# Journal of Medical Sciences

ISSN 1682-4474

science alert

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OPEN ACCESS Journal of Medical Sciences

ISSN 1682-4474
DOI: 10.3923/jms.2020.13.17

# Research Article
# Pattern and Outcome of Drug Induced Dystonia at the Paediatric Emergency Room of a Teaching Hospital in Southwestern Nigeria

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## Abstract

**Background and Objectives:** Drug induced dystonia (DID) is a common reason for unnecessary diagnostic evaluations by the emergency physicians. This study aimed to determine the prevalence, pattern and outcome of DID at the Paediatric Emergency Room (PER) of Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, Nigeria. **Materials and Methods:** A retrospective study of cases of DID that presented at the PER of EKSUTH between January, 2014 to December, 2017 was conducted. Data about age, sex, drug intake and clinical symptoms were obtained from case files. Quantitative variables were summarized using mean and standard deviation while categorical variables were summarized using frequencies and percentages. Data were analyzed using SPSS version 20. **Results:** DID were 0.48% (17/3538) of the total admissions. The mean age of occurrence was 5.7±4.2 years (Range: 1-15 years) and 52.9% of them were females. The drugs implicated were amodiaquine in (7) 41.2%, promethazine (6) 35.2%, metoclopramide (2) 11.8% and haloperidol (2) 11.8%. The abnormal body movements involved the head in 12 (70.6%), neck (7) 41.2%, trunk and limbs (3) 17.6% of the cases. All the patients (100%) had complete resolution within 48 h of admission and were discharged. **Conclusion:** The leading cause of DID was the anti-malarial drug Amodiaquine with the most affected body part being the head region. Clinicians should be familiar with the various ways of presentation DID and have an increased index of suspicion when patients present with movement disorders to prevent misdiagnosis and unwarranted investigations or treatment.

Key words: Drug-induced dystonia, amodiaquine, manifestations, promethazine, metoclopramide

Citation: A.O. Babatola, A.B. Taiwo, E.O. Ogundare, T.O. Ojo, A.B. Ajite, O.I. Oluwayemi, J.O. Fadare and O.S. Olatunya, 2020. Pattern and outcome of drug induced dystonia at the paediatric emergency room of a teaching hospital in southwestern Nigeria. J. Med. Sci., 20: 13-17.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Drug induced dystonia is a common side effect of anti-psychotics medications and some other drugs, the manifestations which are often dramatic and frightening to observers especially laymen are causes of visits to the paediatric emergency room. Dystonia is a movement disorder often present with abnormal sustained or repetitive movements, postures or both[1,2]. It was first described in 1911 by Oppenheim[3]. There are many causes of dystonia, among which are degenerative disorders, brain injuries, vascular disorders, genetic disorders, neoplasms and drugs. Anti-emetics and anti-psychotics are the commonest cause of drug-induced dystonia (DID)[4]. Antimalarials containing 4-aminoquinolines, carbamazepine and some antibiotics such as cefuroxime and cefixime have also been implicated[5-10].

The prevalence of drug-induced dystonia is generally unknown in children, however, there are few reports of some cases in children[4,7,10-12]. The pathogenesis of drug-induced dystonia is not fully known. It is however proposed that blockade of dopaminergic pathway, accumulation of dopamine at the synapses, reduced availability of dopamine at the receptors, hypersensitivity of dopaminergic receptors and unopposed actions of acetylcholine are involved[13,14]. Individual susceptibility may be genetically related[7]. Clinical manifestations depend on the muscle group(s) affected. The common muscles involved are the muscles of the head and neck, which present as tongue thrusting, torticollis and jaw lock. The involvement of other groups of muscles may present as opisthotonus and involuntary repetitive limb movements. It may also present with life threatening manifestations such as laryngospasm and cyanosis. Consciousness and mentation are mostly intact[4-7,12,13].

The diagnosis of drug-induced dystonia is usually clinical, requiring a high index of suspicion; a detailed medication history is cardinal[4,5,15]. Treatment includes supportive measures such as emergency resuscitation, reassurance, withdrawal of the offending drugs and generous hydration. Some classes of drugs such as anticholinergics, dopaminergics, GABAergics and muscle relaxants have been used in the management of DID[16]. However, benztropine, benzhexol, biperidine and diazepam, diphenhydramine and chlorpheniramine are commonly used and reported to be effective in DID treatment[4,5,7,12,13].

