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Safety of IncobotulinumtoxinA in Multipattern Treatment of Upper and Lower Limb Spasticity in Children/Adolescents With Cerebral Palsy: Pooled Analysis of 3 Large Phase 3 Studies

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precipitated by hyperviscosity, the most common management method is IV hydration and observation. However, as in our case, enteral hydration can also be very effective with excellent long-term outcomes.

Poster 094

COL4A1 mutation: Don't miss the antenatal clues!

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Objectives: The COL4A1 (Collagen type IV alpha 1) gene encoding the type IV collagen alpha 1 chain is an essential component of the basal membrane stability. The neurological manifestations of this potentially multi-system disease are well described including porencephaly, cortical malformations and small vessel disease. We report preterm twins who were diagnosed with COL4A1 gene-associated cerebral disease following surveillance antenatal ultrasound scanning demonstrating evolving intracranial haemorrhage and porencephaly.
Methods: A fit and well mother underwent regular antenatal surveillance imaging during her second pregnancy with twins, as her first pregnancy was terminated at 36 weeks following antenatal scans revealing intraparenchymal haemorrhage and cysts. A post-mortem MRI at 37 weeks confirmed a large porencephalic cyst. The antenatal scans for the twins demonstrated progressive intracranial haemorrhage from 20 weeks gestation evolving into cysts by 28 weeks gestation. They were born prematurely at 31 weeks gestation when she went into spontaneous labour.
Results: Although prematurity is associated with intraventicular haemorrhages and subsequent porencephalic cyst formation, this is usually triggered off by the process of labour, which affects the fragility of preterm brain vasculature. In this case, the preceding antenatal evolution of intracranial events warranted further consideration. Genetic testing confirmed a pathogenic heterozygous mutation in COL4A1 in both twins.
Conclusions: COL4A1 mutations are most frequently tested in term infants who are born with porencephalic cysts. We highlight the importance of testing for this in infants of all gestations who present with unexplained spontaneous antenatal intracranial haemorrhage or porencephaly.

Poster 095

Caudal Regression Syndrome type III following gestational diabetes (in a Sri Lankan setting)

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Introduction: Caudal Regression Syndrome is a rare congenital anomaly which has an incidence of approximately 1 per 100,000 new-borns and severe variants are often associated with cardiovascular, pulmonary, gastrointestinal, and musculoskeletal abnormalities. We report a two-month old child in whom the diagnosis of caudal regression syndrome type III was confirmed based on clinical and radiological characteristics.
Case Report: A two-month-old child presented for evaluation of multiple congenital abnormalities. He had two healthy older siblings. Antenatal period was uncomplicated apart gestational diabetes which was not controlled during the second trimester and before the diagnosis was made. He had been having urinary and faecal incontinence since birth. Growth was age appropriate. Physical examination revealed a narrow pelvis, bilateral knee flexion contractures, bilateral leg muscle atrophy, and bilateral congenital talipes equinovarus deformity with diminished ankle joint creases. He had clinical evidence bilateral hip dysplasia with positive Ortolani's and Barlow's test. Other abnormalities included micropenis (stretched penile length – 1 cm), displaced patulous anus with tiny pressure sores and flat, dimpled buttocks (Patient photographs available). Ultrasound revealed complete agenesis of the sacrum and L5 vertebra. The iliac bones were articulated with L4 vertebral body. The cord had terminated abruptly at L1 level. Thickened conus medullaris was seen. There was no evidence of either meningomyelocele or meningocele. Ultrasound of hips revealed bilateral hip dysplasia with shallow acetabula. Overall, the findings were in keeping with type III caudal regression syndrome. Ultrasound abdomen showed no evidence of renal agenesis, neuropathic bladder, vesico-ureteric reflux, or bowel malrotation. Parents were counselled regarding long term prognosis and available supportive treatment options. Long-term follow up was arranged with general paediatrician, paediatric neurologist, and orthopaedic surgeon.
Conclusion: Poorly controlled/undiagnosed gestational diabetes is not an uncommon scenario in a Sri Lankan setting. This report highlights importance of optimal control of antenatal blood sugars to prevent several future complications including sacral agenesis in the new-born.

Poster 096

Safety of IncobotulinumtoxinA in multipattern treatment of upper and lower limb spasticity in children/adolescents with cerebral palsy: pooled analysis of 3 large phase 3 studies

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Introduction: This analysis assessed the safety and tolerability of repeated incobotulinumtoxinA treatment for lower-limb (LL), upper-limb (UL), or combined LL/UL spasticity in ambulant and non-ambulant children/adolescents with cerebral palsy (CP) using pooled data from 3 large Phase 3 studies.
Methods: Pediatric patients with spasticity (2–17 years of age; uni- or bilateral CP; Gross Motor Function Classification System [GMFCS] level I-V; Ashworth Scale [AS] score ≥2 in clinical patterns for treatment; clinical need for treatment) were enrolled.

