Cristella G1, Filippi MC2, Mori M2, Alboresi S2, Ferrari A2.


BACKGROUND: Hemiplegia is the most common form of Cerebral Palsy. Upper Limb is generally more affected than lower one. In fact, hemiplegic children can spontaneously acquire standing and walking ability, while manipulation remains uncertain, with severe limitations in activity and participation, which define child's functional status (International Classification of Functioning - ICF). Several non-surgical tools are currently available to approach upper limb impairments. Studies regarding upper limb multilevel surgery in Hemiplegic Cerebral Palsy are relatively few and inhomogeneous.

AIM: The aim of this study is to propose a surgical approach based on upper limb functional level and manipulation strategy and establish whether multilevel surgery can improve segmental alignment, performance and capacity, that ICF defines as activities and participation qualifiers.

DESIGN: This study is an observational retrospective study.

SETTING: This study involves patients who referred to Children Rehabilitation Unit of IRCCS S. Maria Nuova in Reggio Emilia (Italy), along a period of four years.

POPULATION: It involves children affected by hemiplegic cerebral palsy who underwent upper limb multilevel surgery.

METHODS: For each patient, we previously defined functional use of affected upper limb applying the House classification and the Ferrari one of manipulation pattern. Patients are divided into three groups: synergic hand (House 4, 5), imprisoned hand (House 3), excluded hand (House 0). We recorded goals achievement through Goal Attainment Scale and unimanual and bimanual abilities through Melbourne Assessment of Unilateral Upper Limb Function and through Assisting Hand Assessment respectively.

RESULTS: We record 16 upper limb multilevel surgical interventions in 13 children and report their results.

CONCLUSIONS: This study suggests that surgery can induce a segmental and/or aesthetic and/or a functional change depending on manipulation pattern. It also underlines the importance to analyse results in term of spontaneous manipulation abilities and daily use.

CLINICAL REHABILITATION IMPACT: This study provides a preliminary guide to plan surgery in relation to segmental deformities and overall manipulation pattern and describes their feasible improvement measures. It also suggests the most useful tools to record goal achievements in modifying manipulation function.

Further controlled, randomized and prospective studies are required to support this idea.

PMID: 30156083

Kwon HY1, Kim BJ1.

[Purpose] This study was conducted to examine the effects of task-specific movement patterns during resistance exercise program, which are applied to children with cerebral palsy, on respiratory functions and thickness of abdominal muscles. [Participants and Methods] This study was conducted with randomized double-blinded controlled research was pursued since it is a clinical trial with minors with disabilities as the participants. Seventeen children with cerebral palsy were randomly allocated to both experimental group and placebo group by means of simple randomized sampling. The experimental group wore weighted vest to which loaded-resistance was applied by means of sand bag while the placebo group wore weighted vest without loaded-resistance. Task-specific movement patterns during resistance exercise were performed for 40 minutes 2 times a week over a period of 12 weeks for the participants in both groups. Differences in respiratory functions and thickness of abdominal muscles measured prior to and after 12 weeks of the experiment were compared. [Results] All the measurement values for the respiratory functions and abdominal muscle thickness displayed statistically significant changes between those prior to and after the exercise in both of the experimental group and the placebo group. There were statistically significant differences in the changes prior to and following the exercise between the two groups. [Conclusion] Therefore, task-specific movement patterns in anatomic plane, diagonal patterns and combined forms during resistance exercise program on for children with cerebral palsy can be considered as an effective intervention method in improving respiratory capacity.

PMID: 30154603

Kim DH1, Yoo WG2.


[Purpose] The purpose of this study was to investigate the effect of manual therapy with functional electrical stimulation (FES) on scoliosis curve and quality of life in children with cerebral palsy (CP). [Participants and Methods] Two children with CP performed 30 minutes of manual therapy and 30 minutes of FES three times a week for 3 months. The Cobb's angle and Pediatric Quality of Life Inventory (PedsQL) score were assessed before and after the intervention. [Results] The Cobb's angle and PedsQL score were improved after intervention. [Conclusion] Our results indicate that manual therapy with FES was effective for improving scoliosis curve and quality of life.

PMID: 30154613

4. Factors associated with surgical approach and outcomes in cerebral palsy scoliosis.
Jackson T1, Yaszay B2, Sponseller PD3, Newton PO4, Shah SA5, Miyanji F6, Cahill PJ7; Harms Study Group.


