Fifteen-minute consultation: Management of acute dystonia exacerbation and status dystonicus

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Received 30 March 2024
Accepted 19 May 2024

To cite: Lumsden DE. *Arch Dis Child Educ Pract Ed* Epub ahead of print: [please include Day Month Year]. doi:10.1136/archdischild-2023-326814

ABSTRACT

Dystonia is a common disorder of movement and tone, characterised by sustained or intermittent muscle contractions causing abnormal movements, postures or both. Children and young people with dystonia can experience episodes of acute worsening tone, which require prompt treatment. When most severe, dystonia may become life-threatening—a state called 'status dystonicus'. This guide aims to provide a framework for how to approach the child with acutely worsening dystonia, following an 'ABCD' approach: Addressing the precipitant, Beginning supportive care, Calibrating sedation and Dystonia-specific medications.

INTRODUCTION

Dystonia is defined as 'a movement disorder characterised by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures or both'.[1] Dystonia in childhood has many causes, the most common being cerebral palsy (CP).[2] Dystonic movements may be painful and can interfere with function and the delivery of daily care. Dystonia may occur in isolation, or as part of a more complex motor disorder. At worst, dystonia may become acutely life-threatening, a condition usually termed 'status dystonicus' (SD).[3] Precisely defining SD remains challenging, though a common definition is of 'increasingly frequent and severe episodes of generalised dystonia which had necessitated urgent hospital admission'.[4]

SD has been reported more often in children and young people (CAYP) than adults, with a trigger identified in around ~60% of cases.[5] While >300 episodes of SD have been reported to date, high-quality prospective studies are entirely lacking.[5 6] The true incidence of SD, or of episodes of worsening dystonia resulting in hospital admission, is unclear and very likely significantly underestimated. Around one in four CAYP experiencing SD fail to return to baseline following the episode, with a reported mortality of ~5%.[5] The risk of developing SD is present for all children with dystonia, though has been most frequently reported in CAYP with dyskinetic CP, pantothenate kinase-associated neurodegeneration and in GNAO1-related dystonia.[5] In the absence of a robust evidence base, this guide will focus on a pragmatic approach to the management of acute dystonia exacerbation.[7] For a more general approach to the diagnosis and management of dystonia in childhood, the reader is directed to the review by Forman and colleagues.[8]

GETTING THE RIGHT STATUS: DYSTONIA OR EPILEPSY?

The first challenge when faced in the emergency department (ED) with a CAYP experiencing severe dystonia is being confident that they are not experiencing an epileptic seizure. Prolonged generalised tonic–clonic seizures may be directly harmful to the brain if they continue after 30 min,[9] and in this situation, the aim of treatment is to *turn the seizure off*. In contrast, the aim of acute treatment for severe dystonia is to *turn the dystonia down*. Episodes of SD develop after a period of hours or days of worsening dystonia and lack a clear onset. It usually takes several hours, or even days, to entirely resolve the episode. Figure 1 outlines some of the ways in which status epilepticus (SE) and SD may be distinguished. CAYP will very often have received a dose of benzodiazepine prior to (or shortly following) arrival in the ED, which can impact on their responsiveness. If there is any question as to whether an episode is a seizure or not, encouraging families to record the movements for review later can be very beneficial. CAYP with dystonia often also