Considering the fact that the diagnosis of drug induced dystonia relies heavily on history and physical examination, a good knowledge of DID will enable physicians make accurate diagnosis and manage DID appropriately. This is more important for physicians caring for children given the fact that most children may not be able to describe how they feel when they suffer from DID. To the best of our knowledge, data on DID especially in children is very scarce. This study therefore aimed to determine the prevalence, pattern and outcome of children who presented with drug-induced dystonia at the Ekiti State University Teaching Hospital, Ado-Ekiti, South-west Nigeria.

## MATERIALS AND METHODS

This study was a descriptive study that reviewed medical records of patients seen between January, 2014 and December, 2017 at the Paediatric Emergency Room of Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, Nigeria. Data were obtained from the case files of children who presented and were diagnosed with drug-induced dystonia.

EKSUTH is a state government owned hospital that was established in April, 2008 to serve as a tertiary and referral health center for the secondary and primary tiers of health facilities in Ekiti State, Nigeria, a geopolitical region with a population of about 2.5 million people. The hospital has over 300 beds with 14 beds at the children emergency room. The average number of admissions at the children emergency room is 1200 annually. A clinical proforma was used to extract information from the patients' case files: extracted information included biodata, presenting complaints, drug used, indications for drug use, duration between drug ingestion and onset of symptoms, patient management and outcomes.

**Data analysis:** Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20.0. Frequencies and percentages were used to estimate proportions for categorical variables and continuous variables were summarized using median and range as well as mean and standard deviation as appropriate. Chi-square was used to compare results between groups. A p-value<0.05 was regarded as statistically significant.

**Ethical consideration:** Ethical approval was obtained from Ethics and Research Committee of the Ekiti State University Teaching Hospital, Ado-Ekiti.

## RESULTS

During the study period, 3,538 patients were admitted in the paediatric emergency room, 17 of whom had drug-induced dystonia, giving a prevalence of 0.48%.

Table 1: Characteristics of drug-induced dystonia

| Characteristics | Frequency (%) | Percentage |
|---|---|---|
| **Age group (years)** | | |
| <5 | 9 | 52.9 |
| 6-10 | 6 | 35.3 |
| 11-15 | 2 | 11.8 |
| **Sex** | | |
| Male | 8 | 47.1 |
| Female | 9 | 52.9 |
| **Drug used** | | |
| Amodiaquine | 7 | 41.2 |
| Promethazine | 6 | 35.3 |
| Haloperidol | 2 | 11.8 |
| Metoclopramide | 2 | 11.8 |
| **Onset of symptoms (h)** | | |
| <6 | 4 | 23.6 |
| 7-12 | 3 | 17.7 |
| 13-18 | 0 | 0.0 |
| 19-24 | 7 | 41.2 |
| >24 | 3 | 17.7 |
| **Indication for drug use** | | |
| Vomiting | 12 | 70.6 |
| Fever | 9 | 52.9 |
| Accidental ingestion | 2 | 11.8 |
| **Part of the body involved** | | |
| Head | 12 | 70.6 |
| Neck | 7 | 41.2 |
| Trunk and limbs | 3 | 17.6 |

Table 2: Body part affected among the age groups

| | Age group (years) | | | |
|---|---|---|---|---|
| Body parts affected | <5 | 6-10 | 11-15 | p-value |
| Neck | 4 | 3 | 1 | 0.974 |
| Tongue | 3 | 4 | 2 | 0.164 |
| Eyes | 1 | 2 | 0 | 0.425 |
| Limbs | 2 | 1 | 1 | 0.624 |

Table 3: Drugs and the prescribers

| | Prescriber | | | | |
|---|---|---|---|---|---|
| Drugs | Doctors | Health worker | Patent drug seller | Accidental use | p-value |
| Promethazine | 0 | 6 | 1 | 0 | 0.083 |
| Amodiaquine | 4 | 2 | 1 | 0 | 0.032 |
| Haloperidol | 0 | 0 | 0 | 2 | 0.020 |
| Metoclopramide | 0 | 2 | 0 | 0 | 0.733 |

