

Drug Induced Acute Dystonic Paediatric Emergency Admissions In A Southwestern Nigerian Tertiary Hospital

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Abstract

Background: Drug-induced acute dystonia is an undesirable, sudden, involuntary movement disorder, following the administration of some drugs. The disorder is studied with the aim of documenting the burden of the disease, the implicated drugs, seasonal variation, and their presentation.

Methods: The records of children seen at the paediatric emergency with acute dystonic reactions between January 2018 and December 2024 were studied. Information retrieved from the records includes age and sex of the children and period in the year seen, presumed culprit drug and the prescribers and dispensers.

Results: A total of 42 admissions with acute drug-induced dystonic reactions were recorded over seven years at the Paediatric Emergency unit of Wesley Guild Hospital, Ilesa, giving a prevalence of 0.005%. They comprised 24 boys and 18 girls giving a male to female ratio of 1.33:1. Their ages ranged between 4 months to 15 years with a mean of 6.75 ± 3.40 years. Majority of the dystonic reactions were focal or segmental involving the posturing or movement of the head and neck region, occurring in 64.29 % of the patients. There were more cases of acute dystonic reaction presenting in the wet season months (84.62%) compared to dry season months. Amodiaquine was the most common drug implicated in ADR followed by Metoclopramide in 45.2%, and 21.4% cases respectively. The dystonic reactions were managed with medications and admission spanning between 1-3 days. Six (14.3%) procured their drug from private hospital and pharmacy, 14 (33.3%) from chemists and maternity centres while the rest did not disclose the source of the medication.

Conclusion: Acute drug induced dystonia is a notable cause of paediatric emergency admission in our health facility and antimalarials, especially Amodiaquine are the commonest drugs implicated. Patients present more in the wet than dry season months. Most cases emanated from self, chemist and maternity nurses' prescription compared with prescription by doctors. Ensuring that these medications are only available, prescribed and dispensed by authorized persons should mitigate the burden of this disease.

Keywords: Drug-induced dystonia, Paediatric dystonic reaction, seasonal variation, Amodiaquine, Focal dystonic reaction.

Introduction

Dystonia is an involuntary movement disorder, which usually manifests as sustained or sometimes intermittent muscle contractions, producing repetitive, twisting and patterned movements or abnormal posture.^{1,2} Dystonias may be primary or secondary.¹ Primary dystonia is usually a sign without underlying exogenous nor neurodegenerative aetiology. However, when onset is in children or young adults, genetic abnormality is often the presumed factor. Secondary, dystonia on the other hand is a syndrome where dystonia is a prominent symptom of underlying focal brain lesion, drugs or chemical toxicity¹ or hereditary degenerative conditions such as perinatal injury, medications and brain tumour¹. Drug ingestion is usually the most common reason warranting paediatric emergency consultations^{3,4,5} for secondary dystonia.

Some of the common groups of drugs that can induce acute dystonic reaction include anti-psychotics e.g. Haloperidol and anti-emetics e.g. Metoclopramide. Other medications that may cause acute dystonic reactions include cold and cough preparations containing codeine or antihistamines, expectorants and decongestants.^{6,7} So also are anti-malarials, e.g. amodiaquine and the anti-epileptic carbamazepine.⁴

Awareness of the drugs inducing acute dystonia and its presentation is expected to promote better practices that will reduce disease burden. This study aims to document the

seasonal presentation, drugs identified to induce acute dystonia and factors associated with their administration with a view to proffer recommendations that will reverse the burden of the disease.

Methodology

The records of all cases of children seen with drug induced acute dystonia at the paediatric emergency ward of Wesley Guild Hospital, Ilesa between January 2018 and December 2024 were reviewed. Ethical approval was sought and obtained from the research and ethics committee of the Obafemi Awolowo University teaching Hospital Complex for record retrieval (ERC/2025/03/10). Information obtained from the case notes included age and sex of the subjects, the drug inducing the dystonia, duration for which the patient was admitted and parts of the body presenting with dystonic reactions. Details of the facility where the drug was bought was also recorded and the treatment that was given for the dystonia.

Data collected were entered and analysed with IBM (SPSS) version 22.0. The ranges and means of the patients' ages as well as gender ratio were determined. The drugs implicated in causation of the dystonic reaction were recorded and analysed as a ratio to each other. Comparison of categorical variables and test of association was by chi square test and. p-value of

<0.05 was taken to be statistically significant.

Results

Age, gender and seasonal demographics of the population studied

There were 42 cases of acute dystonia out of 4,447 paediatric emergency admissions giving an hospital prevalence of 0.005%. Annual incidences of presentation with ADR in this study were 0.004%, 0.005%, 0.007%, 0.003%, 0.005%, 0.004% and 0.005% for the respective years analysed. The ages of the children studied ranged from four months to 15 years, with a mean of mean of 6.71 ± 3.40 years. Considering seasonal variation, 6(15.38%) presented in the dry season months of November to March while 33(82.64%) presented in the wet season months. The difference was not statistically significant ($p = 0.125$). Most of the study children were boys. The age and sex distribution of the population studied is shown in Table I.