BACKGROUND: Neuromuscular scoliosis is often treated with posterior spinal fusion, with or without anterior release, and either a same-day or staged, 2-day procedure. METHODS: We retrospectively reviewed 222 patients from a prospectively collected, multi-center database of patients with cerebral palsy scoliosis with 2-year follow-up. Baseline characteristics, perioperative, radiographic, and HRQoL measures were compared in six sub-analyses: (1) staged versus same-day surgeries, (2) posterior-only fusion (PSF) versus anterior-posterior spinal fusion (APSF), (3) same-day versus staged PSF, (4) staged versus same-day APSF, (5) same-day PSF versus same-day APSF, (6) staged PSF versus staged APSF. RESULTS: Staged patients had larger curves and more pelvic obliquity, longer anesthesia and surgical times, longer hospital and ICU stays (p<0.001), and more days intubated (p=0.021). The staged PSF group had larger curves (p=0.006), longer anesthesia (p=0.020) and surgeries (p=0.007), hospital (p=0.009) and ICU stays (p=0.028) compared to same-day PSF. The staged APSF group had longer hospital (p<0.001) and ICU stays (p=0.004) and anesthesia and surgeries (p<0.001). Same-day APSF was associated with larger curves (p<0.002), longer anesthesia (p=0.012) and surgeries (p=0.042), greater residual curves (p=0.035), and greater absolute correction (p=0.007) compared to same-day PSF. The staged APSF group had longer anesthesia times (p=0.001) compared to the staged PSF group. No sub-analysis revealed significant differences in baseline characteristics, complications, or HRQoL. CONCLUSION: Staged and circumferential approaches tend to be used for greater deformity, but were not associated with superior deformity correction, and were associated with longer operative time, hospital stays, ICU stays, and days intubated. However, for the most severe deformity, other patient factors may play more important roles in treatment decisions given that patients treated with a staged PSF or an APSF, whether staged or not, were similar at baseline. LEVEL OF EVIDENCE: III. These slides can be retrieved under Electronic Supplementary Material.

PMID: 30143896
Alexander C1, Elliott C2,3, Valentine J2,4, Stannage K5, Bear N6, Donnelly CJ1, Shipman P7, Reid S1.


AIM: This study aimed to track alterations in muscle volume for 6 months in children with cerebral palsy (CP) after the first exposure to botulinum neurotoxin A (BoNT-A), a commonly used focal spasticity treatment. METHOD: Eleven ambulant children (eight males, three females) with spastic CP, mean age 8 years 10 months (SD 3y 1mo) participated. Participants received injections to the affected gastrocnemius. The muscle volume of the gastrocnemius, soleus, tibialis anterior, and hamstrings was measured using magnetic resonance imaging. Muscle volume was normalized to bone length, and changes analysed relative to baseline. Assessments were conducted 1 week before, and 4 weeks, 13 weeks, and 25 weeks after BoNT-A treatment. RESULTS: All children demonstrated positive clinical and functional gains. Muscle volume of the injected gastrocnemius was found to be significantly reduced at 4 weeks (-5.9%), 13 weeks (-9.4%), and 25 weeks (-6.8%). Significant increases in normalized soleus muscle volume were identified at each follow-up, while hamstrings showed significant increase at 4 weeks only. INTERPRETATION: Absolute and normalized muscle volume of the injected muscle reduces after first BoNT-A exposure, and does not return to baseline volume by 25 weeks. Hypertrophy is seen in the soleus up to 25 weeks; the volume of the plantar flexor compartment is stable. WHAT THIS PAPER ADDS: Muscle atrophy after first botulinum neurotoxin A (BoNT-A) exposure in children with cerebral palsy is noted. Mild BoNT-A-induced muscle atrophy is still apparent 6 months after BoNT-A exposure. Hypertrophy is evident in soleus after gastrocnemius BoNT-A exposure. Total plantarflexor volume is unchanged.

PMID: 30151852

Paget SP1, Swinney CM2, Burton KLO1, Bau K1, O’Flaherty SJ3.


AIM: To identify factors that increase the likelihood of systemic adverse events after botulinum neurotoxin A (BoNT-A) injections in children with cerebral palsy (CP). METHOD: A prospective observational study of patients attending a BoNT-A clinic at a tertiary paediatric hospital (2010-2014). Occurrences of systemic adverse events, defined as lower respiratory tract illnesses, generalized weakness, dysphagia, and death were determined at follow-up. The relationship between systemic adverse events and eight preinjection variables (age, Gross Motor Function Classification System [GMFCS] level, history of dysphagia, gastrostomy, aspiration pneumonia, recent history of illness, BoNT-A dose, and type of sedation) were examined using univariable and multivariable logistic regression with generalized estimating equations methods. RESULTS: In total 591 children underwent 2219 injection episodes with follow-up in 2158 (97%) cases. Systemic adverse events were reported in 77 (3.6%) injection episodes. Univariable analysis suggested that GMFCS levels IV and V, a history of dysphagia, gastrostomy, aspiration pneumonia, and increasing BoNT-A dose increase the likelihood of systemic adverse events. In multivariable analysis, a history of dysphagia (odds ratio [OR] 3.42) and/or aspiration pneumonia (OR 2.31) remained associated with increased likelihood of systemic adverse events. INTERPRETATION: A history of dysphagia and/or aspiration pneumonia are the factors that most increase the likelihood of systemic adverse events after BoNT-A. WHAT THIS PAPER ADDS: Systemic adverse events occur in 3.6% of botulinum neurotoxin A (BoNT-A) injection episodes. Dysphagia and/or aspiration pneumonia are associated with increased likelihood of systemic adverse events. Multivariable models showed no evidence of association between Gross Motor Function Classification System and systemic adverse events. Multivariable models showed no evidence of association between BoNT-A dose and systemic adverse events.

