



A STUDY OF PREVALENCE, PATTERN AND OUTCOME OF DRUG INDUCED DYSTONIA IN CHILDREN: A PROSPECTIVE STUDY

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ABSTRACT

Introduction: This study aimed to determine the prevalence, pattern and outcome of Drug induced dystonia in children. **Methods:** This prospective observational study was carried out at Pediatric department from September 2020 to June 2021. A total number of 130 children (60 females and 70 males), the mean age of 5.7 ± 4.2 years (range 1-15 years) with drug induced dystonia were recruited from Emergency and outpatient department and treated with benzodiazepine in emergency department. All patients were followed for 9 months and there was no recurrence of dystonia at the last follow-up. **Results:** Prevalence rate of drug induced dystonia was 0.051% (130/2520). The most frequent causes of drug-induced dystonic reactions were antipsychotics (46.15%) and antiemetics (46.15%). 46.15 % cases of dystonia were seen with anti-emetic drugs, 46.15% with anti-psychotic drugs and 7.69 % with other drugs. 7.69% cases of Opisthotonos dystonia, 53.84% of cases of dystonia in posturing of head and neck and 38.46% of cases in abnormal posturing in head, neck and limb were seen. There were 61.53% cases of drug over dose in our study. All the patients (100%) had complete resolution within 48 h of admission and were discharged. **Conclusion:** Drug induced dystonia in children were common with antiemetics and antipsychotics either with therapeutic dose or overdose. Benzodiazepines and diphenhydramine were more effective drugs in the treatment of drug induced dystonia in children.

KEYWORDS : Drug-induced Dystonia; Children; Anti-emetic; Anti-psychotic; Benzodiazepines

INTRODUCTION

Dystonia is a neurological movement disorder in which sustained involuntary muscle contractions cause twisting and repetitive movements or abnormal postures of the neck, jaw, tongue or the entire body. Upward or lateral movement of the eyes, dysphagia, dysarthria and difficulty in breathing may also occur. [1, 2] The mechanism of acute dystonia is still unclear.

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 antipsychotics are the commonest cause of drug-induced dystonia (DID). [4] It is proposed that dystonic movements observed in patients receiving dopamine antagonists such as antipsychotics, antiemetics and gastrointestinal motility agents occur due to the imbalance between cholinergic and dopaminergic stimulation and therefore, anticholinergic agents such as biperiden and diphenhydramine are used in the treatment of dystonia. [3-5] Acute dystonic reactions are the most common type of extrapyramidal reactions associated with the use of certain drugs. Drug-induced dystonic reactions (DIDRs) are diagnosed based on the detailed history and physical examination. Drug-induced dystonic reactions (DIDRs) occur due to the many drugs within therapeutic dose or overdose within minutes, hours, or even days of exposure to an inciting drug. Antipsychotics, anticonvulsants, tricyclic antidepressants, and antiemetics are common drugs causing DIDRs. [2] The aim of this study was to study of Prevalence, Pattern and Outcome of Drug Induced Dystonia in children.

MATERIALS AND METHODS

This prospective observational study was conducted between September 2020 to June 2021. Inclusion criteria included a total of one hundred and thirty children aged <15 years who presented to the pediatric emergency department with acute dystonia and with a history of drug ingestion.

The exclusion criteria included children with chronic dystonia, cerebral palsy, and any neurodegenerative disorders.

This study was approved by the institutional ethical committee. A written informed consent was obtained from parents of enrolled children. Data for all the patients such as age, gender, complaints at admission, causative drug for drug-induced dystonic reactions (DIDRs), duration of drug

intake, dosage of the drug (therapeutic dose, overdose, and unknown dose), class of the drug, recommended treatment, and follow-up were recorded. The data were presented as number and percentages.