Table 4: Distribution of diagnosis, treatment and duration of hospital admission

| Parameters | Frequency (n = 17) | Percentage |
|---|---|---|
| **Diagnosis** | | |
| Accurate | 14 | 82.4 |
| Inaccurate | 3 | 17.6 |
| **Treatment** | | |
| Intravenous fluids | 17 | 100 |
| Artane | 3 | 17.6 |
| Diazepam | 9 | 52.9 |
| **Duration of admission (h)** | | |
| <48 | 14 | 82.4 |
| >48 | 3 | 17.6 |

There were more females (52.9%) and the mean age of the cases was 5.7±4.2 years (range 1-15 years). Eighty-seven percent of the cases occurred in patients younger than 10 years. The drugs implicated were amodiaquine, metoclopramide, promethazine and haloperidol. Amodiaquine was involved in 7 (41.2%) of the cases. The common indications for the drugs used included vomiting in 12 (70.6%) of the patients and two of the children ingested haloperidol accidentally. The peak time of onset of symptoms in 14 (82.4%) of the cases was within 24 h. The body part mostly affected was the head, including the tongue and eyes in 12 (70.6%) patients, the neck was affected in 7 (41.2%) of them, while the limbs and the trunks were less commonly affected (Table 1).

**Association between age groups and body part affected:** There was no association between the age of the children and body part involved in the dystonic reaction (p>0.05) (Table 2).

**Drugs involved and the prescribing source:** Six of the patients who had dystonia from promethazine use had the drug prescribed by health workers (non-doctors). Doctors prescribed Amodiaquine for 4 of the 6 patients with dystonia due to Amodiaquine use (Table 3).

**Diagnosis, treatment and outcome of the patients with drug induced dystonia:** The initial diagnosis made at presentation was inaccurate in 3 (17.6%) of the cases. The 3 were initially managed for meningitis. All the patients who presented with DID were admitted and given intravenous fluids; 3 (17.6%) were given Artane®, while 9 (52.9%) were given Diazepam. There was no record of specific time of recovery following the medical interventions instituted while on admission. All cases of DID resolved. Most of the patients (82.4%) spent<2 days (48 h) on admission with an average duration of 15±9.5 h (Table 4).

## DISCUSSION

This study, to the best of the authors' knowledge, is the first of its kind to be conducted among Nigerian children. The prevalence of 0.48% (17 out of 3,538) reported in this study appears low but is comparable with the reports by Park *et al.*[4] in Korea who managed 79 patients with drug induced dystonia over a 10 year period. Derinoz and Caglar in Turkey also reported managing 55 patients over a 6 year period[12]. The cohort of only 17 patients over a 4 year period in this study is however very much lower than the 47 adult patients managed

over 3 years in Port-Harcourt, Nigeria[17]. This higher prevalence among the adult population may be related to higher use of antipsychotics among them. The lower prevalence of DID in children may be due to the lower and less mature dopaminergic/cholinergic receptors in the paediatric age group[6].

This study did not observe any significant gender difference, an outcome similar to reports from studies conducted in Korea and Turkey[4,12]. This is not surprising, given that both the social and biologic factors that could affect the prevalence and nature of DID manifestations are not expected to differ in children because of their age factor.

The drugs mostly implicated in this study, were anti-emetics such as promethazine and metoclopramide; this result is similar to reports from a study conducted by Park *et al.*[4] in Korea and Derinoz and Caglar[12] in Turkey. These antiemetics were supposedly prescribed by health workers who are non-doctors most probably for vomiting which is a non-specific symptom present in most disease conditions. The implication of this is that there is a need for more campaign against drug prescribing by unauthorized persons and caution by authorized persons when prescribing antiemetics.

Amodiaquine, a commonly prescribed antimalarial in the study area, was also implicated in this study, this is similar to previous reports[7,18]. The implication of this is that prescribers of drugs that can cause DID should educate and inform their patients about the condition so that they can know what to do if it occurs. Also adequate drug history should be taken before drug prescription. Haloperidol, a recognized cause of dystonia[12,13,17,19] was also implicated in this study. The two patients who had DID due to haloperidol however, accidentally ingested the drugs; both patients ingested medications meant for their primary care givers. This brings to the fore again the importance of keeping drugs out of the reach of children.

