PROMETHAZINE-INDUCED DYSTONIC REACTION IN A NIGERIAN CHILD: A CASE REPORT AND REVIEW OF LITERATURE

ABSTRACT.

Drug-induced dystonic reactions are reversible movement and posture disorders that occur after administration of certain drugs. They are characterised by intermittent spasmodic or sustained involuntary contractions of various muscles in the body and are often underdiagnosed or misdiagnosed in clinical practice. These reactions occasionally are life threatening and can be distressing to the patients and their families. In developing countries like Nigeria, parents frequently administer promethazine to their kids to alleviate vomiting. However, it is worthy of note that oral administration of promethazine can cause dystonic reactions.

Herein, we describe the management of a 13-month-old male with promethazine-induced dystonic reactions who was misdiagnosed as severe malaria on presentation. Our aim is to increase awareness of promethazine –induced dystonia among clinicians.

Keywords: Acute Dystonia, Medication-induced, Promethazine

INTRODUCTION.

Acute dystonic reactions are reversible extrapyramidal effects that can occur after drug administration and is characterised by intermittent or sustained involuntary contractions of face, neck, trunk, extremities and rarely the larynx.[1,2] Acute dystonic reactions usually occur within a few days following exposure to certain drug and manifests as torticollis, retrocolis, oculogyric crisis(upward eye deviation) or tongue protrusion.[3] These reactions are rarely life threatening but can be distressing to the patients and their families.[2] Medical treatment is usually effective as motor symptoms start to resolve with onset of treatment and discontinuation of offending medication.[1] The diagnosis of medication-induced acute dystonic reactions is clinical. It involves obtaining thorough medication history and

physical examination. Management is pharmacologic and complete resolution may occur following treatment.

CASE REPORT.

A 13-month-old male presented to the Emergency Paediatric Unit of Federal Teaching Hospital Owerri, Imo State Nigeria with history of vomiting of 4 days, abnormal body movements of 2 days and fever of 1 day all prior to presentation. Vomiting was sudden in onset, non- projectile and non –bilious, occurred three to four times each day and contained recently ingested feeds. Abnormal body movements were noted 2 days after the onset of vomiting , involving jerking movements of the upper and lower limbs, smacking of the lips, tongue protrusion and upward rolling of the eyes; aborting spontaneously over one to three minutes and reoccurring multiple times per day. There was no history of postictal loss of consciousness sleep or incontinence. There was no family history of febrile convulsions, epilepsy or similar abnormal body movements. At the onset of his ailment, he was taken to a patent medicine dealer where he received oral promethazine 5mls twice daily for 4 days. Abnormal body movement was noticed 2 days after commencement of oral promethazine.

On examination, he was febrile (38.5^0C), irritable, conscious, pupils were equal and reactive to light, jerking chorea-like movements of the limbs, lip smacking, tongue protrusion with occasional bleeding from the tongue due to biting of the tongue; upward rolling of the eyes, arching of the neck and back with normal tone in between episodes. A working diagnosis of severe malaria (multiple convulsion) to rule out meningitis and space occupying lesion was made. He was admitted to the emergency paediatric unit and was commenced on intravenous Artesunate @3mg/kg/day 0, 12, 24, and 48 hours. He also received intravenous Ceftriazone @ 100mg/kg /day and intravenous phenytoin @ 2.5mg/kg/dose .Serum calcium was normal while serum electrolytes showed mild hypokalaemia (K 3.4 mmol/L) and hyponatremia (132mmol/l), which was corrected with intravenous fluids. Full blood count was essentially normal and blood film for malaria parasite was negative. Brain computed tomography scan done was normal.

A diagnosis of promethazine-induced dystonia was made following review of investigations after 24 hours on admission. Promethasine was discontinued and

intravenous diphenhydramine was prescribed but due to unavailability of the intravenous formulation, syrup diphenhydramine was commenced @ 2mg/kg/ day. Patient showed marked reduction of symptoms (resolution of lower limb jerking) after 72 orals of administering oral diphenhydramine and thereafter the drug was tapered-off over 96 hours and discontinued. Patient was discharged home dystonia free and he is presently on follow-up in neurology clinic.

DISCUSSION

Acute dystonic reactions are reversible extrapyramidal effects that occur after administering drugs.[1] They are characterised by intermittent spasmodic or sustained involuntary contractions of muscle in the face, neck, trunk, pelvis and larynx in either sustained or intermittent patterns leading to abnormal body movements and posture.[2] Dystonic manifestations can affect various muscle groups although they are predominantly observed in the head and neck region.[3] In our patient's case, involvement was primarily noted in the head and neck region. The symptoms may begin immediately the drug is administered or delayed between hours to days. It is documented that 50% occur within 48 hours of initiation of treatment while 90% occur within 5 days.[2] Acute dystonic reactions occasionally are life threatening when they cause laryngospasm, , rhabdomyolysis, acute renal failure, heart arrest, etc. [2-4]

