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METOCLOPRAMIDE-INDUCED DYSTONIA

Metoclopramide is a selective dopamine antagonist (D_2-R) that is used to prevent or treat nausea and vomiting that may result from chemotherapy, surgery or acute migraine attack. However, in view of **increasing number of reports regarding neurological adverse reaction** due to metoclopramide especially **in children and young adult,** the Drug Control Authority (DCA) has issued a directive to **tighten the restriction** regarding the use of metoclopramide in this population. [1]

One of the important neurological side effects of metoclopramide is **dystonia**. Dystonia are extrapyramidal side effects due to **alteration of the dopaminergic-cholinergic balance in the nigrostriatum**. It happens when there is an excess of striatal cholinergic output due to nigrostriatal dopamine D2 receptor (D_2-R) blockade. [2]

It is characterized as **prolonged muscle contractions that result in abnormal movements and postures**. It includes [2]:

Opisthonus: Extreme hyperextension of the body (backward arching of the head, neck, and spine)

Torticollis: Abnormal, asymmetrical head or neck position

Dysarthria: Unclear speech

Trismus: Spasm of the masticatory muscle with difficulty in opening the mouth (lock jaw)

Oculogyric crisis: Temporary period of frequent spasms of eye deviation particularly upward, each spasm lasting from seconds to hours and the entire episode lasting from days to weeks.

Some facts[2]

- **The incidence** of the these reactions due to metoclopramide is 0.2% but can increase to **as high as 25% in young and old patients**
- Dystonia are known to appear more frequently in female patients, at high drug doses, patients with family history of neurological disorders and those who are treated with neuroleptics
- It **can happen at any age** even if it is used **at therapeutic doses** and it is **dose dependent**

In 2019 itself, there have been 2 cases reported in HCTM, one from pediatrics and one in adult patient with underlying epilepsy, both given Metoclopramide for vomiting.

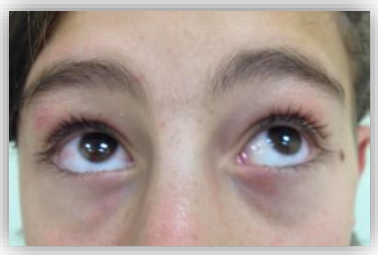

Figure 1: Metoclopramide induced oculogyric crisis[2]

REMINDER [1]

- **Restrict** the indication as **second-line option,** especially for **pediatric patients** (1-18 years old)
- **All** metoclopramide products are **contraindicated for patients <1 year old**
- **Restrict duration** of use (up to 5 days)
- **Maximum** daily dose of **30mg or 0.5mg/kg/day for adult** and **0.5mg/kg/day (0.1-0.15mg/kg OD to TDS) for pediatrics**
- Keep the **interval of at least 6 hours between each dose** even if vomiting or rejection of the dose occurs
- **IV** must be administered as **slow bolus (≥3min)**
- **Contraindicated** in patients with **history of neurological disease** especially epilepsy and **avoid concomitant use** with **drug that may cause extrapyramidal symptoms**.

References:
1. National Pharmaceutical Control Bureau (NPRA) Directive [BPFK/PPP/07/25 (24)]
2. Koban Y, Ekinci M, Cagatay H, Yazar Z. Oculogyric crisis in a patient taking metoclopramide. Clinical Ophthalmology. 2014;:567
3. BNF & BNF for Children

Treatment available in HCTM during Emergencies

Treatment of dystonia is symptomatic as no curative therapies are available. The table below shows the available treatment of dystonia available in HCTM[3].

Drugs	Dosing	Comments
Procyclidine 10mg/2mL inj. **(Kemadrin®)**	**Child 10 years and above, Adult:** IM or IV injection 5-10mg, repeated after 20 minutes if necessary (max: 20mg/day) **Child 2-9 years**: IM or IV 2-5mg for 1 dose **Child 1 month-1 year**: IM or IV 0.5-2mg for 1 dose	Effective emergency treatment for acute drug induced dystonic reactions. Usually effective within 5-10 minutes, but may need 30 minutes for relief for dose more than 10mg Unlicensed use in children
Benzhexol/ Trihexyphenidyl 2mg tab. **(Artane®)**	**Adult**: Oral 1mg daily, then increased in steps of 2mg every 3-5 days, adjusted according to response. Maintenance: Oral 5-15mg daily in 3-4 divided doses (Max: 20mg/day) **Child 3 months–17 years:** Oral Initially 1-2mg daily in 1-2 divided dose, then increased in steps of 1mg every 3-7 days. (Max 2mg/kg/day)	Usually as a second line treatment. Tablets can be taken with or without food
Diazepam 10mg/2mL inj. **(Valium®)**	**Adult**: IV injection 5-10mg, then 5-10mg after at least 10 minutes as required. **Child 12-17 years:** IV injection 5-10mg, repeated if necessary, to be given over 3-5 minutes **Child 1 month-11 years:** IV injection 100mcg/kg, repeated if necessary, to be given over 3-5 minutes.	For life threatening acute drug-induced dystonic reaction. To be administered into large vein. Infants and children: Do not exceed 1 to 2 mg/min IV push. Adults: 5 mg/min.

Please be informed that manufacturer will be introducing a **new formulation** of **Cerumol Ear Wax Softener replacing the Cerumol Ear Drops** effective September 2019. Do check with pharmacy regarding stock availability. Details of the Old and New Formulation as below:

Properties	Cerumol Ear Drops (Old Formula)		Cerumol Ear Wax Softener (New Formula)	
Active ingredients	**Arachis Oil 57%**	Lubricant	**Propylene Glycol Dicaprylocaprate**	Solvent
	Paradichlorobenzene 2%	Insecticide & and to reduce viscosity	**Butoxyl**	Viscosity surfactant, surface wetting agent
	Chlorobutanol 5%	Antibacterial, antifungal and to reduce viscosity	**Turpentine Oil**	Wax penetration & solvent
			Chlorocresol	Preservative
Volume	11mL per bottle		10mL per bottle	
Shelf life	5 years		3 years	
Registration category	Pharmaceutical product		Medical device	

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