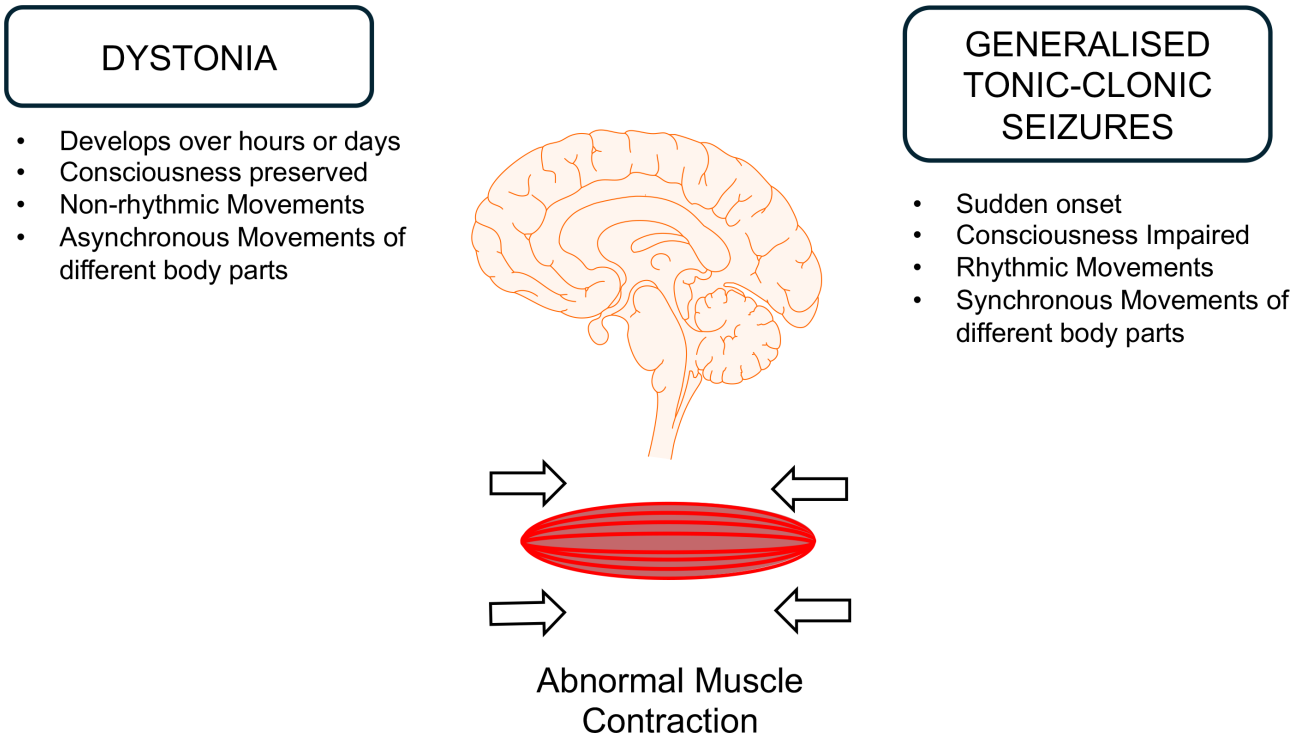

Figure 1 Differentiating episodes of 'status dystonicus' from 'status epilepticus'.

present with other hyperkinetic movement disorders—particularly chorea and myoclonus. These movements may also be exacerbated when dystonia worsens, which can further complicate differentiation from SE. Choreiform movements are typically non-rhythmic, random-appearing multiplanar non-purposeful movements. Myoclonic movements are brief, shock-like movements of a muscle group. Myoclonus may be epileptic (cortical myoclonus) or driven by subcortical mechanisms. Differentiation of the two at the bed side is difficult in practice, and an electroencephalogram recording is usually required.

MANAGING EPISODES OF ACUTE DYSTONIA EXACERBATION

A flow chart outlining an approach to managing episodes of acute dystonia exacerbation in CAYP is provided in figure 2. This emphasises an 'ABCD' approach. In contrast to the ABCD of Advanced Paediatric Life Support algorithms, these should be considered in parallel rather than sequentially. Grading the severity of dystonia for a CAYP is an important starting point, recognising that symptoms lie on a spectrum of severity, with SD at the most extreme. The Dystonia Severity Action Plan (DSAP) provides a simple 5-point scale for grading dystonia, which is useful for directing the urgency of intervention.[10] CAYP scoring 4 or 5 on this scale are in SD. Most children presenting acutely will be at DSAP grade 3, presenting an opportunity for intervention to prevent any further worsening of symptoms.

WHY HAS DYSTONIA WORSENED?—ADDRESSING THE PRECIPITANT

It is difficult to put a fire out if fuel keeps getting thrown onto it. Episodes of worsening dystonia will often (but not always) have a clear trigger, which is important to recognise and treat directly. Figure 3 provides a summary of common triggers for worsening dystonia, which should be considered for each CAYP. For frank SD, the common triggers differ between CAYP and adults,[5] and include intercurrent infection and changes to medications (either introductions or discontinuation). It is important for all presentations to specifically check if any new medications have been added or discontinued. Each CAYP should also be checked for an implanted device (deep brain stimulator or intrathecal baclofen pump). If one is present—the clinical team managing the device should be contacted urgently.

