

CEREBRAL PALSY & NEURODISABILITY

FP01

GLIAL PRECURSOR CELL TRANSPLANTATION IMPROVES BEHAVIORAL AND NEUROPATHOLOGICAL OUTCOME IN A MODEL OF NEONATAL WHITE MATTER INJURY

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Aims: Perinatal White Matter Injury (PWMI) is the leading cause of cerebral palsy and other neurocognitive deficits in prematurely born children. There is currently no restorative therapy available in PWMI, but cell therapy has been widely discussed. The objective of this study was to determine the fate and effect of glial restricted precursor cell (GRP) transplantation in an ischemic mouse model of PWMI.

Methods: Neonatal CD-1 mice underwent unilateral carotid artery ligation on postnatal day 5 (P5); at P22, intracallosal injections of either eGFP-GRP cells or normal saline were performed in control and ligated mice. Neurobehavioral, and postmortem studies were performed at various time points between 1, 4 or 8 weeks post-transplantation

Results: GRP survival was comparable at 1 month but significantly lower at 2 month post-transplantation in PWMI mice compared to control. Surviving cells showed better migration capability in controls, however, the differentiation capacity of transplanted cells was similar in control and PWMI mice. There was a significant increase in mean hemispheric myelin basic protein density along with a significant decrease in SMI32 staining in GRP-transplanted PWMI mice compared to saline-treated PWMI mice. Saline-treated PWMI mice showed a significant reduction of startle amplitude compared to controls, while this abnormal behavioral response was completely abolished in GRP-transplanted animals.

Conclusion: Despite reduced survival of transplanted GRP cells, these cells improved behavioral and neuropathological outcomes in an ischemia-induced PWMI model. Further research is needed to determine the mechanisms by which these precursor cells lead to amelioration of PWMI.

FP02

GO FOR THE CAUSE: SIGNIFICANT GENOMIC REARRANGEMENTS IN CRYPTOGENIC CEREBRAL PALSY

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Introduction: Cerebral palsy (CP) is an "umbrella term" for motor disability diagnosed in childhood, which is caused by various brain injuries. Genomic rearrangements (GRs) are micro-deletions/duplications that were reported in children with neurodisabilities. We investigated the prevalence and characteristics of GRs in individuals for whom the etiology of CP is unknown, termed 'cryptogenic CP'.

Methods: 51 participants, age 10.5±7.8 years, with non-progressive pyramidal and/or extra-pyramidal signs since infancy and no identified etiology were enrolled. GRs were tested using Affymetrix platform and classified as: pathogenic GRs, likely pathogenic, likely benign or no GRs. Main outcome measures were: positive (pathogenic and likely pathogenic GRs) or negative (likely benign and no GRs) findings.

Results: 38 GRs were found in 25/52 (48%) participants, most of which were considered positive (10/25 pathogenic and 6/25 likely pathogenic versus 9/25 likely benign) and were not previously reported to cause motor disability (12/16). Multiple GRs and de-novo findings were more common in the positive GRs group than in the negative group ($p < 0.0001$ for both). De-novo GRs were common among individuals with a first and/or a second degree relative with a significant neurological disorder ($n=4/8$). Dysmorphic features and non-motor comorbidities were more prevalent in individuals with significant/positive GRs ($p < 0.05$ for both).

Conclusion: GRs are common in individuals with cryptogenic CP. They are more likely to be multiple and de-novo even in families with another affected member. This useful test should be performed in individuals with CP of unknown etiology.

FP03

DEVELOPMENT OF A PORTABLE ELECTRONIC GONIODYNAMOMETER FOR THE EVALUATION OF EQUINUS FOOT IN CEREBRAL PALSY.

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The assessment of the equinus foot in children with spastic cerebral palsy (CP) contributes significantly to the identification of musculoskeletal disorders and to the treatment of abnormal gait.

Methods: A newly developed Portable Electronic Goniodynamometer (PEGD) was designed to passively move the ankle joint toward dorsiflexion at speeds imposed through specific software and to provide measurements of range of motion and resistance to movement. A pilot study was conducted on 26 equinus foot to investigate the reliability of the measures provided by the new equipment and by the isokinetic dynamometer in passive mode (IDPM) the method most frequently used in the literature for such measures. The intra- and interclass reliabilities of both devices were checked at three speeds (10, 30 and 60°/sec) to verify which is more reliable for this measurement, and the test results provided by the devices were compared.

Results: For PEGD, a high intraclass correlation was found for peak torque and angle of peak torque at a 10°/s passive ankle dorsiflexion, and there was a high interclass correlation for all speeds, tests and variables. The IDPM displayed no agreement in any of the test situations. There was also no correlation between PEGD and IDPM data.

Conclusions: PEGD is a portable device able to passively move the ankle joint and provide reliable measurements of range of motion and resistance to dorsiflexion movement at 10°/s.