Table I: Socio-demographic characteristics of the study participants

Age category	Frequency (N=42)	Percentage
≤ 5 years	13	30.9
6 - 10 years	23	54.8
11 – 15 years	6	14.3
Mean	6.75 ± 3.4 years	
Sex distribution of the population studied		
Male	24	57.1
Female	18	42.9
Socio-economic class (n = 38)		
Upper	3	7.1
Middle	16	38.1
Lower	19	45.2
Seasonal variation (n = 39)		
Dry season	6	15.38
Wet season	33	84.62

Name of drugs administered, and where drugs was procured

The most common drugs recorded to induce dystonia was the anti-malarial Camoquine (Amodiaquine) followed by anti-emetic Metoclopramide. Other drugs recorded to induce dystonia are documented in Table 2. Chemists were the most common personnels that prescribed the drugs while doctors were the least associated to prescribe the drugs leading to development of dystonia. The chemist shop was the most usual place of purchase of the drug while Local Government Area maternities were the least common location for obtaining the drugs. Details of the source of procurement of the drugs are stated in Table 2.

Table II: Name of drugs causing dystonia, and where drugs was bought

Categories	Number (N= 42)	Percentage
Drug administered		
Amodiaquine	19	45.2
Artemisinin	2	4.8
Metoclopramide	9	21.4
Promethazine	1	2.4
Chloroquine	1	2.4
Haloperidol	1	2.4
Unidentified	9	21.4
Where drug was procured		
Not stated/probably self	17	40.5
Chemist	14	33.3
Pvt hospital/Pharmacy	6	14.3
LGA maternity	5	11.9

Indications for drug use

While one (2.4%) of the studied children used a worm expeller to deworm and 8(19.0%) used it to stop vomiting, 21 (50.0%) used the implicated drug to treat fever or presumed malaria, while 11 (26.2%) did not indicate the purpose for which the offending drug was administered. However, one (2.4%) of the children was administered haloperidol by an unsupervised adult with psychiatric condition.

Dose of drugs taken and blood levels of the drugs

The details of the dose of the drugs administered were not recorded by the attending physician. Blood levels of the administered drugs were not assayed as we do not have facilities for such.

Parts of the body involved with the dystonic reaction

The neck was the most frequently involved part of the body followed by the mouth and tongue and the eyes, then the limbs as focal or segmental dystonia while the rest of the children had a generalized body involvement. Details of the parts of the body involved with the acute dystonic reactions are stated in Table 3.

Table III: Parts of the body involved in the manifestation of dystonia

Part of the body involved	Frequency (N = 42)	Percentage
Focal/Segmental:	27	64.3
Head/Neck	16	38.1
Eye	11	26.2
Mouth/Tongue	11	26.2
Limbs	4	9.5
Generalized (whole body)	15	35.7

Duration of admission and associated body parts involved

All patients were admitted for a period ranging from 12 hours to 72 hours. Twenty-four (58.5%) children were admitted for one day only. Thirteen (31.7%) were admitted for two days while four (9.8%) were admitted for three days. The other one had this information missing from the records.

Treatment on admission

All the forty-two admitted children were given one form of treatment or the other. Intravenous fluids were administered to 34(81.0%) of them to keep the vein open, administration of treatment drugs or hydration. The drugs commonly administered to manage the acute dystonic reaction were diazepam in 29(69.0%), benzhexol in 1(2.4%), both in 5(11.9%) phenobarbitone in one (2.4%), and phenobarbitone with diazepam in one case respectively while five (11.97%) had no medication given.

There was a significant association between body parts affection and the duration of admission as higher proportion of patients with 1-2 days of admission had focal/segmental presentation while none of those that stayed 3 days had such presentation ($X^2 = 10.183$, $p=0.006$).

Discussion

Drug induced acute dystonic reactions encountered in paediatric emergency consultation is not an uncommon disorder. Previous studies document this disorder as a common reason for paediatric emergency consultation.^{2,7,8} The abnormal posturing and movement

disorder coupled with the acute onset of the disorder is usually a cause of concern and worry to the patient or the parents. Fear emanating from the presumably unknown cause and outcome of unremitting acute bizarre posturing is a strong motivation for seeking urgent care.

Most of the children admitted with drug induced dystonia were under the age of ten years, especially the preschool ages. This age group is also prone to frequent malaria attacks. Treatment of symptoms of malaria was the most common circumstance for using the drug implicated as inducing the acute dystonia in our series. This is even corroborated by the finding of more cases in the wet, malaria season. Our findings on the age group affectation are consistent with previous reports.^{7,9} A mean age of 11.3 years was however recorded among Korean children with acute drug induced dystonia. Drugs for gastrointestinal disorders were the most common culprits among the Korean children³ unlike the present study. More boys compared to girls had drug induced dystonia, however this gender affectation difference was not much.

Antimalarials were the most common drugs inducing the acute dystonia. Previous reports also suggest that the anti-malarials and antihistamines are common causes of drug induced dystonia. The next most common drug identified was the prokinetic, dopamine receptor antagonist Metoclopramide used to treat vomiting. Other antimalarials identified to cause acute dystonia include arthemeter¹⁰ and chloroquine. Amodiaquine is a recommended drug for Artemisinin-based combination therapy. Thus, it is important to do further studies to establish the association between Amodiaquine based ACT combinations and dystonia with the view of reviewing the policy and preventing this reaction.