PMID: 30146721

7. Onabotulinum toxin-A (Botox) for spastic equinus in cerebral palsy: a prospective kinematic study.
Hastings-Ison T1,2, Sangeux M1,2,3, Thomason P1,2, Rawicki B4,5, Fahey M6, Graham HK2,7,8.


Purpose: Botulinum toxin-A (or Botox) is widely used for the management of equinus gait in children with cerebral palsy but few recent studies have included instrumented gait analysis. Methods: This was a prospective cohort study. Gait analysis was performed four weeks before and four weeks after Botulinum toxin-A injection for spastic equinus to detect the maximum
effects on gait kinematics. Outcome measures included the Gait Profile Score (GPS), the Gait Variable Score (GVS) for the ankle, maximal ankle dorsiflexion and maximal knee extension at midstance. Results: In all, 37 children participated (20 boys); mean age five years seven months (4 years 1 month to 8 years 2 months); 19 with unilateral and 18 bilateral involvement. At a mean four weeks post-injection, the GPS and ankle GVS were unchanged. However maximum ankle dorsiflexion increased for the whole group; median 7.7° (confidence interval (CI) 4° to 10.6°) to 11.5° (CI 7.7° to 12.9°), p = 0.02. Maximum midstance knee extension was unchanged for the whole group, but median knee flexion increased in children with bilateral involvement; 10.9° (CI 7.4° to 20.8°) to 16.5° (CI 8.4° to 19.7°), p = 0.58. Conclusion: Injections of the gastrocsoleus for spastic equinus did not result in objective improvements in overall gait. Improvements in ankle dorsiflexion for children with bilateral involvement may be offset by deterioration at the knee. Level of Evidence: II - prospective cohort study, before and after intervention.

PMID: 30154931

8. Walk to run transition in children with cerebral palsy.
Scharr S1, Salami F2, Staut L2, Krautwurst B2, Wolf S2.


The motion data of three patients with cerebral palsy were used to analyze velocity, stride length and stride time parameters during walk to run transition. The results showed that subjects were able to perform the transition while keeping their dynamic equilibrium.

PMID: 30143427

Carollo JJ1, Worster K2, Pan Z3, Ma J4, Chang F5, Valvano J6.


BACKGROUND: The purpose of this retrospective study was to explore lower limb intersegmental coordination as a clinically important indicator of motor control mechanisms in individuals with cerebral palsy exhibiting stiff-knee gait. We used the relative phase of thigh and foot segments around foot-off to describe motor control, given the relevance of the pre-swing phase of gait to the existence of stiff-knee gait. METHODS: Traditional gait parameters and thigh/foot intersegmental coordination were calculated using pre-and postoperative kinematic data from a cohort of 54 subjects (92 legs) with spastic cerebral palsy. All participants had stiff-knee gait, walked without assistive devices, and underwent rectus femoris transfer surgery to improve swing period knee flexion. Analyses included correlations between a) preoperative intersegmental coordination and gait variables (knee flexion range, rate and gait performance) and b) pre-to-postoperative intersegmental coordination change and change in gait variables. FINDINGS: Thigh/foot intersegmental coordination significantly (P < 0.001) correlated with knee flexion range, rate and walking speed. Postoperative intersegmental coordination was significantly more uncoupled than preoperative. Pre-to-postoperative intersegmental coordination improvement also significantly correlated with improvements in knee flexion range, rate and walking speed. Pre-to-postoperative changes in intersegmental coordination accounted for 43% and 36% of variance in knee flexion range change and knee flexion rate change respectively. INTERPRETATION: Interssegmental coordination is a clinically important factor in knee flexion limitations associated with stiff-knee gait for individuals with cerebral palsy. These findings are a foundation for further study of intersegmental coordination measures as complements to traditional instrumented gait analysis.

PMID: 30145412

10. Ground reaction and solid ankle-foot orthoses are equivalent for the correction of crouch gait in children with cerebral palsy.
Ries AJ1, Schwartz MH1,2.


AIM: To investigate any performance differences between the solid ankle-foot orthosis (SAFO) and ground reaction ankle-foot orthosis (GRAFO) designs for correcting crouch gait in children diagnosed with cerebral palsy (CP). METHOD: We
retrospectively analyzed 147 individuals seen at our center who: (1) were diagnosed with diplegic CP, (2) walked with crouch gait, (3) had bilateral SAFO or GRAFO prescription, and (4) had three-dimensional gait analysis collected for both barefoot and orthosis walking conditions. RESULTS: Overall, no performance gap was identified between the SAFO and GRAFO groups (p = 0.828). A series of bootstrapped stepwise regression analyses indicated that ankle-foot orthosis (AFO) design was not predictive of crouch gait improvements. Improvements in crouch gait were instead shown to be predicted by AFO neutral angle and four patient factors: amount of dorsiflexion in stance, level of knee flexion contracture, age, and severity of crouch. INTERPRETATION: Our results show that the SAFO and GRAFO designs are equally effective at correcting crouch gait for individuals diagnosed with CP. WHAT THIS PAPER ADDS: No performance difference was detected between solid ankle-foot orthoses and ground reaction ankle-foot orthoses designs for crouch gait correction. Crouch gait improvement from ankle-foot orthoses (AFO) is influenced by AFO neutral angle. Other factors of influence include: dorsiflexion in stance, level of knee flexion contracture, age, and severity of crouch.