FP04

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION EFFECTS ON MOTOR LEARNING IN PERINATAL STROKE: SHORT-TERM OUTCOMES FROM THE PLASTIC CHAMPS TRIAL.

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Background: Perinatal stroke causes hemiparetic cerebral palsy. Developmental plasticity models have informed central therapeutic targets. Repetitive transcranial magnetic stimulation (rTMS) can modulate motor learning in adult stroke but is untested in perinatal brain injury.

Methods: PLASTIC CHAMPS (www.clinicaltrials.gov/NCT01189058) was a randomized, blinded factorial trial of rTMS and constraint therapy (CIMT) in stroke-induced cerebral palsy. Children 6-18 years participating in a 2 week goal-directed motor learning camp were randomized to inhibitory rTMS (1Hz, 1200 stimulations) over non-lesioned motor cortex, CIMT, both or neither. Primary short-term outcome was 1 week post-camp Melbourne Assessment (MA). Additional outcomes included Assisting Hand Assessment (AHA), Canadian Occupational Performance Measure (COPM), and safety/tolerability. Corticospinal tract (CST) orientation was defined using single-pulse TMS.

Results: All forty-five children completed the trial (median 11.4yrs, 67%/33% arterial/venous, mean MA (SD) 74(23) %). All improved on multiple measures at 1 week. Compared to sham, rTMS was associated with greater gains in MA (5.51(5.9) versus 1.89(4.7), $p=0.027$). CIMT did not affect 1 week MA. Group comparison suggested greater improvements for rTMS alone compared to CIMT alone ($p=0.06$). rTMS and CIMT effects did not appear synergistic. rTMS did not decrease function in children with ipsilateral CST projections (MA increased 5.1(4.6) %, $p=0.04$). Unaffected hand function did not decrease with rTMS or CIMT. Procedures were well tolerated with no serious adverse events.

Conclusions: Non-invasive brain stimulation trials are feasible in children with perinatal stroke. Inhibitory, contralesional rTMS may enhance motor learning therapy in stroke-induced cerebral palsy. Long-term outcomes will help determine clinical relevance.

FP05**COMPARATIVE STUDY OF BACLOFEN AND TIZANIDINE IN REDUCING SPASTICITY IN CEREBRAL PALSY- A RANDOMIZED CONTROLLED TRIAL**

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Aims: To compare efficacy of oral baclofen and tizanidine in reducing spasticity in cerebral palsy.

Methods: This randomized controlled trial includes 66 spastic cerebral palsy cases aging 1- 5yrs. 33 received Baclofen and another 33 received Tizanidine. Cases were assessed before starting studied drugs for i) **Muscle tone** through Modified Ashworth Scale (MAS) ii) **Angle for crouch** measured by Goniometer and iii) **Foot contact with ground**. The angles for crouch gait and foot contact were described by **Physician Rating Scale**. Finally the overall **Motor function** was measured by **GMFCS**. Intensive physiotherapy was given uniformly to both groups. The cases were re-assessed 4 weekly till 5 months follow-up through above scales to compare drug effects and side effects if any.

Results: At 3 month follow up Tizanidine showed significant improvement in foot contact and gross motor function over Baclofen, $p=0.013$ and $p=0.024$ respectively. At 5 month Tizanidine demonstrated significant reduction of muscle tone over Baclofen ($p=0.026$). Tizanidine demonstrated statistically significant superior efficacy in reducing spasticity over Baclofen regarding reduction of muscle tone, improvement in foot contact and gross motor function ($P < 0.001$, $P < 0.001$, $P = 0.001$ respectively). Tizanidine also had less side effects.

Conclusion: Tizanidine had superior efficacy over Baclofen in reducing spasticity with regards to muscle tone, foot contact and gross motor function. It had also fewer side effects than Baclofen.

FP06**CEREBELLAR VERMIAL INVOLVEMENT IN PATIENTS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY AND RELATION TO COGNITIVE FUNCTIONS.**

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Introduction: The cerebellum contributes to attention, language and visuo spatial function.

Aim of the study: we aimed to evaluate degree of cerebellar involvement in magnetic resonance imaging (MRI) of patients with neonatal hypoxic ischemic encephalopathy (HIE), to assess the relevance of cerebellar vermian atrophy to severity of the disease and its relation to patients' cognitive function tests.

Methods: Thirty children with HIE were enrolled. They were investigated by MRI, VEP and cognitive functions assessment.