Most drugs were ingested at the usual therapeutic doses with the exception of haloperidol where the doses ingested could not be ascertained. This gives credence to the fact that occurrence of dystonia following drug ingestion is not likely to be dose-dependent[4,10-12], although this study did not include assays for serum drug levels. Majority (82%) of our patients in this study presented within 24 h of ingestion of the implicated drugs, there are, however, reports of occurrence of DID even after weeks of drug ingestion[4,12].

Similar to other studies, the face especially the tongue and eyes were most commonly involved in our study[4,12,20]. The reasons for this observation is not known but may be related to the distribution and concentration of dopaminergic receptors in the areas of the brain involved with motor movements of the face and tongue. This possibility could be explored in further studies.

The chances that a patient with DID will be misdiagnosed was also highlighted in this study[21,22]. This is not surprising, as DID may mimic other conditions like meningitis, seizure, hypocalcaemia, etc. In this study, the three cases that were misdiagnosed were initially managed for meningitis and empirical antibiotics were commenced for them. Antibiotics use occasioned by DID misdiagnosis can contribute to excessive and misuse of antibiotics which are known drivers of the growing grave problem of antibiotic resistance. This, therefore suggests that clinicians need to be well knowledgeable about DID to prevent unnecessary interventions, waste of resources and further worsening of the growing problem of antibiotics resistance .

The management of DID is not elaborate: all affected patients had intravenous fluid, majority had diazepam and 3 were given benzhexol with good clinical outcomes and they were discharged home. Similar observations have been reported in some earlier cited studies[4,5]. This suggests that clinicians need to be able to recognize the symptoms and signs of drug induced dystonia early and manage as appropriate so as to avoid unnecessary healthcare costs due to unwarranted investigations and treatments.

The major limitation to this study is its small number of patients with DID, identified in this single facility which did not allow for investigations of associations between variables. The lack of similar studies conducted within the African continent with which to compare our findings is another limitation. Also, being a retrospective study, the time of resolution of symptoms following medical interventions could not be ascertained as this was not documented in the patients' medical records. Despite the limitations mentioned above, the study has documented the prevalence and common causative agents of DID among pediatric patients in Ado-Ekiti, South-West Nigeria. The reasons for variations in the timing of the occurrence of dystonia following drug ingestions will be our focus in further studies.

## CONCLUSION

The reported prevalence of DID in our study was low with amodiaquine and promethazine being the most common implicated drugs. There is a need for physicians to have high index of suspicion so as not to mis-diagnose this often very dramatic condition. Drug prescribers need to be aware of common drugs that may cause DID in children and prescribe them only when necessary. Caregivers should always keep drugs out of reach of children to avoid accidental ingestion of drugs that can cause DID.

## SIGNIFICANCE STATEMENT

There are many previous studies on drug induced dystonia among adults but similar studies in children are very scanty. This study describe for the first time among children in the study locality the occurrence of drug induced dystonia and its manifestations, thus showing that the phenomenon is not also uncommon among children. Therefore findings from this study will help to sensitize health care workers involved in the care of children about the occurrence of drug induced dystonia in children and its manifestations, thereby raising awareness and the need for proper and adequate management of drug induced dystonia. In addition, it is an important contribution to knowledge on the subject in the study area.

## ACKNOWLEDGMENT

The authors appreciate Dr. Fatunla O.T. and Dr. Abdulraheem F.O. for the assistance in collection of data.

