonatal and 2-year outcomes in very premature infants born 5 years apart. **Methods:** Prospective observational study of infants born before 33 weeks' gestation in 2000 or 2005 admitted to a neonatal intensive care unit in France. We collected perinatal data and evaluated motor, cognitive, neurosensory, and behavioral outcomes at 2 years of age. **Results:** We included 170 infants in 2000 and 173 in 2005. The significant differences in neonatal outcomes were decreases in postnatal corticosteroid use and in percentage of infants with head circumference below the 3(rd) percentile on days 7 (25% vs. 13%) and 30 (30% vs. 17%). At 2 years of age, rates of follow-up were 87% in 2000 and 94% in 2005. The cerebral palsy rate was 6% in both cohorts. The overall rate of motor disabilities diminished from 30% (41/137) to 18% (26/142) and the rate of mild motor disabilities decreased from 24% to 12%. Rates of cognitive, behavioral and neurosensorial impairments were similar. **Conclusion:** Between 2000 and 2005, motor impairments at 2 years of age diminished in very preterm children (but not cerebral palsy rates). We observed a reduced use of postnatal corticosteroids and a decreased percentage of neonates with head circumference below the third percentile. © 2012 The Author(s)/Acta Paediatrica © 2012 Foundation Acta Paediatrica.

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**11. Curr Opin Obstet Gynecol. 2012 Mar 23. [Epub ahead of print]**

**Delayed childbearing: effects on fertility and the outcome of pregnancy.**

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**PURPOSE OF REVIEW:** The proportion of women who are intentionally delaying pregnancy beyond the age of 35 years has increased greatly in the past few decades because of the clash between the optimal biological period for women to have children with obtaining additional education and building a career. This article highlights the effects of delayed childbearing on fertility and obstetric and perinatal outcome. **RECENT FINDINGS:** Demographic studies indicate that fertility rates are falling in many countries, Europe being the continent with lowest total fertility rate. Female employment and childrearing can be combined when the reduction in work-family conflict is facilitated by state of policy intervention. It has been traditionally accepted that fertility is more related to the age of the female than the male partner but recent literature suggests trends that increased paternal age is also associated with lower fertility, an increase in pregnancy-associated complications and an increase in adverse outcome in the offspring. Delayed childbearing is rarely a conscious choice and women are unaware that, at present, with the exception of egg donation, assisted reproductive technology has no answer yet to age-related decline of female fertility. There is no evidence of a beneficial effect of preimplantation genetic screening for women of advanced maternal age. Concerning perinatal outcomes, apart from the known effects of advanced maternal age on common fetal and obstetric complications, recent evidence increasingly points toward an independent association between maternal (and paternal age) and cerebral palsy, neurocognitive and psychiatric disorders. **SUMMARY:** The consequences of advancing maternal and paternal age are not only relevant for the risk of natural and assisted conception, but also for the outcome of pregnancy. Although the absolute rate of poor pregnancy outcomes may be low from an individual standpoint, the impact of delaying childbearing from a public health perspective cannot be overestimated and should be in the agenda of public health policies for the years to come.

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**12. Dev Med Child Neurol. 2012 Mar 28. doi: 10.1111/j.1469-8749.2012.04274.x. [Epub ahead of print]**

### **Characteristics of children with cerebral palsy in the ORACLE children study.**

Marlow N, Pike K, Bower E, Brocklehurst P, Jones D, Kenyon S, Kurinczuk JJ, Taylor D, Salt A.

Institute for Women's Health, University College London, London; Health Sciences Department, University of Leicester, Leicester; University Rehabilitation Research Unit, Southampton General Hospital, Southampton; National Perinatal Epidemiology Unit, University of Oxford, Oxford; School of Health and Population Sciences, University of Birmingham, Edgbaston; Maternal and Newborn Health Initiative, International Federation of Gynaecology and Obstetrics, London; Great Ormond Street Hospital for Children and Institute of Child Health, University College London, London, UK.

**Aims:** We have identified an excess of children with cerebral palsy (CP) born to women who received antibiotic treatment for spontaneous preterm labour (SPL). This nested study investigated the profile of impairment among children with CP in the ORACLE Children Study (OCS), and contrasted outcomes with those in 4Child, a population CP registry. **Method:** The study group comprised 167 children aged from 7 to 10 years (100 males, 67 females) with CP from the OCS, who were subdivided into a preterm rupture of membranes (PROM) group (87 children) and an SPL group (80 children). The OCS sought follow-up information regarding the health and behaviour of surviving children at 7 years of age in the UK using a parent-report postal questionnaire. Families provided further information to define wider aspects of function and were offered a physiotherapy assessment. **Results:** The prevalence of CP was higher among children in the OCS than among those in 4Child (standardized morbidity ratios: SPL group, 3.12 [95% confidence interval {CI} 2.47-3.87]; PROM group: 1.56 (CI 1.24-1.92)). The proportion of children with CP born after 32 weeks of gestation was higher in the SPL group (73%) than in the PROM group (30%); the prevalence of CP was higher in the SPL group than in the PROM group or 4Child. Children with CP in the OCS tended to have similar distributions of neuroimpairment as children in 4Child, but motor impairment and associated vision and hearing problems were found to be less severe. **Interpretation:** The pattern of CP in both the PROM and the SPL groups was similar, but functional outcomes were milder, compared with children with CP in the general population. However, in these groups the risk of CP was increased independently of gestational age. This is consistent with findings that ongoing inflammatory damage can cause CP.