PMID: 30146679

11. Lower limb muscle fatigue during walking in children with cerebral palsy.
Eken MM1,2, BrAEndvik SM3,4, Bardal EM3, Houdijk H2,5, Dallmeijer AJ1, Roeleveld K3.


AIM: To investigate whether more prominent signs of muscle fatigue occur during self-paced walking in children with cerebral palsy (CP) compared to typically developing peers. METHOD: In this case-control study, 13 children with CP (four males, nine females; mean age [SD] 11y 4mo [3y 8mo]; nine in Gross Motor Function Classification System [GMFCS] level I, three in GMFCS level II, and one in GMFCS level III) and 14 typically developing peers (nine males, five females; mean age [SD] 9y 10mo [1y 10mo]) walked 5 minutes overground at a self-selected walking speed. Electromyography (EMG) median frequency and root mean square (RMS) were identified per gait cycle from EMG recordings of the tibialis anterior, gastrocnemius medialis, soleus, rectus femoris, and semitendinosus. Rate of change in those variables was analysed using mixed linear model analyses. RESULTS: The decrease in EMG median frequency of gastrocnemius medialis and soleus and increase in EMG-RMS of tibialis anterior, gastrocnemius medialis, and soleus were significantly larger in the most affected leg of children with CP compared with typically developing peers. INTERPRETATION: Increased selective muscle fatigue of the lower leg muscles was observed during self-paced walking in children with mild-to-moderate severe CP. This could contribute to and account for limited walking capacity. WHAT THIS PAPER ADDS: Children with cerebral palsy (CP) show more signs of lower leg muscle fatigue than typically developing peers. No signs of muscle fatigue were observed in upper leg muscles of children with CP.

PMID: 30156008

Takahashi K1, Mutsuzaki H2,3, Matakita Y3, Yoshikawa K1, Matsuda M1, Enomoto K1, Sano K1, Kubota A1, Mizukami M4, Iwasaki N2,5, Yamazaki M6.


[Purpose] This study aimed to determine the safety and immediate effect of a single training session with the Hybrid Assistive Limb (CYBERDYNE) on walking ability in patients with cerebral palsy. [Participants and Methods] This study included 20 patients with cerebral palsy (15 males, 5 females, mean age 15.0 ± 6.3 years; 19 with spastic cerebral palsy, 1 with athetoid cerebral palsy; Gross Motor Function Classification System level I: 4, II: 3, III: 9, and IV: 4). Participants completed a single 20-minute gait training session using the Hybrid Assistive Limb. The safety and immediate effect were evaluated. The immediate outcomes were gait speed and mean step length, and cadence before and after training. [Results] Two participants were excluded because they were not tall enough to use the Hybrid Assistive Limb. Eighteen participants performed the training. There were no serious adverse events during the training. Since 14 participants were able to walk on their own, walking evaluations were performed before and after training. Statistically significant improvements were observed in gait speed and mean step length. [Conclusion] Gait training using the Hybrid Assistive Limb is safe for patients with cerebral palsy and can produce immediate effects on walking ability in ambulatory patients with cerebral palsy.

PMID: 30154591
13. Use of 3D gait analysis as predictor of achilles tendon lengthening surgery outcomes in children with cerebral palsy. 
Pilloni G1,2, Pau M3, Costici F4, Condoluci C5, Gaffl M6.


BACKGROUND: In children with spastic Cerebral Palsy (CP), the treatment of equinus foot with Achilles tendon lengthening (ATL) surgery is associated with high incidence of overcorrection, which may result in crouch gait. AIM: We aimed to assess if gait pattern in preoperative time could be a predictor of the surgery outcome. DESIGN: Cross-sectional retrospective study. SETTING: Movement Analysis Lab, IRCCS San Raffaele Pisana Hospital, Rome (ITALY). POPULATION: Eighteen children (mean age 9.6±4.7 years) with spastic diplegia CP who underwent bilateral ATL surgery to correct equinus foot were involved. METHODS: Participants underwent 3D gait analysis before and approximately 12 months after surgery. Primary measures were spatiotemporal, kinematic (summarized by Gait Variable Scores, GVSs) and kinetic parameters. The gait patterns for each leg was defined from kinematic data, using a quantitative classification: Plantar Flexor Knee Extension (PFKE) index. The CP group was split into true equinus and jump gait. RESULTS: The equinus foot was successfully corrected as demonstrated by the improvement of GVS ankle dorsiflexion. However, there was a high rate of overcorrection in the true equinus, characterized by increases in knee flexion-extension GVS (8.7° pre vs. 16.7° post P<0.05) and knee flexion angle at initial contact (5.2° vs. 20.6° P<0.05) and by a decrease in the maximum ankle power generated at push-off (1.49 vs. 0.83 W/kg P<0.05). CONCLUSIONS: Assessment of motor phenotype in preoperative time are good predictors of the results of ATL surgery. In children with true equinus gait, the increase of knee flexion subsequent to ATL is an early indicator that this technique will lead to crouch gait. These results show the influence of true equinus and jump gait patterns on the outcomes of the ATL. CLINICAL REHABILITATION IMPACT: Therefore, we propose that this approach could have clinical value to evaluate and prescribe rehabilitation in children with CP disease, proposing different solutions depending on motor phenotype.