GENERAL MANAGEMENT—BEGINNING SUPPORTIVE CARE

As episodes of worsening dystonia take some time to improve, supportive care is required, as are treatments for any complications which may arise. This can include fluid management, pain relief and constipation management. An outline of supportive measures is provided in table 1, along with the complications acute dystonia exacerbation may cause to different organ systems. Depending on the severity of the episode, admission to a high dependency (CAYP at DSAP grade 4) or, less commonly, intensive care (CAYP at DSAP

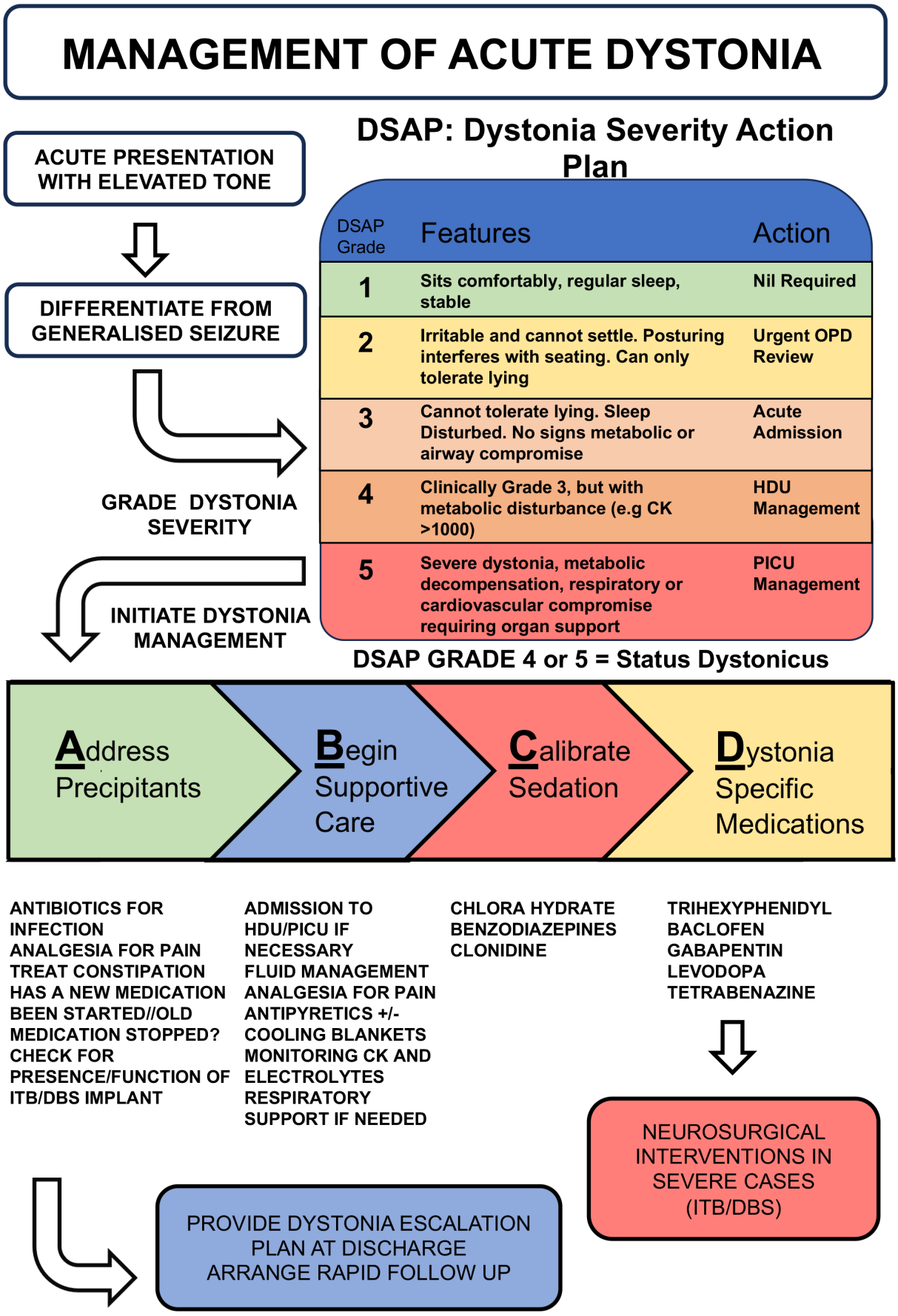

Figure 2 An approach to managing acute dystonia. CK, creatine kinase; DBS, deep brain stimulation; HDU, high-dependency unit; ITB, intrathecal baclofen; OPD, outpatient dystonia; PICU, paediatric intensive care unit.