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13. *Dev Med Child Neurol.* 2012 Mar;54(3):200. doi: 10.1111/j.1469-8749.2011.04207.x. Epub 2012 Jan 23.

**Alcohol consumption during pregnancy: the growing evidence.**

Day SM.

Comment on

*Dev Med Child Neurol.* 2012 Mar;54(3):224-30.

[PMID: 22268630](#) [PubMed - indexed for MEDLINE]

14. *J Paediatr Child Health.* 2012 Mar 27. doi: 10.1111/j.1440-1754.2012.02430.x. [Epub ahead of print]

**Can the early condition at admission of a high-risk infant aid in the prediction of mortality and poor neurodevelopmental outcome? A population study in Australia.**

Greenwood S, Abdel-Latif ME, Bajuk B, Lui K; the NSW and ACT Neonatal Intensive Care Units Audit Group.

Department of Newborn Care, Royal Hospital for Women School of Women's and Children's Health, University of New South Wales Neonatal Intensive Care Units' Data Collection, NSW Centre for Perinatal Health Services Research, Sydney New South Wales Department of Neonatology, Canberra Hospital School of Clinical Medicine, Australian National University, Canberra, Australian Capital Territory, Australia.

**Aim:** The aim of this article was to evaluate the Revised Clinical Risk Index for Babies' (CRIB-II) severity of illness score as a predictor of moderate to severe functional disability (FD) in very premature infants. **Methods:** Population study of infants born <29 weeks' gestation cared for in all Neonatal Intensive Care Unit in New South Wales and the Australian Capital Territory between 1998 and 2003. FD at 2-3 years corrected age was defined as developmental delay (quotient < 2 standard deviation), non-ambulatory cerebral palsy (needing aids to walk), blindness (acuity <6/60 in better eye) or deafness (hearing aids). Sensitivity and specificity of CRIB-II scores to predict FD were performed by receiver operating characteristic curve analysis. **Results:** Of study population of 2210, 480 (21.7%) died before hospital discharge. Among 1328 infants assessed, 217 (16.3%) had FD, 109 (8.2%) developmental delay, 75 (5.6%) cerebral palsy and 54 (4.1%) blindness or deafness. CRIB-II performed significantly better than gestation or birthweight (BW) alone in predicting mortality (area under the curve (AUC)  $\pm$  standard error  $0.83 \pm 0.01$ , vs.  $0.78 \pm 0.01$  and  $0.76 \pm 0.01$ , respectively). CRIB-II scores were significantly higher in FD than non-FD children ( $11.9 \pm 2.9$  vs.  $10.1 \pm 2.6$ ), but the AUC for CRIB-II ( $0.68 \pm 0.02$ ) did not significantly differ from that of gestation ( $0.65 \pm 0.02$ ) and BW ( $0.65 \pm 0.02$ ). **Conclusion:** CRIB-II improved prediction of mortality but did not perform better than gestational age or BW in predicting FD. We would caution clinicians against using the infant's condition at admission to predict long-term outcome.

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15. *J Transl Med.* 2012 Mar 23;10(1):58. [Epub ahead of print]

**Safety and feasibility of countering neurological impairment by intravenous administration of autologous cord blood in cerebral palsy.**

Lee YH, Choi KV, Moon JH, Jun HJ, Kang HR, Oh SI, Kim HS, Um JS, Kim MJ, Choi YY, Lee YJ, Kim HJ, Lee JH, Son SM, Choi SJ, Oh W, Yang YS.

**ABSTRACT:** **Backgrounds** We conducted a pilot study of the infusion of intravenous autologous cord blood (CB) in children with cerebral palsy (CP) to assess the safety and feasibility of the procedure as well as its potential efficacy in countering neurological impairment. **METHODS:** Patients diagnosed with CP were enrolled in this study if their parents had elected to bank their CB at birth. Cryopreserved CB units were thawed and infused intravenously over 10~20 minutes. We assessed potential efficacy over 6 months by brain magnetic resonance imaging (MRI)-

diffusion tensor imaging (DTI), brain perfusion single-photon emission computed tomography (SPECT), and various evaluation tools for motor and cognitive functions. RESULTS: Twenty patients received autologous CB infusion and were evaluated. The types of cerebral palsy were as follows: 11 quadriplegics, 6 hemiplegics, and 3 diplegics. Infusion was generally well-tolerated, although 5 patients experienced temporary nausea, hemoglobinuria, or urticaria during intravenous infusion. Diverse neurological domains improved in 5 patients (25%) as assessed with developmental evaluation tools as well as by fractional anisotropy values in brain MRI-DTI. The neurologic improvement occurred significantly in patients with diplegia or hemiplegia rather than quadriplegia. CONCLUSIONS: Autologous CB infusion is safe and feasible, and has yielded potential benefits in children with CP.

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