PMID: 30156089

14. Results of Ilizarov External Fixation in Rigid Equinus Deformity: An Experience of 30 Patients.
Ahmad K1, Ahmad Bhat S1, Avtar Agrawal R1, Agrawal R1.


BACKGROUND: Equinus deformity is associated with congenital disorders, trauma, infections, burns and neuromuscular diseases. Tip-toe gait resulting from equinus deformity often makes ambulation difficult. Many modalities of treatment are available but most of them are challenging due to high risk of skin and soft tissue complications. The purpose of this study was to evaluate the results of Ilizarov external fixator with or without minimal soft tissue release in patients with rigid equinus deformity. MATERIALS AND METHODS: 30 patients, with 21 (70%) males and 9 (30%) females, were included in this study. 17 (56.66%) patients had right foot, 10 (33.33%) had left foot and 3 (10%) had bilateral feet involvement. 17 (56.66%) had polio, 8 (26.66%) had cerebral palsy, 3 (10%) had posttraumatic and 2 (6.66%) had post-burn equinus deformities. Mean duration of equinus deformity was 5.1 years (range 1 to 11). The ankle range of motion and radiographic lateral tibiotalar angle were assessed preoperatively and at last final follow-up. Kling et al. criteria were used to assess the morphological and functional outcome. RESULTS: The mean preoperative rigid equinus deformity was -32° (range -40 to -20). The mean duration of Ilizarov external fixation required to correct the equinus deformity was 3.6 months (range 2-5.5 months). The mean preoperative tibiotalar angle was 150.2° (range 113° to 169°), which reduced to a mean angle of 102.8° (range 87° to 117°) at final follow-up. Mean dorsiflexion and plantar flexion at final follow-up was 15° (range -5° to 10°) and 31° (15° to 40°), respectively. 4 (13.33%) patients had superficial pin tract infection which was treated by serial dressings and oral antibiotics. 2 (6.66%) patients had a recurrence of 10° of equinus deformity. Excellent to good results were seen in 93.33% of patients whereas 6.66% had poor results. CONCLUSION: Ilizarov external fixation being a minimal invasive procedure allows a greater degree of equinus deformity correction.

PMID: 30152762

Sgandurra G1,2, Biagi L3, Fogassi L4, Sicola E1, Ferrari A5,6, Guzzetta A1,2, Tosetti M3, Cioni G1,2.

Little is known about the action observation network (AON) in children with unilateral cerebral palsy (UCP). Using fMRI, we aimed to explore AON and sensory-motor network (SMN) in UCP children and compare them to typically developed (TD) children and analyse the relationship between AON (re-)organization and several neurophysiological and clinical measures. Twelve UCP children were assessed with clinical scales and transcranial magnetic stimulation (TMS). For the fMRI study, they underwent a paradigm based on observation of complex and simple object-manipulation tasks executed by dominant and nondominant hand. Moreover, UCP and TD children carried out a further fMRI session to explore SMN in both an active motor and passive sensory task. AON in the UCP group showed higher lateralization, negatively related to performances on clinical scales, and had greater activation of unaffected hemisphere as compared to the bilateral representation in the TD group. In addition, a good congruence was found between bilateral or contralateral activation of AON and activation of SMN and TMS data. These findings indicate that our paradigm might be useful in exploring AON and the response to therapy in UCP subjects.

PMID: 30147718

16. Biological and Social Influences on the Neurodevelopmental Outcomes of Preterm Infants.
Burnett AC1, Cheong JLY2, Doyle LW3.


Although very preterm birth and very low birthweight are recognized risk factors for longer term developmental difficulties, there is a wide spectrum of outcomes for children and adolescents born preterm. Biological and social variables have the potential to explain this variability. Although current understanding of these influences and how they interact is incomplete, perinatal factors are related to permanent neurosensory impairments such as cerebral palsy, blindness, and deafness. Cognitive and academic outcomes are variably associated with biological and social variables across development, and the most robust correlates of behavior and mental health difficulties include early behavioral problems and family influences.

PMID: 30144851

17. Validation of the Spanish version of the Franciscan Hospital for Children Oral Health-Related Quality of Life questionnaire.