## REFERENCES

1. Albanese, A., K. Bhatia, S.B. Bressman, M.R. DeLong and S. Fahn *et al*., 2013. Phenomenology and classification of dystonia: A consensus update. Movement Disord., 28: 863-873.
2. Duma, S.R. and V.S.C. Fung, 2019. Drug-induced movement disorders. Aust. Prescr., 42: 56-61.
3. Newby, R.E., D.E. Thorpe, P.A. Kempster and J.E. Alty, 2017. A history of dystonia: Ancient to modern. Movement Disord. Clin. Pract., 4: 478-485.
4. Park, H.W., J.R. Kwak and J.S. Lee, 2017. Clinical characteristics of acute drug-induced dystonia in pediatric patients. Clin. Exp. Emerg. Med., 4: 133-137.
5. Oyewole, A.O., A.O. Adelufosi and O. Abayomi, 2013. Acute dystonic reaction as medical emergency: A report of two cases. Ann. Med. Health Sci. Res., 3: 453-455.
6. Oshikoya, K.A., H. Chukwura, O.F. Njokanma, I.O. Senbanjo and I. Ojo, 2011. Incidence and cost estimate of treating pediatric adverse drug reactions in Lagos, Nigeria. Sao Paulo Med. J., 129: 153-164.
7. Fajolu, I.B. and F.E.A. Lesi, 2010. Drug-induced acute dystonia in a 7 year old child following the use of artesunate-amodiaquine: A case report. Int. J. Risk Saf. Med., 22: 111-114.
8. Fadare, J.O. and L.F. Owolabi, 2009. Carbamazepine-induced dystonia, a case report. Neurol. Asia, 14: 165-166.
9. Busari, O.A., J. Fadare, S. Agboola, O. Gabriel, O. Elegbede and Y. Oladosu, 2013. Chloroquine-induced acute dystonic reactions after a standard therapeutic dose for uncomplicated malaria. Sultan Qaboos Univ. Med. J., 13: E476-E478.
10. Bayram, E., M.T. Bayram, S. Hiz and M. Turkmen, 2012. Cefixime-induced oculogyric crisis. Pediatr. Emerg. Care, 28: 55-56.
11. Yilmaz-Topal, Ö., N. Tuygun, H. Akça, E. Polat and C.D. Karacan, 2015. Cetirizine and albendazole induced dystonia in a child. Turk. J. Pediatr., 57: 407-408.
12. Derinoz, O. and A.A. Caglar, 2013. Drug-induced movement disorders in children at paediatric emergency department: 'dystonia'. Emerg. Med. J., 30: 130-133.
13. Van Harten, P.N., H.W. Hoek and R.S. Kahn, 1999. Acute dystonia induced by drug treatment. Br. Med. J., 319: 623-626.
14. Marano, M., L. di Biase, G. Salomone, A. di Santo, A. Montiroli and V. di Lazzaro, 2016. The clinical course of a drug-induced acute dystonic reaction in the emergency room. Tremor Other Hyperkinet. Mov., Vol. 6. 107916/D87P8ZS1.
15. Işıkay, S., M. Almacıoğlu and K. Yılmaz, 2012. Metoclopramide induced acute dystonic reaction in a child: A case report. J. Emerg. Med. Case Rep., 3: 59-61.
16. Jinnah, H.A. and S.A. Factor, 2015. Diagnosis and treatment of dystonia. Neurol. Clin., 33: 77-100.
17. Nkporbu, A.K., C.U. Okeafor, C.N. Stanley, O.N. Onya and C.S. Princewill, 2016. Prevalence and pattern of drug induced movement disorders in University of Port Harcourt Teaching Hospital (UPTH): A 3-year review. EC Neurol., 4: 36-40.
18. McEwen, J., 2012. Artesunate-and amodiaquine-associated extrapyramidal reactions. Drug Saf., 35: 667-675.
19. Yaginuma, K., M. Watanabe, K. Miyazaki, A. Ono and H. Murai *et al*., 2019. Haloperidol-induced dystonia due to sedation for upper gastrointestinal endoscopy: A pediatric case report. Case Rep. Emerg. Med., Vol. 2019. 10.1155/2019/3591258.
20. Sharawat, I.K. and R. Suther, 2018. Drug induced acute dystonic reaction. Indian Pediatr., 55: 1003-1003.
21. Dingli, K., R. Morgan and C. Leen, 2007. Acute dystonic reaction caused by metoclopramide, versus tetanus. Br. Med. J., 334: 899-900.
22. Incecik, F., Y. Onlen, C. Ozer and K. Ozcan, 2008. Metoclopramide induced acute dystonic reaction: Two case reports. Marmara Med. J., 21: 159-161.