In our series, 2 (4.8%) of the patients reported Artemisinin as inducing the dystonia while one implicated Chloroquine. The mechanism for dystonia is believed to be extrapyramidal effects of many of the drugs, especially anti-psychotics and anti-emetics like metoclopramide.^{9,11} The mechanism with the anti-malarials, Amodiaquine and Chloroquine is believed to be due to the reduction of catecholamine levels in the forebrain and inhibition of neuronal calcium uptake and with the involvement of GABA in dystonia and improvement in this symptom with administration of diazepam is understandable.^{12,13,14,15} Acute dystonic reactions to chloroquine and amodiaquine can also be idiosyncratic, as they can occur at standard or toxic dosage.^{14,15,16} Unfortunately, the drug levels of all the drugs associated with dystonia were not measured because the facilities for this estimation were not accessible. Thus, it was not possible to decide whether the acute dystonic reactions were true toxicities or mere side effects. Therefore, it is important to do further studies to establish the association between Amodiaquine-based Artemisinin combinations and dystonia with the view to reducing or preventing this reaction.

The most common parts of the body affected by dystonia in the present study were the neck, eye and tongue which is consistent with previous studies.^{2,3} Some also involved the limbs either separately or with the head, eyes or tongue. These by current classification of dystonia are focal or segmental as compared to generalised, defined as affectation of the whole body. Generalized dystonia was also common in this series. Affectation of the most visible parts of the body such as the face and neck make it difficult to conceal the disease and probably contributes to early detection and urgent health seeking behaviour.

Concerning the morbidity associated with drug induced dystonic reactions, most of the cases were hospitalized for average of two

days and this may be warranted for fear of progression to development of respiratory symptoms, especially when mouth and or tongue are involved or merely to manage the anxiety of the caregiver as they may seek alternative care that may complicate the situation. They were admitted with diazepam and intravenous fluid administration, the latter to keep vein open and hydration to aid elimination of the drug implicated. Diagnosis was clinical, requiring no investigations as reported by most studies except for the underlying disease that warranted taking the dystonia causing medication.

Outcome in all the patients studied was also good, without sequelae or complication and requiring short duration of hospitalisation (less than 72 hours). That more body parts affected was associated with longer the duration of hospitalisation is not unexpected. It may be a correlation or degree of drug receptor affectation and severity outcome in terms of duration of occurrence and extents of body parts involvement. Our findings on morbidity and outcome are also similar to previous reports.^{1,4,9}

Most of the children were from low socio-economic status families which could have influenced the choice of healthcare facility they approached for treatment and procurement of the drugs for their earlier symptoms. Most of the drugs inducing the dystonia were prescribed by non - doctors and most of the prescriptions were not obtained in pharmacies. It could be noted that these drugs are over-the-counter medications. Chemists and maternity nurses were the professionals mostly associated with the prescription of the dystonia inducing drugs. A similar finding was obtained in another study conducted in Nigeria, informing the study suggestion that unauthorized persons should not prescribe.⁷

There is a need to increase the awareness of these dystonia inducing drugs among nurses and chemists with a view to discourage similar prescription patterns. Awareness of dystonia inducing drugs should also include non health professionals, as our study revealed that some of the drugs were obtained from the home stock of the patient/caregiver and this did not require consultation with any health practitioner.

Rational prescription of medicines may have a place in the reduction of the burden of acute drug induced dystonia. A previous report has established that irrational prescription of drugs is a public health issue in low- and middle-income countries.^{17,18} Most of the professionals who prescribed the dystonia inducing drugs were not trained to undertake medical consultation and prescription. Furthermore, most of these professionals lack the required knowledge of pharmacology and rational prescription. It may be possible to prevent this disorder or reverse this menace by enforcing that medicines are prescribed and dispensed only by authorized persons. This practice is expected to ensure rational prescription and increase the safety margin in avoidance of unwanted drug side effect.

Conclusion: Acute drug induced dystonia is a notable cause of paediatric emergency admission in our health facility and antimalarials, especially Amodiaquine are the commonest drugs implicated. Patients present more in the wet than dry season months. Very few of the implicated drugs were procured at recognised private hospital/pharmacies. Most cases of dystonic reactions emanated from self, chemist and maternity nurses' prescription compared with prescription by doctors and the implicated drugs were same as in the past previously documented. Ensuring that these medications are only available, prescribed and dispensed by authorized persons should mitigate the burden of this disease.

Inability to measure serum drug levels precluded knowing which drug in the fixed combination antimalarials was responsible for the dystonic reaction.

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Contributions of each author:

Oseni SBA: Conceptualization and Review of literature; Design of methodology; Data collection; Data analysis and presentation of findings; Discussion of findings; Final authorization of completed work.

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Oyededeji O: Conceptualization and Review of literature; Design of methodology; Data collection; Data analysis and presentation of findings; Discussion of findings; Final authorization of completed work.

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