BACKGROUND: The Franciscan Hospital for Children Oral Health-Related Quality of Life questionnaire (FHC-OHRQOL-Q) is an instrument designed specifically for parents and caregivers of patients with special needs that has not yet been applied in Spain. The aim of this study was to adapt it to Spanish and evaluate its reliability and validity in patients with intellectual disability (ID) treated under general anesthesia. MATERIAL AND METHODS: The study was conducted in two different stages: a) cross-cultural adaptation of the original questionnaire, and b) cross-sectional study on 100 parents and caregivers who completed the piloted FHC-OHRQOL-Q. The patients were examined according to the WHO methodology. Dental treatments performed were recorded. Statistical tests were used to evaluate reliability (internal consistency) and validity (content, criterion, construct and discriminant) of the instrument. RESULTS: The mean age was 24 years (range=4-71 years). The most frequent causes of ID were psychomotor retardation (25%) and cerebral palsy (24%). The items most frequently answered by parents and caregivers were eating and nutrition problems (80%) and bad breath/taste (57%). Reliability (Cronbach's alpha coefficient) was considered excellent (alpha=0.88-0.95). The analysis of the factorial validity yielded similar results to the original questionnaire. The high response rate of items (>96%) allowed content validity. Criterion validity was confirmed by a significant correlation with questions on oral health and oral well-being. Discriminant validity was demonstrated by the significant association of ≥21.5 years of age with worse oral symptoms (p=0.034) and parental concerns (p=0.005), DMFT index ≥3 with daily life problems (p=0.02), ≥4 decayed teeth with daily life problems (p=0.001), and >2 dental extractions with oral symptoms (p=0.000), daily life problems (p=0.002) and parent's perceptions (p=0.043). CONCLUSIONS: The FHC-OHRQOL-Q in Spanish is a reliable and valid instrument to apply in clinical practice to evaluate the impact of OHRQOL in mostly adult patients with ID, accessible to Spanish-speaking parents and caregivers.

PMID: 30148470

Sheng N1, Ma J1, Ding W1, Zhang Y2.


Childhood chronic conditions have a considerable effect on the quality of life (QoL) of pediatric patients and their caregivers. The purpose of this meta-analysis was to evaluate the effects of caregiver-involved interventions on the QoL of children and adolescents with chronic conditions and their caregivers. METHODS: The PubMed, EMBASE, Web of Science, Cumulative Index of Nursing and Allied Health Literature, Academic Search Complete, Education Resource Information Center, and PsycINFO databases were searched for published randomized controlled trials from inception to April 2016. Two reviewers (NS and JM) independently screened included studies and assessed study quality. The meta-analyses and meta-regressions using random-effects models were performed with the Comprehensive Meta-analysis software (version 3, Biostat, Englewood, NJ). RESULTS: Fifty-four studies involving 10075 pediatric patients diagnosed with asthma, diabetes, cancer, hypersensitivity, cerebral palsy, arthritis, or sickle cell diseases and 10015 caregivers were included in our analysis. The interventions mainly involved education about disease, skill training, environment change, psychological intervention, physical exercise, experience sharing, monitoring, or social support. The results demonstrated that caregiver-involved interventions significantly improved the health-related QoL (HRQoL) of caregivers [standardized mean difference (SMD) = 0.26, 95% CI 0.14-0.38, p < 0.001], particularly those delivered through the face-to-face mode (SMD = 0.32, 95% CI 0.21-0.43, p < 0.001). However, no improvements in the QoL (SMD = 0.00, 95% CI -0.22 to 0.22, p = 1.00) and HRQoL (SMD = 0.06, 95% CI -0.02 to 0.14, p = 0.16) of children and both caregivers and children (SMD = 0.04, 95% CI -0.08 to 0.17, p = 0.52) were observed. CONCLUSIONS: This meta-analysis provides evidence on the positive effects of caregiver-involved interventions on the HRQoL of caregivers. Moreover, face-to-face mode is the delivery approach with a promising effect on the HRQoL of caregivers. Further research on conditions not found in this review is warranted.

PMID: 30167936

19. [Clinical cases of multiple sclerosis in children with cerebral palsy].

Sivertseva SA1, Bykova OV2, Bakhtiyarova KZ3, Prilenskaya AM1, Sivertsev MY4, Kandala NS1, Bazhukhin DV1, Smirnova NF5, Guseva ME5, Boyko AN5.


The careful differential diagnosis is very important in pediatric cases of multiple sclerosis (MS). It has special difficulties, if MS started in patients with residual neurological pathology. Two cases of development of MS in children with cerebral palsy (CP) are presented. The clinical features and diagnostic difficulties in such comorbid situations are discussed.

PMID: 30160669


Carratala-Marco F1, Andreo-Lillo P1, Martinez-Morga M2,3, Escamz-Martinez T3, Botella-Lopez A2, Bueno C2, Martinez S2.


