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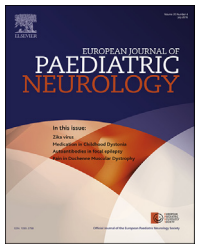

Original Article

Medication use in childhood dystonia

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ABSTRACT

Background: Data around current prescription practices in childhood dystonia is limited. Medication use may be limited by side effects, the incidence of which is uncertain. For a large cohort assessed by our supra-regional service we aimed to:

i) Review medications used at the point of referral.

ii) Determine the prevalence of adverse drug responses (ADR) resulting in discontinuation of drug use.

iii) Identify clinical risk factors for ADR.

Methods: Case note review of 278 children with dystonia referred to our service. Data collected on medications, ADR, dystonia aetiology, Gross Motor Function Classification System (GMFCS) level and motor phenotype (pure dystonia/mixed dystonia-spasticity). Logistic regression analysis was used to identify risk factors for ADR.

Results: At referral 82/278 (29.4%) children were taking no anti-dystonic medication. In the remainder the median number of anti-dystonic medications was 2 (range 1–5). Medications use increased with worsening GMFCS level. The commonest drugs used were baclofen (118/278: 42.4%), trihexyphenidyl (98/278: 35.2%), L-Dopa (57/278: 20.5%) and diazepam (53/278: 19%). Choice of medication appeared to be influenced by dystonia aetiology.

ADR had been experienced by 171/278 (61.5%) of children. The commonest drugs responsible for ADR were trihexyphenidyl (90/171: 52.3%), baclofen (43/171: 25.1%) and L-Dopa (26/171: 15.2%). Binary logistic regression demonstrated no clinical risk factors for ADR.

Conclusions: ADR is commonly experienced by children with dystonia, regardless of dystonia severity or aetiology. A wide variation in drug management of dystonia was identified. Collectively these findings highlight the need for a rational approach to the pharmacological management of dystonia in childhood.

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1. Introduction

Dystonia in childhood may be defined as "*A movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both.*"[1] Childhood dystonia is frequently secondary in aetiology, may be associated with spasticity[2,3] and expressed on the background of a maturing central nervous system, potentially altering the response to pharmacological agents.[4,5] Childhood dystonia is unlikely to remit spontaneously[3,6] and negatively affects a child's life including activity and participation.[7]

The evidence-base for pharmacological managements of dystonia is limited, with the exception of botulinum toxin and trihexyphenidyl.[8] Recent guidelines for the treatment of childhood dystonia are based largely upon expert opinion.[4,9]

Although clinicians recognize that the use of the common anti-dystonic agents maybe limited by adverse drug reactions (ADR), the frequency of these reactions remains to be established. A better understanding of ADR is required to counsel parents and carers on medication choices. We aimed for a cohort of children with dystonic movement disorders referred to our tertiary centre to:

i) Review medications used at referral
ii) Determine the prevalence of ADR
iii) Identify clinical risk factors for ADR.

2. Methods

Data were collected retrospectively from the clinical notes of Children and Young People (CAYP) referred to the Complex Motor Disorders Service between July 2005 and January 2012. Clinical notes were available for 294/315 (93.3%) CAYP, with 16 subsequently excluded (15 having a pure spastic phenotype on clinical examination and 1 insufficient information documented on medication use at baseline). This left 278 CAYP for study. Demographic features of children included in this cohort have previously been reported.[3] A pro-forma procedure was used to record patient details at initial contact with our service, including age at presentation, aetiological classification of dystonia,[6] presence of spasticity, functional classification as measured by Gross Motor Function Classification System (GMFCS),[10] duration of dystonia, proportion of life lived with dystonia (calculated by normalizing duration of dystonia to age) and source of referral.

Regular maintenance medication use at presentation, previous history of medication use, and the occurrence of ADR was also recorded. In case ADR had occurred, it was recorded to what medication ADR had been attributed. ADR was defined as an adverse side effect to the medication sufficiently severe to result in discontinuation of the medication.

Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Differences in the number of medications used across aetiological classifications and functional level was measured using the Kruskal–Wallis test. Differences in the occurrence of ADR between aetiological classifications or functional level were assed by Chi-squared testing. In both cases a P-value <0.05 was considered statistically significant. Ordinal regression with a logit link function was used to explore which factors independently related to number of medications at presentation. Binary logistic regression was performed to explore possible factors relating to ADR.

3. Results

Median age at presentation was 9.75 years (6.6–13.0, 25th–75th centile), with a median duration of dystonia of 7.75 years (4.6–10.9, 25th–75th centile).

The median proportion of life lived with dystonia was 0.95 (0.80–0.99, 25th–50th centile).

Dystonia was classified as primary for 30/278 (10.8%), Secondary 200/278 (71.9%), Heredodegenerative 29/278 (10.4%) and Primary-Plus 19/278 (6.8%). GMFCS levels were I = 26, II = 26, III = 14, IV = 40 and V = 172. For 79/278 (28.4%) of the cohort spasticity was found coincident with dystonia.

The commonest source of referral (123/278) was tertiary paediatric neurologists, followed by Consultants in Paediatric Neurodisability (78/278). Remaining referrals were received from General Paediatric Services (41/278), Community Paediatric Services (34/278), with 1 case referred by an Orthopaedic Surgeon and 1 further case referred from General Practice.

A total of 18 different anti-dystonic medications were identified at the point of referral. Across the cohort as a whole, the 3 commonest anti-dystonic medications were baclofen (118/278, 42.5%), trihexyphenidyl (98/278, 35.3%) and L-DOPA (57/278, 20.5%) (Table 1, Fig. 1). The profile of medication use differed by dystonia aetiology. In the secondary and heredodegenerative group the commonest 2 anti-dystonic medications used were baclofen and trihexyphenidyl, in the primary group L-DOPA followed by trihexyphenidyl, with more limited medication use in the Primary-Plus group. The number of anti-dystonic medications varied across the group from 0 to 5 (median 2). No anti-dystonic medication was in used for 82/278 (29.5%) CAYP. A greater number of anti-dystonic medications were used by those CAYP with lower function, i.e. higher GMFCS level, (Chi-squared P < 0.001) (Table 2). Medication use also differed by aetiology, with greater medication use in the Secondary and Heredodegenerative dystonia groups (Kruskal–Wallis test, P = 001). The number of medications used did not differ between those children with or without spasticity (Mann–Whitney U-test, P = 0.241). Baclofen use was higher in CAYP with co-incident spasticity (50/79 or 63% with spasticity, 68/179 or 37.9% without spasticity, Chi-squared test P < 0.001).

ADR had been experienced by 171/278 (61.5%) CAYP, caused by 11 different medications. For the cohort as a whole, and regardless of aetiology, the drug most commonly causing ADR was trihexyphenidyl. Baclofen was the drug next most commonly reported as causing ADR, except in the primary dystonia and primary-plus dystonia groups, where L-DOPA and clonazepam respectively were the second most common drugs. Experience of ADR did not differ by dystonia aetiological (Chi-squared, P = 0.302) (Table 3), GMFCS level (Chi-squared, P = 0.079), Proportion of life lived with dystonia (Kruskal–Wallis, P = 0.42) or presence/absence of co-incident