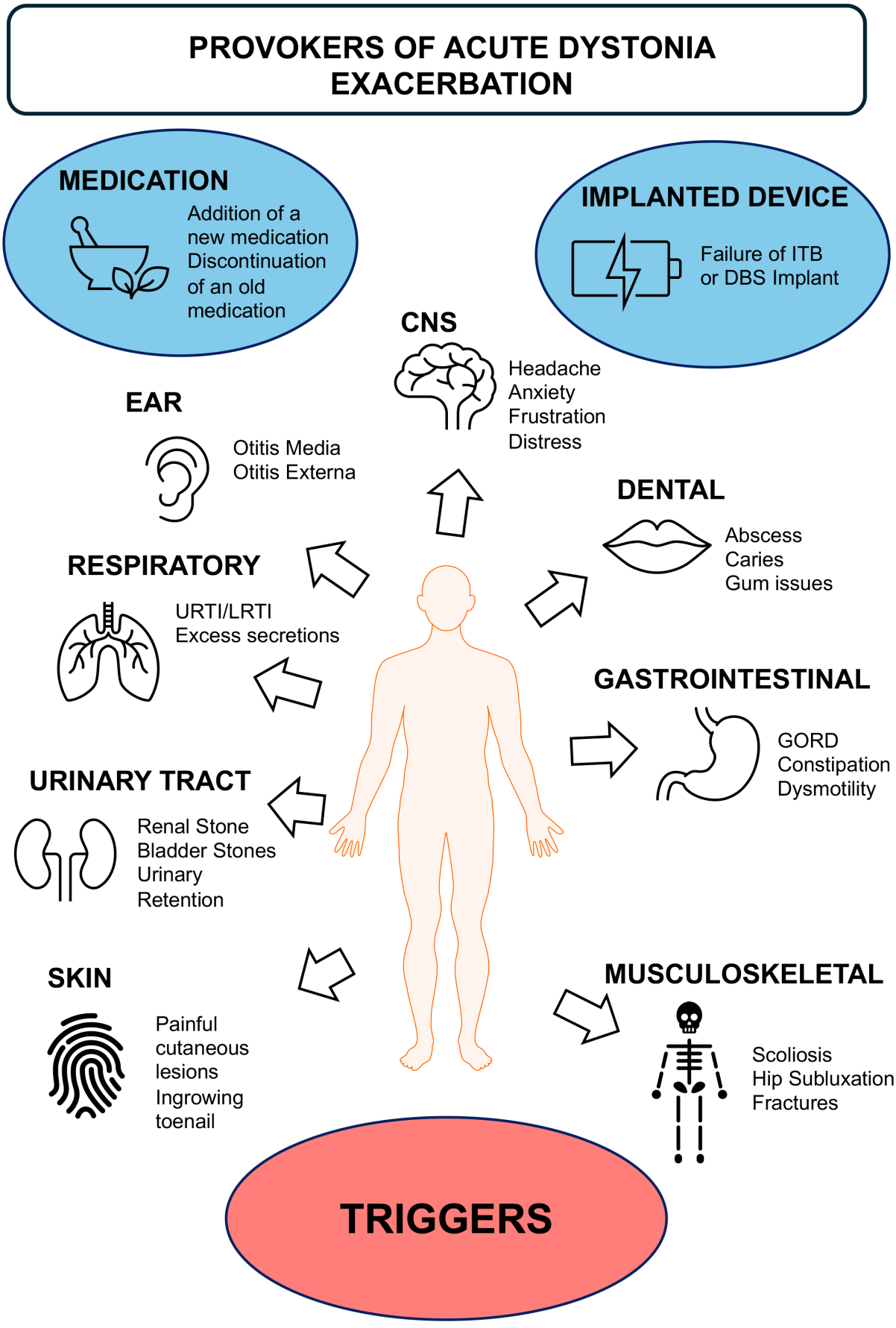

Figure 3 Triggering factors which may provoke worsening dystonia. CNS, central nervous system; DBS, deep brain stimulation; GORD, gastro-oesophageal reflux disease; ITB, intrathecal baclofen; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection.