Patients received total body incobotulinumtoxinA doses of 16 U/kg body weight (BW, ≤400 U) for LL spasticity in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL/UL treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Adverse events (AEs) were assessed in the pooled population.

Results: In total, 907 patients (59.6% male, mean [SD] age 6.7 [4.2] years, BW 23.3 [13.9] kg) received multipattern treatment; 753 patients (83.0%) completed the studies and received up to 6 ICs. Across all ICs, 363 (40.0%) experienced an AE; 33 (3.6%) had ≥1 treatment-related AE. The most common AEs were nasopharyngitis, bronchitis, and upper-respiratory tract infection. Serious AEs (SAEs) and AEs of special interest (AESIs) were reported for 49 (5.4%) and 18 (2.0%) patients, respectively. AESIs reported in >1 patient were muscular weakness (6 patients, 0.7%), dyspnea, constipation, and dysphagia (3 patients, 0.3% each). There was no increased incidence of AEs, SAEs, or AESIs with repeated dose. No deaths were reported in these studies.

Conclusions: IncobotulinumtoxinA was safe and well tolerated for LL, UL, or combined multipattern treatment over up to 6 ICs in a comprehensive population of ambulant and non-ambulant pediatric patients with spasticity (GMFCS levels I-V).

Poster 097

Improvement of spasticity-related pain with Incobotulinumtoxina treatment in children/adolescents with cerebral palsy: pooled analysis of 3 phase 3 studies

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Introduction: Spasticity-related pain (SRP) in children and adolescents with cerebral palsy (CP) is common, often neglected, and impacts daily quality of life. We assessed the effect of incobotulinumtoxinA on SRP using pooled data from 3 large Phase 3 pediatric studies.

Methods: Ambulant and non-ambulant patients (2–17 years of age; uni- or bilateral CP; Ashworth Scale score ≥2 in clinical patterns for treatment) were enrolled. Patients received total body incobotulinumtoxinA doses of ≤16 U/kg (≤400 U) for lower-limb (LL) treatment in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL and upper-limb (UL) treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Changes in self-reported (child/adolescent) or observed (parent/caregiver) SRP were assessed using the Questionnaire on Pain caused by Spasticity (QPS) in patients with LL (TIM, TIMO, and XARA) and UL treatment (TIMO and XARA).

Results: Assessments for 849 patients with LL and 454 patients with UL treatment were included. Of these, 340 (40.0%, LL: 61.2% male, mean [SD] age 9.3 [3.8], body weight [BW] 32.6 [14.8] kg) and 160 (35.2%, UL: (61.9% male, mean [SD] age 10.3 [3.7] years, BW 36.8 [16.5] kg) were able to assess SRP by interviewer- or self-administered QPS. Most (81.9% LL; 69.7% UL) reported pain at baseline for ≥1 activity. SRP increased with activity demands. Complete SRP relief at Week 4 post-treatment in each IC was seen (Table) and was highest in IC4. Observed SRP frequency was consistent with self-reported SRP and was supported by respective QPS item scores (all $P<0.001$ for responder rates).

Conclusions: In this large, pooled analysis, repeated incobotulinumtoxinA injections led to sustained pain reduction in children and adolescents with spasticity, with complete pain relief in the injected limb during activities in ≤54.8% of patients.

Poster 098

Common features in children with known genetic cause for cerebral palsy.

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Background: Cerebral palsy (CP) has a complex aetiology with several contributing factors such as prematurity, infection and hypoxic-ischaemic injury which are well understood and have guided clinical treatment and prevention, reducing prevalence. There is an emerging understanding of the genetics behind this complex disorder with Increasing knowledge of both genetic susceptibility genes, copy number variants and rarer monogenic mutations, which can drive research towards targets for intervention and precision medicine.

Objectives: To characterise the clinical presentation of children with an underlying genetic cause for their cerebral palsy and to identify common features possibly predictive of underlying genetic abnormality.

Methods: From a cohort of 221 patients in Cambridgeshire aged 0–18 years who all had a clinical presentation consistent with CP, we identified 11 cases with a genetic diagnosis identified. We analysed their clinical records to identify common themes likely from literature to be atypical.

Results: Of 9 patients, 4 were male (36.3%) and 7 were female (63.6%). Identified features more likely to be seen in genetic CP included: normal gestation and delivery, epilepsy type or severe intellectual disability out of keeping with presentation, congenital abnormalities, dysmorphic features, atypical MRI findings and a family history. 9/11 (81.8%) patients had at least 4 of the 7 features we have identified in total and 6/11 (54.5%) patients had at least 5 out of the 7 features we have identified in total. The most common features included: unexpected severe intellectual disability (9/11 patients), normal gestation and delivery (8/11 patients), dysmorphic features (9/11 patients) and atypical MRI findings (9/11 patients).

Conclusions: In patients with a genetic underlying cause identified for their cerebral palsy, there are a number of common features