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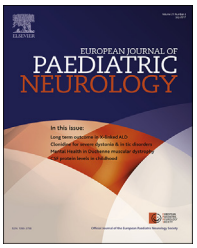

Original article

Clonidine use in the outpatient management of severe secondary dystonia

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ABSTRACT

Objective: To evaluate the safety, efficacy and effective dosage of clonidine in the outpatient (OP) management of secondary dystonia.

Methods: A retrospective analysis of children and young people (CAYP) prescribed clonidine in an OP clinic between January 2011 and November 2013 for dystonia management. Of 224 children receiving clonidine, 149/224 did not have a movement disorder and 12/224 had no data leaving 63 movement disorder cases, 15/63 managed as in-patients, 15/48 suffered from tics leaving 33/63 for OP evaluation. Clonidine effectiveness was assessed by 'yes/no' criteria in improving 5 areas: seating, sleep, pain, tone and involuntary movements.

Results: 2/33 motor cases had insufficient data; 7/33 had concurrent therapy leaving 24/33 for analysis. Improvement in at least one area was reported by 20/24 (83%) CAYP: Improved seating tolerance 14/24, and sleep 15/24; reduced pain 15/24; improved tone 16/24 and involuntary movements 17/24.

Starting doses ranged from 1 mcg/kg OD to 2 mcg/kg TDS with optimum doses reached on average at 9.5 months follow-up. Maximum dose reached was 75 mcg/kg/day given in 8 divided doses. Average maximum daily dose was 20 mcg/kg/day. The commonest frequency of administration was 8 hourly.

Side effects were reported in 11/24 CAYP and discontinued in 1/24 for lack of clinical effectiveness, 1/24 for side effects and 4/24 due to both lack of effectiveness and side effects.

Conclusion: Clonidine was effective in secondary dystonia management in 83% of cases. A starting dose of 1 mcg/kg TDS was well tolerated and safely escalated. Prospective objective evaluation is now required to confirm the efficacy of clonidine.

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What is known	What this paper adds
Childhood dystonia is a debilitating condition that causes great daily challenges and can lead to musculoskeletal deformity. Current commonly used medications are often insufficient to control dystonia, can cause side effects and polypharmacy is common	Clonidine is a potential new addition to the pharmacological management of dystonia. It is tolerated well and works in cases in whom other medications had been trialled and failed.

1. Introduction

Dystonia is a movement disorder characterised by intermittent or sustained involuntary muscle contractions causing abnormal movements, postures or both.[1] Dystonia can greatly adversely affect a child's ability to function in daily life, irrespective of dystonia aetiology, rendering essential tasks such as washing and dressing a time-consuming, difficult and sometimes painful process. Carers of patients referred to a tertiary centre have reported that the dystonia improves in <10% of patients, remains statically severe in 31% and in 2/3 of cases worsens over time.[2] The long-term effects of dystonia on the body can be debilitating, unfortunately there are no proven medical means of preventing an inexorable progression to musculoskeletal deformity in children with dystonia, which is particularly prominent in severe secondary dystonias the majority of which have cerebral palsy (CP).[3] There is a paucity of high quality trials to inform the pharmacological management of dystonia in childhood.[4,5] However, the limited efficacy of medication in some children increases the likelihood of polypharmacy in severely affected children and the risks of side effects need to be carefully balanced against the benefit.[6] Anti-dystonic agents commonly used include, trihexyphenidyl, benzodiazepines and baclofen,[6] all of which may commonly cause significant adverse effects.[7] There is interest in exploring other potential options in the pharmacological management of dystonia and we have recently reported the benefit of gabapentin in childhood dystonias in a retrospective audit of 69 children.[8] A comprehensive survey of the management strategies in dystonia and other movement disorders of childhood has been recently reviewed[9] and specifically in the cerebral palsies.[10]

Clonidine is a centrally-acting alpha-2 agonist first developed as an antihypertensive agent in adults.[11] Clonidine is currently used in a number of different clinical settings, including as a peri-operative sedative adjunct to anaesthesia to improve post-operative pain,[12] as a benzodiazepine sparing sedative in the intensive care setting,[13,14] in the management of ADHD[15] and sleep disorders.[16] Within the field of movement disorders it is most known for the management of tics in Tourette's disorder,[17,18] with more limited experience reported in other conditions, particularly paroxysmal autonomic instability in dystonia.[19,20] Effectiveness in spasticity has also been demonstrated.[21]

Effective clonidine dosages used in these different clinical settings vary, e.g. sleep disorders/ADHD receive doses of 25–150 mcg BD, premedication for anaesthetic has shown effectiveness with minimal side effects at doses of up to 4 mcg/kg,[22,23] for sedation in the PICU setting doses of 5 mcg/kg TDS have been used.[13] Reported use in movement disorders has had a similarly wide dosage range. In Tourette's disorders low doses are used, starting with 25 mcg at night. The literature mainly focuses on clonidine use in status dystonicus with PAID, in this indication a clonidine infusion starting at 0.25 mcg/kg/hour and escalating to 2 mcg/kg/hour has been suggested.[19] The side effects in these doses include dry mouth, somnolence, bradycardia and relative hypotension in sleep not requiring treatment. In the poisoning literature doses of 11 mg (11000 mcg) have been described with respiratory depression and hypotension.[24]

Our service started using clonidine as a benzodiazepine-sparing sedative agent to promote sleep in the acute setting for management of status dystonicus. We progressed to using it in severe cases of dystonia in the outpatient setting when other medications had a limited effect. It is this outpatient use of clonidine that is evaluated here.

For a cohort of children with secondary dystonia we aimed to:

1) Determine the efficacy of Clonidine in reducing dystonic symptoms
2) Determine the dose ranges and regimens required to achieve relief of dystonic symptoms
3) Establish the frequency of side effects experienced.

2. Methods

All children prescribed and issued clonidine by the Evelina London Children's hospital pharmacy between 2010 and 2013 (inclusive) were identified by the pharmacy medications tracker. Children's electronic notes were accessed and the prescribing condition for clonidine was identified. All patients who had been prescribed clonidine primarily for movement disorder were included. Data was collected from patient notes using a standardised pro-forma. Data collected included age at clonidine initiation, motor phenotype (dystonia, spasticity or mixed, as assessed by a consultant paediatric neurologist with experience in movement disorders), underlying pathology, GMFCS level (I-V)[25] (in non-cerebral palsy cases a "GMFCS equivalent" score was applied as reported previously by our group[26,27]), weight, starting dose, dose increase amounts, interval times (days) of dose increases, maximum dose reached, effectiveness reported in pattern of sleep, and severity respectively of dystonia, involuntary movements, pain,