Results: Abnormalities in MR images were mainly confined to posterior putamen, ventrolateral thalamus and paracentral white matter. According to total scores of changes in these areas, patients were grouped into group I of 20 patients (66.7%) having scores of 5 of 9 or less and group II of 10 patients (33.3%) having scores of 6 of 9 or more. Seven patients (23.3%) had high T2 signal intensity in the cerebellar vermis and high signal lesions in affected sites. The presence of vermian involvement was significantly associated with MR evidence of severe hypoxic damage in typically affected sites ($p=0.038$). Cognitive function tests were significantly impaired in patients of group II and in patients with cerebellar vermian atrophy compared to patients of group I and patients without vermian atrophy, respectively ($p<0.05$). Abnormal VEP were more frequent in patients of group II compared to group I.

Conclusion: Our results may suggest that vermian atrophy in MR images of patients with HIE can predict cognitive impairment and thus may be suggesting early intervention for learning disabilities.

FP07**PREVALENCE & RISK FACTORS FOR NEUROLOGICAL DISORDERS IN CHILDREN AGED 9-15 YEARS IN NORTHERN INDIA**

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Aim: To compute prevalence and study risk factors for neurological disorders (ND) – epilepsy, intellectual disability, motor, vision and hearing defects in children aged 9-15 years in the community.

Methods: A new instrument – Lucknow Neurological Screen (LNS) was developed and validated. This was used in a two stage community survey for NDs in rural and urban areas of Lucknow, India. Screen positives and a random proportion of screen negatives were validated using predefined criteria. Prevalence of different NDs was calculated by weighted proportions. Demographic, socioeconomic and medical risk factors were compared between validated subjects who were positive and negative for ND by univariate and logistic regression analysis. Final etiological diagnoses were recorded.

Results: Of 6431 children screened (mean age (SD) 139.2 (24.3) months; male 3412, female 3019) 221 were positive. 214 screen positives and 251 screen negatives were validated. Combined prevalence of NDs was 31.3 per 1000 children of this age (weighted 95% confidence intervals 16.5, 46.4). The final model for risk factors for ND on logistic regression included older age ($p=0.0142$), mud house ($p < 0.001$), delayed cry at birth ($p=0.0291$) and previous head injury ($p=0.0354$). Wide-ranging causes of ND were identified in the community including postpolio paralysis, tuberous sclerosis, Duchenne muscular dystrophy and sub acute sclerosing panencephalitis.

Conclusions: Prevalence of ND is high in this region. Lower socioeconomic status, perinatal difficulties and head injury are predictors of ND. These factors are largely modifiable.

FP08**NEUROLOGICAL MANIFESTATIONS OF INCONTINENTIAPIGMENTI**

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Introduction: Incontinentia Pigmenti (IP) is a condition that may affect several organs, including the skin, teeth, eyes, and central nervous system (CNS). The aim of the research is to present a descriptive study of neurological manifestations in 25 cases of IP, and to determine the type and severity of these anomalies.

Methods: Retrospective analysis was performed on the clinical data of 25 children with IP, including clinical manifestations (cutaneous, hair, nail, teeth and ophthalmologic abnormalities), age of onset, family history, psychomotor development, CNS types of anomalies, radiological [ultrasonography, computed tomography and magnetic resonance (MRI)] and neurophysiological findings [electroencephalogram (EEG)].

Results: The average age of onset was 8.1 months; CNS anomalies were diagnosed for 32%: the most common were developmental delay (20%), mental retardation (20%), microcephaly (16%), and epilepsy (12%): 1 West Syndrome who evolved to partial epilepsy, and 2 partial epilepsies. One of the patients presented muscle hypotonia, muscle weakness with no reflexes, neurogenic damage in electromyography, Spinal Muscle Atrophy molecular genetic test negative. EEG revealed characteristic findings in 20% patients (2 generalized EEG abnormalities, 2 focal EEG abnormalities and 1 hypsarrhythmia). MRI showed 8% patients with white matter hyperintensities and 4% polymicrogyria.

Conclusion: We found similar number of neurological features than literature has reported. Neurological impairments were the most severe consequences. A wide spectrum of neurological presentations was found. Due to this, and because neurological anomalies usually occur from the neonatal through the early infantile period, fast referral to Pediatric neurologists should be routinely considered

FP09**HEMIPLEGIC CEREBRAL PALSY- ETIOLOGY, CLINICAL FEATURES AND OUTCOME**

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Cerebral Palsy (CP) is defined as a group of disorders of development of movement and posture, which limits activity that is attributed to non-progressive disturbances that occur in the developing fetal or infant brain.

Our study investigated the etiology, clinical features and outcome of a cohort of children with hemiplegic CP recruited from 3 medical centers in Israel.

The cohort includes 135 children, aged between 4 to 28 years: 71 (53%) males, 58% full-term and 42% who were premature, out of which 16% were born at 30 weeks and below. Nineteen (14%) children were twins, of whom 17 were preterm and 2 were full-term ($p < 0.001$). The right side was involved in 60% of the cases and left side in 40% of the cases. Apgar scores after 1 minute were 8 ± 2.4 at full-term and 6.8 ± 2.8 in premature ($p < 0.05$). There was no difference in the 5 minute Apgar score.

