

Neurology

G106 A REVIEW OF ANTIEPILEPTIC THERAPY AND SEIZURE CONTROL IN A SPECIALISED CENTRE FOR YOUNG PEOPLE WITH EPILEPSY (NCYPE)

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Objective: The NCYPE is a national residential centre for students with complex epilepsy. The aim of the study was to compare the treatment with specific reference to usage of anticonvulsant drugs at admission and at discharge, and attempt to classify their epilepsy.

Methods: A retrospective review of case notes, seizure diaries, EEG, and neuroimaging of the student graduates in July 2004 was undertaken comparing the initial and final 12 months of their placement at NCYPE. Classification of their epilepsy was attempted based on the terminology proposed by the ILAE (2001).

Results: 38 of the 47 graduates (age 16.9 to 24.1 years; 24 males, 14 females) had a diagnosis of epilepsy; 24 (63.2%) with symptomatic/probably symptomatic focal epilepsy, 5 of whom underwent epilepsy surgery. The remaining diagnostic groups included idiopathic generalised epilepsy, 6 (15.8%); SMEI, 2 (5.3%); Lennox Gastaut syndrome, 1 (2.6%); and unclassifiable in 5 (13.2%). The median length of stay was 4.9 years. Their median number of AEDs remained unchanged (2 AEDs/patient). A total of 30 (78.9%) students had a reduction in reported seizure frequency, with 16 (42.1%) having more than 75% reduction in the frequency of seizures. Twelve (31.6%) had a reduction of 25% or more in the reported use of rescue medications; with no change in 20 (52.7%). Five students (13.2%) had a >75% reduction in the frequency of status epilepticus, whereas it remained unchanged in the rest.

Conclusions: This study suggests that management of refractory epilepsy in specialised epilepsy centres may have beneficial effect on seizure frequency and morbidity. In contrast to other studies, seizure outcome was more favourable in this group with complex epilepsy. The majority of diagnoses in our study group also suggested an underlying focal pathology, stressing the importance of thorough assessments in the evaluation of patients with complex epilepsy.

G107 ACQUIRED MICROCEPHALY: AN OBSERVATIONAL STUDY

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Aim: To study the patterns, causes, and effects of acquired microcephaly.

Methods: Acquired microcephaly was defined as a decrease in head circumference z score (1 SD) of >1 from an initial value above -2, using Child Growth Foundation norms. We studied growth patterns, causes, motor (Touwen) and psychometric outcomes (IQ/DQ: BSID-II/WPPSI-R/WISC-III); literacy, numeracy, specific abilities, and behaviour (WORD; WONDI; NEPSY; CBCL). Statistical analysis used odds ratios and group comparison of means.

Results: Thirty four patients (17 boys) had mean z scores initially -0.7 (range -2 to 1.4) which decreased by 3 (-5.7 to 0.6; includes later recovery); two thirds decreased by >2. Three patterns occurred: (a) decreased, then grew parallel (19); (b) continued decrease (10); and (c) later recovery (3). Two were too young to classify. Seven had poor weight gain and three global growth delay. Causes were idiopathic (5); familial (1* relative -2SD) (11); syndromic (14); and symptomatic (post insult) (4). Most syndromic causes were non-specific. Most idiopathic cases had pattern (a); familial and syndromic cases could have any pattern. Twenty one were ≥2 z-scores by 1 year: pattern (a) between 6 and >36 months and (b) between 3 and 12 months. There were weak non-significant correlations between final z scores and motor or intellectual outcomes. Idiopathic cases had higher IQ/DQ scores than other causes. Compared with pattern (a), pattern (b) was more likely to show poorer gross motor skills (OR 2.5; 95% CI 0.2 to 29.3). Accompanying weight or growth impairment was linked to poorer social skills (OR 2.0; 95% CI 0.3 to 14.8), global developmental delay and specific neuropsychological deficits.

Conclusion: Most cases did not have a diagnosable cause. Patterns and causes are linked to each other and to outcome.

G108 MANAGEMENT OF BENIGN INTRACRANIAL HYPERTENSION. A NATIONAL AUDIT

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Aim: Benign Intracranial Hypertension (BIH) is a serious condition in children (1:10 000). Misdiagnosis and mismanagement can be associated with serious morbidity, related to visual impairment and debilitating headache. Significant number of such patients are seen and managed by general Paediatricians. As there are no standard national guidelines for management of BIH, we speculate wide variability amongst Paediatricians in managing such patients. This audit is aimed to examine the standard of care delivered to such patients by the general paediatricians across the country.

Methods: A questionnaire was sent to all the Paediatricians in the UK registered with RCPCH and the responses of the treating group were analyzed using Microsoft access.