The engrailed homeobox protein (EN) plays an important role in the regionalization of the neural tube. EN distribution regulates the cerebellum and midbrain morphogenesis, as well as retinotectal synaptogenesis. In humans, the EN1 and EN2 genes code for the EN family of transcription factors. Genetic alterations in the expression of EN2 have been related to different neurologic conditions and more particularly to autism spectrum disorders (ASD). We aimed to study and compare the phenotypes of three series of patients: (1) patients with encephalic structural anomalies (ESA) and abnormalities in the genomic (DNA) and/or transcriptomic (RNAm) of EN2 (EN2-g), (2) ESA patients having other gene mutations (OG-g), and (3) ESA patients free of these mutations (NM-g). Subjects and Methods: We have performed a descriptive study on 109 patients who suffer from mental retardation (MR), cerebral palsy (CP), epilepsy (EP), and behavioral disorders (BD), showing also ESA in their encephalic MRI. We studied genomic DNA and transcriptional analysis (cDNA) on EN2 gene (EN2), and in other genes (OG): LB1, PTAFR, PAFAH1B2, PAFAH1B3, FGF8, Pax2, D17S379, D17S1866, and SMG6 (D17S5), as a
routine genetic diagnosis in ESA patients. Results: From 109 patients, fifteen meet the exclusion criteria. From the remaining 94 patients, 12 (12.8%) showed mutations in EN2 (EN2-g), 20 showed mutations in other studied genes (OG-g), and 62 did not showed any mutation (NM-g). All EN2-g patients, suffered from MR, nine EP, seven BD and four CP. The proportions of these phenotypes in EN2-g did not differ from those in the OG-g, but it was significantly higher when comparing EN2-g with NM-g (MR: p = 0.013; EP: p = 0.001; BD: p = 0.0001; CP: p = 0.07, ns). Groups EN2-g and OG-g showed a 100 and a 70% of comorbidity, respectively, being significantly (p = 0.04) greater than NM-group (62.9%). Conclusion: Our series reflects a significant effect of EN2 gene alterations in neurodevelopmental abnormalities associated to ESA. Conversely, although these EN2 related anomalies might represent a predisposition to develop brain diseases, our results did not support direct relationship between EN2 mutations and specific clinical phenotypes.

PMID: 30147646

Thumar V1, Squires JH2, Spicer PJ3, Robinson AL4, Chan SS.


Ultrasound is one of the most important imaging modalities in pediatric imaging because of its accessibility, portability, lack of ionizing radiation, and ability to generally perform examinations without need for sedation. Ultrasound elastography can measure the stiffness of various tissues. This review article aims to discuss how ultrasound elastography has performed in evaluating multiple pathologies in the pediatric population. The best studied pediatric applications are in liver diseases such as fibrosis, biliary atresia, and hepatic vascular congestion. Measuring muscle stiffness in cerebral palsy is the most promising pediatric musculoskeletal application, but many other applications are in the early stages of research. Other applications in pediatric small organ imaging have been explored and still need more study before gaining clinical relevance.

PMID: 30169493

22. Neuroprotective exendin-4 enhances hypothermia therapy in a model of hypoxic-ischaemic encephalopathy.
Rocha-Ferreira E1,2, Poupon L3, Zelco A3, Leverin AL1, Nair S1, Jonsdotter A1, Carlsson Y1, Thornton C4, Hagberg H1,5, Rahim AA3.


Hypoxic-ischaemic encephalopathy remains a global health burden. Despite medical advances and treatment with therapeutic hypothermia, over 50% of cooled infants are not protected and still develop lifelong neurodisabilities, including cerebral palsy. Furthermore, hypothermia is not used in preterm cases or low resource settings. Alternatives or adjunct therapies are urgently needed. Exendin-4 is a drug used to treat type 2 diabetes mellitus that has also demonstrated neuroprotective properties, and is currently being tested in clinical trials for Alzheimer's and Parkinson's diseases. Therefore, we hypothesized a neuroprotective effect for exendin-4 in neonatal neurodisorders, particularly in the treatment of neonatal hypoxic-ischaemic encephalopathy. Initially, we confirmed that the glucagon like peptide 1 receptor (GLP1R) was expressed in the human neonatal brain and in murine neurons at postnatal Day 7 (human equivalent late preterm) and postnatal Day 10 (term). Using a well characterized mouse model of neonatal hypoxic-ischaemic brain injury, we investigated the potential neuroprotective effect of exendin-4 in both postnatal Day 7 and 10 mice. An optimal exendin-4 treatment dosing regimen was identified, where four high doses (0.5 µg/g) starting at 0 h, then at 12 h, 24 h and 36 h after postnatal Day 7 hypoxic-ischaemic insult resulted in significant brain neuroprotection. Furthermore, neuroprotection was sustained even when treatment using exendin-4 was delayed by 2 h post hypoxic-ischaemic brain injury. This protective effect was observed in various histopathological markers: tissue infarction, cell death, astrogliosis, microglial and endothelial activation. Blood glucose levels were not altered by high dose exendin-4 administration when compared to controls. Exendin-4 administration did not result in adverse organ histopathology (haematoxylin and eosin) or inflammation (CD68). Despite initial reduced weight gain, animals restored weight gain following end of treatment. Overall high dose exendin-4 administration was well tolerated. To mimic the clinical scenario, postnatal Day 10 mice underwent exendin-4 and therapeutic hypothermia treatment, either alone or in combination, and brain tissue loss was assessed after 1 week. Exendin-4 treatment resulted in significant neuroprotection alone, and enhanced the cerebroprotective effect of therapeutic hypothermia. In summary, the safety and tolerance of high dose exendin-4 administrations, combined with its neuroprotective effect alone or in conjunction with clinically relevant hypothermia make the repurposing of exendin-4 for the treatment of neonatal hypoxic-ischaemic encephalopathy particularly promising.