The overall frequency of epilepsy in the cohort was 26%. There was no difference in the frequency at full-term compared to premature cases. Eighty-five children (64%) in the cohort had a normal cognitive level and 36% were below the normal level. No statistical significant difference was found when comparing the cognitive level of full-term to premature children. However, the percentage of normal cognitive children was higher in the CP children without epilepsy as compared to the group with epilepsy ($p < 0.05$).

The most common etiologies were: prenatal stroke (17%), perinatal stroke (16%), periventricular leucomalacia (PVL, 13%) and intraventricular hemorrhage (IVH, 13%).

In conclusion, prematurity plays a significant role in hemiplegic CP. Preterm children do not differ from full-term in their outcome in terms of the prevalence of epilepsy and cognitive dysfunction. PVL and IVH are common causes for hemiplegic CP after pre- and perinatal stroke.

FP10**STUDY OF CLINICAL PATTERNS AND RISK FACTORS OF CEREBRAL PALSY IN CHILDREN IN RURAL HOSPITAL, INDIA**

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Introduction: Cerebral palsy (CP) is a common pediatric disorder occurring in about 2 to 2.5 per 1000 live births. It is a chronic motor disorder resulting from a non-progressive (static) insult to the developing brain. The aim of study was to identify the risk factors & clinical patterns of CP

Methods: A case-control study was conducted to investigate the risk factors of CP. The cases were 60 CP children who were admitted to AVBRH hospital, Sawangi from Jan 2012 to Dec 2012 and controls ($n=120$) matched for sex & age were selected without CP who were admitted during the same period. The detailed history and neurological examination was done to confirm the diagnosis of CP.

Results: Spastic CP was the commonest type (76%), while mixed and atonic CP was the least type. Quadriplegic CP (68%) was the commonest topographical subtype. 72% of cases were born at term whereas 28% were preterm. Factors associated with an increased risk of CP were: abruptio placenta, premature rupture of membranes, prematurity, preterm labour, cesarean section and low birth weight. Septicemia,

meningitis, hyperbilirubinemia and neonatal convulsion were associated with an increased risk of CP in the neonatal period. In the logistic regression models prematurity and asphyxia were significantly associated with an increased risk of CP.

Conclusion: The most common clinical pattern of CP was spastic quadriplegic CP. Neonatal convulsion, neonatal jaundice, neonatal infection and antepartum hemorrhage are significant risk factors that can increase the prevalence of CP.

FP11**THE STUDY ON QUALITY OF LIFE OF CHILDREN WITH CEREBRAL PALSY**

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Aim: To study the quality of life of children with cerebral palsy.

Methods: With the PedsQL4.0, 113 children with cerebral palsy were studied, and 52 children with common illness and 314 normal children were also studied and compared. With the PedsQL of school functioning, the children of these three groups who had been to school or kindergarten were also studied and compared.

Result: The score of physiology functioning, communication functioning and total score of PedsQL in children with cerebral palsy were lower than those in the children with common illness and normal children. The difference has statistical significance. The score of emotional functioning in children with cerebral palsy was only lower than that in the normal children, the difference has statistical significance. The score of school functioning in children with cerebral palsy was significant lower than that in children with common illness and normal children ($P < 0.01$).

Conclusion: The quality of life of children with cerebral palsy is much lower than children with common illness and normal children. The illness has severe effect on the school functioning of children with cerebral palsy. Therefore, the whole improve of quality of life is the goal for the rehabilitation of children with cerebral palsy

FP12**MULTIPLE REGRESSION ANALYSIS OF QUALITY OF LIFE IN CHILDREN WITH CEREBRAL PALSY**

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Objective To analyse the correlation factors influencing quality of life (QOL) in children with cerebral palsy (CP).

Methods 80 children with CP and 80 healthy children were measured by Pediatric Quality of Life Inventory Version 4 (PedsQL4.0) to assess their QOL and then compared differences in QOL of children between two groups. Children with CP were also assessed using Gesell Developmental Scale(GDS) and Gross Motor Function Classification System(GMFCS) to test their developmental quotient(DQ) and severity degree(GMFCS), and then the correlation among QOL, age, sex, family income, clinical type, severity degree, intelligence degree of children with CP were analysed by multiple regression analysis.

Results Significant differences in mean scores favouring control group were found in physical functioning/aspect, emotional functioning, social functioning, psychological aspect and total score ($P < 0.01$). Intelligence degree and severity degree correlated to total score of QOL. Severity degree, intelligence degree and age correlated to physical aspect. Intelligence degree correlated to psychological aspect.

Conclusion CP reduces children's QOL in full-scale. Severity degree and intelligence degree are two important factors influencing QOL in children with CP.