Results: Out of the 2475 Paediatricians identified, 2203 (89%) responded. Referral to the neurologist was stated as always in 85% of the responders. 145 were excluded (different subspecialties). Paediatric Neurologists (65 responded) were analyzed separately. Results are not included in this abstract. Of the remaining 1993 Paediatricians, Only 544 (27%) had seen patients with BIH. 287/544 (53%) always referred to the neurologist. The remaining 257/544 (47%) treated their patients. 240/257 (93%) sought neurological advice (54% always, 39% sometimes). 93% performed lumbar puncture (26% always, 62% sometimes). The most common single investigation was MRI scan of the brain 47%, while only 22% perform thyroid function test. All the baseline investigations were performed by 7%. The treatment threshold was at 20-24 cm of CSF pressure by 67% as against 29% for 15-19cm and 5% for 25-30 cm. 22% sought advice from the neurologist for determining the treatment threshold. The first line treatment was variable, most common was serial LP 20%, single LP 19%, acetazolamide 10%, different combinations 12%, and as per advice 24%. The referral to the ophthalmologist was stated as sometimes in 87% and always in only 9%, and never by 2%. The second line treatment regime was highly variable but 35% sought advice, and 40% used different combinations most common was acetazolamide and steroid 11%.

Conclusion: The number of Paediatricians who treated children with BIH is relatively small but significant. Although neurologist advice was sought actively, there was great variation in the investigations and treatment modalities. Referral to the ophthalmologist was patchy and inconsistent. This audit highlighted the need for national guidelines to unify the standard of care delivered to such patients and hence prevent serious morbidity related to visual impairment and debilitating headache.

G109 HEAD UP TILT TESTING AND EXTERNAL OCULAR COMPRESSION IN CHILDREN: CLINICAL AUDIT OF A REGIONAL PAEDIATRIC CLINICAL NEUROPHYSIOLOGY SERVICE

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Aims: External ocular compression was employed infrequently at Birmingham Children's Hospital from 1993 to 2000 in pre-school children with severe or frequent possible reflex asystolic syncope (with reflex anoxic seizures, RAS) and head up tilt testing from 1997 onwards for school age children with possible neurally mediated syncope (including RAS and vaso-vagal syncope) that was unusually severe or frequent. The clinical impression was that results were frequently uninformative, particularly for the head up tilt testing. Prospectively collected data were therefore analysed to audit the tests' use and usefulness.

Methods: Basic demographic and clinical data and test results were collected prospectively on all patients and entered on a database. Further analysis of the clinical usefulness of the investigations by clinic letter review is underway.

Results: 116 unselected consecutive children were tested from 1997 to 2003.

External Ocular Compression: 37 children 6 months to 5 years. 14/37 (38%) reported positive, including 7/37 (19%) sinus arrest (asystolic) for 5 or more seconds.

Head Up Tilt Testing: 79 children 6 years to 17 years. 15/79 (19%) reported positive, including 6/79 (8%) with sinus arrest (asystole) for 5 or more seconds. Further analysis of the data set is underway.

Conclusions: Both tests, when used in selected patients, identified a significant minority with clearly abnormal excessive vagal type cardiac inhibition. Asystole was more frequently seen in the younger children

undergoing external ocular compression, generally for severe possible RAS. However, even in older children head up tilt testing was positive/reproduced symptoms in 1/5, half of whom had significant sinus arrest (asystole). A cardiac arrhythmia was disclosed in 0/116 (95% CI 0 to 3%). The measurement of beat to beat blood pressure during head up tilt testing would help define the mechanism in those with reproduced symptoms without significant asystole.

G110 CLINICAL EXPERIENCE OF LEVETIRACETAM (KEPPRA) IN CHILDREN WITH INTRACTABLE EPILEPSY: PRELIMINARY RESULTS

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Aim: To audit our experience of levetiracetam in children with intractable epilepsy in four neurology units in the UK.

Method: Unselected children prescribed levetiracetam from 2001 to 2004 were ascertained systematically from routine prospective pharmacy records or from departmental patient databases. A retrospective chart review of patients using a standard proforma to assess changes in seizure frequency and adverse events was undertaken.

Results: So far 164 patients (100 male) aged 1–17 years (mean 8 years 3 months) comprising 143 patient years of exposure have been studied. Mean age of onset of epilepsy was 2.9 years (2 days – 14.8 years). 72 had focal and 92 had generalised epilepsies. 148 had previously been prescribed 2 or more AEDs, 34 had received more than 5 AEDs. Levetiracetam dose ranged from 8 mg–100 mg/kg/day (mean 39 mg/kg) (data maybe skewed by seven patients receiving a dose of ≥ 80 mg/kg). Duration of treatment ranged from 1–28 months (mean 14.9 months). 13/164 achieved LEV monotherapy. 71 (43%) had a more than 50% reduction in seizure frequency, including 31 (19%) obtaining seizure freedom for a minimum of 3 months of which 19 (11%) were seizure free for 6 months or more. Levetiracetam was withdrawn in 49 (30%) patients, 22 (13%) due to possible adverse effects.