PMID: 30165597
23. Therapeutic cooling is associated with better function in children with cerebral palsy due to birth asphyxia according to the national health care quality registry CPUP.
Westbom L.1, Hägglund G.2.


Hypothermic treatment after birth asphyxia was introduced as a recommended practice in Sweden in 2007. CPUP is a national quality register and surveillance program that encompasses the total population of children with cerebral palsy (CP) in Sweden. In an analysis of CPUP data children with CP and asphyxia treated with cooling were compared to children with CP and asphyxia who were not cooled. A lower proportion of severe motor and cognitive impairments were observed in the group that did receive the cooling/hypothermic treatment.

PMID: 30152852

24. Long-Term Neurodevelopmental Outcome of Monochorionic Twins after Laser Therapy or Umbilical Cord Occlusion for Twin-Twin Transfusion Syndrome.
Schou KV1,2, Lando AV3, Ekelund CK1, Jensen LN1, Jørgensen C1, Nørgaard LN1, Rode L4, Sogaard K1, Tabor A1,2, Sundberg K1.


INTRODUCTION: We sought to assess the incidence of severe neurodevelopmental impairment (NDI) in monochorionic twins treated for twin-twin transfusion syndrome (TTTS) and compare it to the incidence in uncomplicated monochorionic twins. MATERIAL AND METHODS: We included TTTS pregnancies treated by fetoscopic selective laser coagulation (FSLC) or umbilical cord occlusion (UCO) in 2004-2015. Primary outcome was severe NDI defined as cerebral palsy, bilateral blindness or bilateral deafness (ICD-10 diagnoses), and severe cognitive and/or motor delay (assessed by the Ages and Stages Questionnaires [ASQ]). RESULTS: A total of 124 children after TTTS and 98 controls were followed up at 25 months of age (SD 11.4). Severe NDI was found in 8.9% of the TTTS children (10.5% [9/86] after FSLC; 5.3% [2/38] after UCO) compared to 3.1% in the control group (p = 0.10). The odds ratio for severe NDI was 1.8 in cases versus controls (p = 0.37). The total ASQ score was significantly lower in the TTTS group than in controls (p = 0.03) after FSLC (p = 0.03) and after UCO (p = 0.14). DISCUSSION: Children after TTTS appear to have a higher risk of severe NDI and score significantly lower on the ASQ compared to monochorionic twins from uncomplicated pregnancies.

PMID: 30149379

25. Early Diagnosis and Treatment of Cerebral Palsy in Children with a History of Preterm Birth.
Spittle AJ1, Morgan C2, Olsen JE3, Novak I2, Cheong JLY4.


Infants born preterm are at increased risk of cerebral palsy (CP), with the risk increasing with decreasing gestational age. Although preterm children are at increased risk of CP compared with their term-born peers, most preterm children do not have CP and thus, it is important to have a standardized process for detecting those children at high risk of CP early. A combination of clinical history, neuroimaging, and physical examination is recommended to ensure early, accurate diagnosis. Early detection of CP is essential for timely early intervention to optimize outcomes for children and their families.

PMID: 30144846

Herrera TI1, Edwards L2, Malcolm WF2, Smith PB3, Fisher KA2, Pizoli C4, Gustafson KE2, Goldstein RF2, Cotten CM2, Goldberg RN2, Bidegain M5.

BACKGROUND: Therapeutic hypothermia reduces the risk of death, or moderate to severe neurodevelopmental impairment (NDI) in term infants with hypoxic–ischemic encephalopathy (HIE). Reports of its safety and efficacy in preterm infants are scarce. OBJECTIVE: Report short and long-term outcomes of preterm infants with HIE who received therapeutic hypothermia. METHODS: A retrospective cohort analysis of all preterm infants <36 weeks' gestation with HIE who received whole body hypothermia in a single center from January 2007 to April 2015. The primary outcome was death or moderate to severe NDI defined by moderate or severe cerebral palsy, severe hearing or visual impairment, or cognitive score < 85 on the Bayley Scales of Infant Development III (BSID III) at 18-24 months' adjusted age. RESULTS: 30 infants with a median gestational age and birthweight of 35 weeks' (range; 33-35) and 2575 g (1850-4840) and a median first postnatal blood pH of 6.81 (6.58-7.14). Complications included coagulopathy (50%), early clinical seizures (43.3%), arterial hypotension (40%), persistent metabolic acidosis (37%) and thrombocytopenia (20%). Four infants died before or soon after discharge (18.2%). Eighteen surviving infants (69.2%) had follow up data; 7 of them had moderate to severe NDI (38.9%). Cognitive, motor and language mean composite BSID III scores were 84 (54-110), 83 (46-118), and 78 (46-112). Death or moderate to severe NDI occurred in 11/22 (50%) infants with known outcomes. CONCLUSION: Large randomized trials on efficacy and safety are needed in this highly vulnerable population as the incidence of complications and the combined outcome of death and NDI is concerning.

PMID: 30144709

27. Cerebral palsy.
Barnett R.


PMID: 30152380

28. A patient-centered research agenda for cerebral palsy: an important tool for the future.
Samson-Fang L1.


PMID: 30151945