Table 1 Complications of status dystonicus and support required, organ system by organ system

System	Potential complications	Supportive measures
Respiratory	Airway compromise Bulbar dysfunction Aspiration Diaphragmatic compromise Exhaustion/poor respiratory effort	Airway adjuncts (may be poorly tolerated) Oxygen where necessary Intubation/ventilation (rarely required)
Renal/urinary tract	Acute kidney injury Urinary retention	Adequate hydration/hyperhydration Haemofiltration/renal replacement therapy (rarely required) Urethral catheterisation
Cardiovascular	Dehydration Dysautonomia	Adequate hydration
Gastrointestinal	Bulbar dysfunction GORD/gastric status Constipation	NG tube insertion Reflux treatment/gastric protection Laxatives
Musculoskeletal	Pain Fractures (rare)	Analgesia Support with positioning in bed and seating
Metabolic	Electrolyte disturbance Rhabdomyolysis Hyperpyrexia	Electrolyte replacement Hydration/hyperhydration Antipyretics Haemofiltration/renal replacement therapy (rarely required)
Psychological/emoting	Distress and anxiety PTSD symptoms longer term	Recognition that CAYP is alert and aware during episode (unless significantly sedated) Psychological support

CAYP, children and young people; GORD, gastro-oesophageal reflux disease; NG, nasogastric; PTSD, post-traumatic stress disorder.

grade 5) environment may be required. This may be due to the direct impact of dystonic movements, or the side effects of sedative and other medications (see below) required to control symptoms. One important risk with acute dystonia exacerbation is of rhabdomyolysis resulting in acute kidney injury, which in severe cases may result in the need for renal replacement therapy. While monitoring of plasma electrolyte and creatine kinase levels is necessary, frequency of blood sampling needs to be balanced against the disruptive impact of blood sampling itself on the CAYP. One of the goals of acute treatment is sedation—efforts which painful blood sampling will counteract. Severe dystonia places a significant energy demand on the body, and CAYP may rapidly become catabolic. Early placement of a nasogastric tube should be considered in CAYP without a surgical feeding tube already in place. The safety of a CAYP's swallow may be compromised by severe dystonia (particularly when this affects the head and neck), further compounded by the adverse effect of sedative medications.

TEMPORISING MEASURES—CALIBRATING SEDATION

While triggers are treated, and more dystonia-specific medications are changed (see below), a level of sedation is usually required to reduce distressing symptoms of dystonia. For mild episodes, this may be the very sparing use of a single agent, while for severe episodes of SD, a more complex regimen may be required. Table 2 provides some details of commonly used tone-reducing medications (TRMs), sedative and non-sedative. A number of different sedative medications have been described in the acute management of severe dystonia, including benzodiazepines, clonidine and chloral hydrate.[11] In all cases, care must be taken with regard to the risk of airway compromise and/or respiratory depression. For severe episodes of SD, particularly with concurrent rhabdomyolysis, intubation and ventilation may be required. In recent years, concerns have been raised about the use of chloral hydrate outside of the current UK licensing of short-term (not more than 2 weeks) treatment of insomnia in children with neurodevelopmental disorders. Consensus guidance has been produced to provide a framework for the use of this medication for CAYP with severe movement disorders.[12]

IMPROVING ABNORMAL TONE—DYSTONIA-SPECIFIC MEDICATIONS

Sedative strategies provide a period of symptom control while changes are made to background TRMs. A large number of TRMs have been described in the management of worsening dystonia and SD, with varying efficacy reported.[3 11] Table 2 provides details of some of the more commonly used medications, along with common side effects. Factors to consider when selecting a TRM are outlined in Box 1. For episodes of severe SD, the potential benefits of neurosurgical interventions such as deep brain stimulation (DBS) have been increasingly reported.[5 13] It remains unclear which CAYP are optimal candidates for DBS (or in some cases intrathecal baclofen) and at what time point during an episode of SD. All children admitted