RESULTS

During the study period, 2520 patients were admitted in the paediatric emergency room, 130 of whom had drug-induced dystonia, giving a prevalence of 0.051%. There were more males (53.84%) and the mean age of the cases was 5.7 ± 4.2 years (range 1-15 years). Below the age of 5 years, 30.76% (40/130) patients of drug induced dystonia were seen. Between 6-10 years, 23.07% (30/130), and 11-15 years, 46.15% (60/130) cases were seen. 46.15 % cases of dystonia were seen with anti-emetic drugs, 46.15% with anti-psychotic drugs and 7.69 % with other drugs. 7.69% cases of Opisthotonos dystonia, 53.84% of cases of dystonia in posturing of head and neck and 38.46% of cases in abnormal posturing in head, neck and limb were seen. There were 61.53% cases of drug over dose in our study. (Table 1)

The most frequent causes of drug-induced dystonic reactions (DIDRs) were antipsychotics (46.15%) and antiemetics (46.15%). Risperidone was the most commonly used drug within antipsychotics in this study. The diagnosis of patients, who had taken antipsychotic drugs, was attention deficit hyperactivity disorder (ADHD) (50/130), and autism spectrum disorder (ASD) (50/130). All patients with DIDRs due to antiemetics were within 10 years of age and were prescribed for vomiting and gastroesophageal reflux disease (GERD). Among 130 patients, seven patients received combination of two drugs. In fifty patients (38.46%), dystonic reactions emerged due to drugs that were prescribed by a pediatrician and psychiatrist. However, in 80 patients (61.53%) who had dystonia from drug use had the drug prescribed by health workers (non-doctors). 33.3% of the patients obtained the drugs as over the counter (OTC) drugs. Routine blood investigations (complete blood count, serum electrolytes, creatinine, and liver function test) were normal in all children. Electroencephalogram (EEG) was done in seven patients and all had normal findings. Neuroimaging was done in twenty-two infants who were normal in both. All the patients were treated with benzodiazepine in emergency department. A total of sixty-two patients received oral diphenhydramine for 3 days. The follow-up period was 9 months and there was no recurrence of dystonia at the last follow-up.

DISCUSSION

Drug-induced dystonic reactions (DIDRs) occur due to the many drugs within therapeutic dose or overdose within minutes, hours, or even days of exposure to an inciting drug. Antipsychotics, anticonvulsants, tricyclic antidepressants, and antiemetics are common drugs causing DIDRs. [2] The mechanism of acute dystonia is still unclear. It is proposed that dystonic movements may be due to the imbalance between cholinergic and dopaminergic stimulation. [3,4] Thus, blockade of these receptors by drugs causes the disappearance of the inhibiting effect of dopamine on acetylcholine, and as a result, cholinergic system becomes relatively more dominant and leads to the development of extrapyramidal movement disorders, such as dystonia. [5] In our study, the prevalence rate of drug induced dystonia was 0.051%. 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, 7-12] 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, 10, 11] in Korea and Derinoz and Caglar[12-17] in Turkey. In our study, 46.15 % cases of dystonia were seen with anti-emetic drugs, 46.15% with anti-psychotic drugs and 7.69 % with other drugs. 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] In the present study, 7.69% children had taken amodiaquine. 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 was also implicated in this study. [12, 13, 17, 19] The two patients who had DID due to haloperidol however, accidentally ingested the drugs; both patients ingested medications meant for their primary care givers. In the present study, 46.15% children had taken anti-psychotic drugs. All the children were fully recovered without complication. 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 are 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.

CONCLUSION

The reported prevalence of drug induced dystonia in our study was low with amodiaquine (anti-malarial) and anti-emetic and anti-psychotic drugs 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. We need to be aware of common drugs that may cause drug induced dystonia in children and prescribe them only when necessary. we should always keep drugs out of reach of children to avoid accidental ingestion of drugs that can cause drug induced dystonia.

Table 1: Clinical Profile of Drug-induced Dystonic Reactions in Children

Characteristics	Frequency	Percentage (%)
Age group (years)		
<5	40	30.76
6-10	30	23.07
11-15	60	46.15
Sex		
Male	70	53.84
Female	60	46.15
Drug used		
1. anti emetic Metoclopramide Promethazine	60	46.15
2. anti sychotic Risperidone Heloperidol Clorpromazine	60	46.15
3. Others Amodiaquine	10	7.69
Types of dystonia		
1. Opisthotonus	10	7.69
2. posturing of head and neck	70	53.84
3. Abnormal posturing of head, neck, and extremities	50	38.46
Dosage		
Therapeutic dose	50	38.46
Overdose	80	61.53
Duration of drug use		
<12 h	50	38.46
12-48 h	40	30.76
2-7 days	40	30.76

Funding: None

Acknowledgement: None

Conflict of Interest: None

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