Conclusion: Levetiracetam appears effective and well tolerated in a variety of intractable childhood epilepsies.

G111 ARE SPINAL MAGNETIC RESONANCE SCANS PREDICTIVE OF BLADDER AND BOWEL NEUROPATHY IN PATIENTS WITH CLOSED NEURAL TUBE DEFECTS

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Aims: To assess the risk of bladder and bowel neuropathy in patients with closed neural tube defects.

Methods: 69 patients (43 females, 26 males) between the ages of 3 and 62 (median age 10.5 years, interquartile range 6.2–14.1 years) were reviewed. Radiological findings on MR scan were compared with clinical features and a review of urodynamic data and renal tract imaging. The patients were divided into three groups according to MR findings. Group 1 had sacral agenesis/hypoplasia or evidence of caudal regression among their lesions. Group 2 had a meningocele or lipomyelomeningocele with their abnormalities but features of group 1. Group 3 had other lesions.

Results: Overall 35 (50.7%) had a neuropathic bladder and bowel. Twenty two (31.9%) had lower limb neurological abnormalities. Only 11 patients with lower limb dysfunction had bladder and bowel neuropathy. The risk of bladder and bowel neuropathy was significantly greater in group 1 patients. Of 17 patients in group 1, 16 (94%)

had bladder and bowel neuropathy. This compared with 9 of 14 in group 2 (64%) and 11 of 38 (29%) in group 3 (group 1 v groups 2+3, $p < 0.0005$. Group 1 v group 3, $p < 0.0001$. Group 2 v group 3, $p < 0.0276$). For those in group 3 there was no relationship between MR abnormalities (long/tethered cord, lipoma, diastem, and split cord or syringomyelia) and the presence or absence of bladder and bowel neuropathy.

Conclusions: These data are important information for antenatal and postnatal counselling as well as being an important guide to the investigation and management of these patients. The absence of an association between bladder and bowel neuropathy and spinal lesion in group 3 patients raises a question mark over the role of surgery in this group.

G112 IGG DEPOSITION AND ENTRY INTO THE CNS AS COMPONENTS OF THE AUTOIMMUNE RESPONSE IN BATTEN DISEASE

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Introduction: A mouse model (*Cln3*^{-/-}) and individuals with Batten disease raise autoantibodies against glutamic acid decarboxylase (GAD65)¹ and a range of brain directed autoantigens.² However, it is unclear how these autoantibodies access and exert effects on the central nervous system (CNS).

Aims: To explore the occurrence of IgG deposition in the CNS and to evaluate how these immunoglobulins, including autoantibodies, gain access to the brain parenchyma.

Methods: Paraffin-fixed postmortem tissue from patients with Batten disease and appropriate controls were used to determine IgG deposition using a sensitive immunoperoxidase technique. To study lymphocyte infiltration into the CNS we quantified subclasses of lymphocytes in the CNS of *Cln3*^{-/-} mice and age-matched controls at three different stages of disease progression. We investigated the integrity of the blood brain barrier (BBB) using (a) intravenous injections of fluorescently labelled lectins or dextrans of different sizes and horse radish peroxidase (HRP), and (b) intraperitoneal injections of human sera, in *Cln3*^{-/-} mice and controls.

Results: There was increased IgG deposition across various regions of the CNS in Batten patients compared with controls and an increased association of IgGs with CNS tissue in *Cln3*^{-/-} mice. Significant lymphocyte infiltration occurred in *Cln3*^{-/-} mice, especially later in the disease, but was not of the activated T or B cell subsets that are capable of producing antibodies. A size selective breach of BBB allowing passage of molecules between 70 to 100 kD (IgG 150 kD) was evident in *Cln3*^{-/-} mice from the early phase of disease. Intraperitoneal injection of control human sera in *Cln3*^{-/-} mice and controls, revealed an increased perivascular accumulation of these human immunoglobulins in the CNS of diseased animals.

Conclusion: Collectively these data show that the deposition of immunoglobulins that occurs in the CNS of patients with Batten disease is unlikely to result from the size selective breach in BBB, nor central antibody production. Instead it may occur as a result of peripherally produced antibodies that have passed through to the CNS via active transport mechanisms. Although the ability of these immunoglobulins to target a variety of subpopulations of neurons is apparent,² their precise pathogenic role remains to be evaluated.

1. Chattopadhyay, et al. *Human Molecular Genetics* 2002;11(12): 1421–31.
2. Lim, et al. *Neuropathology and Applied Neurobiology* 2004;30:9.