The incidence of drug induced dystonia is unknown primarily due to prevalent misdiagonsis and underreporting in medical literature.[1] Documented risk factors include male gender, younger age, potency of dopamine blocker and previous dystonic episode.[2-4] In this case, our patient had two significant risk factors namely male gender and young age. Drug-induced dystonic reaction may be caused by antiemetics especially metoclopramide and promethazine, neuroleptics and antidepressant drugs. [1]

Promethazine is a first-generation antihistamine used to treat various ailments[2] and is not recommended for use in children less than 2 years. It is a strong H1 agonist with moderate anticholinergic and antidopaminergic activity.[5] This gives it the potential to cause movement disorders. Its use intravenously has been noted to have lower threshold for causing dystonia as compared to oral intake.[6] Oral formulation of promethazine procured

from a patent medicine dealer was administered to our patient. This probably explains why the patent suffered dystonic reaction.

Dystonic reactions are often unpredictable and idiosyncratic. They are due to an imbalance between cholinergic and dopaminergic pathways in the nigrostratum of the basal ganglia.[2] Acetylcholine has grossly inhibitory effect on movement while dopamine has grossly excitatory effects on movements. Most drugs produce dystonic reactions by nigrostriatal dopamine D2 receptor blockade, which leads to an excess of striatal cholinergic output.[1,2]

The diagnosis of drug induced dystonia is made from a thorough history and examination.[1,2] A detailed history involving medication history and a comprehensive physical examination should be done and conditions such as stroke and seizures should be ruled out.[2] Initially, the patient was diagnosed with severe malaria with meningitis as a differential diagnosis. Diagnosing drug induced dystonic reactions requires a high index of suspicion given the resemblance dystonic movement to seizures. ~~Drug –induced dystonic reaction is confirmed clinically when there is rapid resolution of symptoms following treatment. However, clinicians should consider an alternative diagnosis when there is a no resolution of symptoms following treatment.[2,7]~~ In this case, initiation of oral diphenhydramine led to significant improvement, thus supporting the diagnosis of promethazine-induced dystonia. Fever can manifest with ongoing dystonic reactions or as a result of neuroleptic malignant syndrome.. Sepsis and malaria were ruled out as the probable cause of fever in our patient as evidence by normal full blood count result and negative blood film for malaria parasite. Notably, the fever observed in the index case was due to dystonic reaction and not neuroleptic malignant syndrome which usually occur one month after drug administration.[4]

Acute dystonic reaction in children poses serious challenge for the paediatrician as the disease closely resembles meningitis, tetanus, neuroleptic malignant syndrome, orbital/mandibular fractures, hypocalcaemia, focal seizure, strychnine poisoning.[2,3] Consequently, there is a high probability of misdiagnosis and delay in instituting appropriate medication.

The aim of treatment is to re-establish the disrupted dopaminergic-cholinergic balance in the basal ganglia and discontinue the offending drugs.[2] Anticholinergics (Diphenhydramine, benztropine) and benzodiazepines are used to reverse or reduce symptoms in acute dystonic reactions.[2] Supportive measures such as oxygen or assisted ventilation should be provided if indicated.

Diphenhydramine is first line therapy and has anticholinergic effect and central nervous system penetration. Intravenous administration is preferred to other routes of administration owing to its faster onset of action.[2] Dosing is 1-2mg/kg/dose 6 hourly not to exceed 50mg in 24 hours and followed by oral administration 6 hourly for 24-72 hours to prevent recurrence of symptoms[2] and taper off to prevent withdrawal symptoms. Our patient received only oral formulation of Diphenhydramine and had complete resolution of symptoms within 72 hours of treatment and neither had any recurrence nor withdrawal symptoms. Benztropine has significant CNS penetration, but is not for use in paediatric age group.[2] Second line therapy is with IV benzodiazepine 0.1mg/kg or IM lorazepam 0.05-0.1mg/kg may be considered if anticholinergic therapy fails.[2]

~~Prognosis is good because dystonic reactions are typically not life threatening and result in no long-term effects. Complete resolution of symptoms can not occur following treatment.~~ It is noteworthy that symtoms may reoccur after 72 hours following treatment. The index patient had complete resolution of symptoms and there was no recurrence throughout the duration of treatment .~~No long-term sequelae are expected once the agent is identified and discontinued.~~ The patient has visited the Paediatric neurology clinic for follow up without any neurological sequelae documented.

CONCLUSION.

In developing countries like Nigeria where over the counter prescriptions are prevalent, patients have easy access to promethazine often prescribed to stop vomiting. Consequently, clinicians should have high index of clinical suspicion of drug –induced dystonia in any child presenting with abnormal body movement particularly if the child received promethazine prior to presentation. .

ETHICAL APPROVAL AND CONSENT

Ethical approval for this study was obtained from the Ethical committee of the Federal Teaching Hospital Owerri Nigeria. Parental written consent was also obtained and preserved by the authors.

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