Table 2 Tone-reducing medications (TRMs) used in the management of dystonia

Category	Medication	Mechanism of action	Main side effects
Acutely sedative TRM	Benzodiazepines (eg, midazolam, diazepam)	Enhances affinity of GABA-A receptors for agonists	Dependency and tolerance with longer-term use, respiratory depression, adverse cognitive effects
	Chloral hydrate	Hypnotic and sedative with similar action to barbiturates	Dependency and tolerance with longer-term use, GI upset
	Clonidine	Centrally acting adrenergic agent (α_2 adrenoreceptor agonist)	Dependency and tolerance with longer-term use, drowsiness, bradycardia, hypotension, dizziness (hypertension at very high doses)
Longer-term TRM	Baclofen	$GABA_B$ receptor agonist	Vomiting/GI upset, worsening airway secretions, impairing bulbar function, exacerbating axial hypotonia
	Trihexyphenidyl	Centrally acting anticholinergic (muscarinic) agent	Dry mouth, thicker secretions, pupil dilation, constipation
	Gabapentin	Disrupts regulatory action of $\alpha_2\delta$ calcium channel subunit (NOT gabanergic action, despite the name)	Tiredness, dizziness, GI upset, behavioural change, concerns about respiratory depression at high doses
	Levodopa	Precursor of the neurotransmitter dopamine	Vomiting/GI upset, potential for chorea with higher doses in children with dopamine deficit
	Tetrabenazine	Dopaminergic depletion (blocks synaptic release of dopamine)	Depression/low mood, Parkinsonism, neuroleptic malignant syndrome

GABA, gamma-aminobutyric acid; GI, gastrointestinal.

to an intensive care setting due to dystonia should be discussed early with a service which is experienced in the delivery of DBS to CAYP.

The evidence base for TRMs used in the management of dystonia is extremely limited,[14] and side effects limiting use are commonly experienced by CAYP.[15] During severe exacerbation of dystonia, it may be necessary to introduce or increase several TRMs, and it is important following an episode that there is close follow-up to try and rationalise ongoing medication use.

Box 1 Factors to consider when selecting tone-reducing medications (TRMs)

- TRMs the CAYP is already receiving.
- Background comorbidities which might be particularly worsened by the specific side effects of a given medication (eg, for a severely constipated child, an anticholinergic medication like trihexyphenidyl would be used with caution).
- The overall profile of the motor disorder for a CAYP (eg, co-incident spasticity would suggest potential benefits with the addition of baclofen).
- The speed at which symptom control is required (eg, a slow titration of trihexyphenidyl is required to limit the impact of anti-cholinergic side effects which may in term limit its use in a very acute situation).
- Whether a TRM could additionally help with treating a trigger (eg, gabapentin may have an additional analgesic effect in the CAYP with worsening dystonia due to pain from a subluxation of the hip).

CAYP, children and young people.

AFTER THE EPISODE: FOLLOW-UP AND AFTER CARE

CAYP experiencing an episode of worsening dystonia or SD will require close follow-up, for the reasons outlined in Box 2. Unfortunately, CAYP who have experienced an episode of worsening dystonia are at risk of experiencing further such episodes in the future. Given this risk, and the lack of standardised guidelines for the management of worsening dystonia, all children who have experienced an episode of worsening dystonia necessitating hospital admission should be provided with a personalised plan for dystonia management, providing (a) guidance on medication

Box 2 Reasons for close follow-up after an episode of worsening dystonia

- To consider if and when doses of TRMs increased during the episode of worsening dystonia can be reduced.
- To monitor for significant side effects from elevated doses of TRM.
- To ensure completed treatment/management of the trigger for an episode (if one has been identified).
- To monitor any complications encountered during the episode of worsening tone.
- To enable assessment of changed needs for the CAYP and family/carers if dystonia does not return to baseline.
- To provide support for the well-being of the CAYP and their family after what will typically have been a difficult episode.

CAYP, children and young people; TRM, tone-reducing medication.

changes to be made if dystonia acutely worsens, (b) advice on how to manage medications if CAYP are made nil by mouth and (c) the contact details for the team responsible for managing a CAYP's dystonia. The British Paediatric Neurology Association provides blank dystonia passports which can be adapted to an individual CAYP, along with guidance as to how these forms should be completed.[16] These plans should be documented in patient notes, with a copy provided to parents/carers to carry.

CONCLUSION

Episodes of acute worsening of symptoms are not uncommon in children with dystonia. A systematic approach is required to treatment, with a particular focus on identifying and treating triggers. Following discharge, CAYP require close follow-up and should be provided with guidance to support the management of any future episodes experienced.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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