

EMERGENCY THERAPEUTIC ATTITUDE IN A CASE OF ACUTE INTOXICATION WITH METOCLOPRAMIDE IN THE PEDIATRIC PATIENT

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ABSTRACT: Metoclopramide is authorized through the national procedure in the EU Member States, is a selective dopamine receptor blocker, (D2) and serotonin (5-HT₃), inhibits chemoreceptors residing within the trigger, lessens the sensitivity of the nerves that transmit impulses visceral the pylorus and duodenum to induce vomiting. Reevaluation of drugs containing metoclopramide was initiated in December of 2011, at the request of France, in accordance with the provisions of article 31 of Directive (EC) 2001/83/EC. This was followed by another reevaluation metoclopramide-containing drugs used in children, made by EU Member States, as provided for in article 45 of Regulation (EC) No. 1901/2006 on medicinal products for pediatric, and after which, in 2010, it has identified the risk of neurological adverse reactions and have been recommended a series of measures to reduce risk to a minimum.

Keywords: pediatric patient, metoclopramide, adverse reaction

INTRODUCTION:

Metoclopramide is an emetic central actions. Normalizes motility of gastro-intestinal and gallbladder, antispasmodic effects, stimulation of esophageal peristalsis, gastric and duodenal and pylorus does to relax. Compared to other antiemetics and antispasmodic action, provides central predominantly, the specific centers that regulate digestive activity. (Bateman et al, 1985, Dingli 2007) Metoclopramide can give side effects in children, even after therapeutic doses, a dyskinetic extrapyramidal syndrome (oculogyric crisis, in the facial muscle contractures- tongue or neck-torticollis), reversible, persist syndrome 8-12 hours after the suspension of treatment. (Fahn et al, 2007, Yis et al 2005). These side effects generally occur after 1-3 hours after starting treatment (sometimes even after a single administration) and impose its discontinuation. The incidence of dystonic reactions in children and young adults is greater at high doses over 0,5 mg/kg per day.

The preparation is known since 1964. Metoclopramide is rapidly absorbed from the digestive tract with a bioavailability of $76 \pm 38\%$ (with large individual variations).

C_{max} is reached in less than an hour from healthy volunteers after administration of a single dose of 20 mg metoclopramide orally, and in 2.5 hours after oral administration or nazogastric doses of 0,10-0,15 mg/kg

administered 4 times a day at preterm, C_{max} having value of 80 ng/ml in healthy volunteers and 18 ng/ml in preterm newborns. Metoclopramide is widely distributed into tissues, including the CNS. The apparent volume of distribution is 2,2-3.4 l/kg. In small proportion binds to plasma proteins by 40%.

Hepatic metabolism of metoclopramide is made in part from the first passage through the liver and glucuronocjugation lime. Half life is 4-6 hours. The preparation is excreted from the body mainly through the kidney within 24-72 hours approximately 85% of the administered dose, of which 30% as unchanged.

MATERIALS AND METHODS:

Patient b. C aged 10 years, without personal history or collateral-significant, critically important in urban areas is accompanied by dad, the UPU service in Pediatrics, so as a result of accidental ingestion 30 drops metoclopramide (a bottle containing water solution of Metoclopramide 0,665 g%-1 mg = 3 drops) in place of vitamin C. Ingestion occurred after 60 minutes.

Clinical examination shows general status influenced, G-30 Kg,-1.40, present in the skin of generalised maculo-pruritic papules with a tendency to combine, vicious neck-position stiff neck, drowsiness-affirmative symptoms appeared at 40 minutes for

ingestion of metoclopramide. Examination of the cardio-respiratory apparatus highlights: FR-18 r/min, rhythmic heart FC-78 b/min, TA-100/70 mmHg, SaO₂-98%.

Laboratory tests in emergency had highlighted both the normal values test biochemical or hematologic.

The clinical diagnosis of adverse reactions to metoclopramide, accidental administration of 10 mg active substance (therapeutic dose required per day is 15 mg, at 30 kg-0.5 mg/kg):

- from the central nervous system-drowsiness and extrapyramidal effects-stiff neck
- immediate hypersensitivity- cutaneous eruption

Treatment goals were:

- . prevention of drug absorption
- . toxic elimination from the body while placing
- . the administration of antidotes
- . symptomatic treatment

Detoxication methods enable were divided into the following groups:

1. Methods of stimulation of the natural detoxication processes-gastrointestinal tract clean out-challenge the vomiting reflex
2. Methods of therapy type antidote (pharmacological)
 - administration of antiparkinson drug - 2 mg akineton-biperiden-1/2 po, together with administration of diazepam 5 mg IV
 - antihistamine - claritine-loratadinum 10 mg po together with administration of corticosteroids iv. - hemisuccinat of hydrocortisone 10 mg/kg
3. Artificial methods of detoxication, went along with the support of vital functions monitored throughout therapy with dynamic control of hemodynamic indices and acid-base balance.

Infusion is applied to reduce the concentration of toxic substances in blood by the parenteral administration of hydro-electrolytic solutions (intravenous infusion with saline and glucose) and create conditions for the effective stimulation of dieresis.

Clinical evolution was favorable with the disappearance of both the neurological phenomena of drowsiness and extrapyramidal reaction, as well as those of the immediate type hypersensitivity. The patient has left the emergency module in 6 hours, on his father's

signature, without returning this later for another checkup.

RESULTS AND DISCUSSION:

In situations of acute intoxication with metoclopramide aims to:

- Clinical diagnosis (lab) intoxication exogenous clinic interpretation of obtained results.
- Application of advanced methods of treatment of intoxication, including accelerated disposal measures of mitigation in the body toxicity by using formulae and application of symptomatic therapy antidote, correction and support the vital functions of the body, which had been damaged by the action of toxic.
- Prevention-an explanation of how parents of metoclopramide; referral of possible reactions to the therapeutic doses or overdose.
- In 2009, the USFDA required all manufacturers of metoclopramide to issue a black box warning regarding the risk of tardive dyskinesia with chronic or high-dose use of the drug.

CONCLUSIONS:

Caution is advised in case of metoclopramide in children and young adults because of the risk of neurological side effects.

Drug toxicology study of a therapeutic index of medicinal preparations, adverse reactions and their dangerous actions on the body and develop measures on prevention and treatment of drug poisoning.

Diagnose and quick therapeutic attitude leads to a favourable evolution of adverse reactions caused by metoclopramide.

REFERENCES:

- Bateman DN, Rawlins MD, Simpson JM. Extrapyramidal reactions with metoclopramide. *BMJ* 1985; 291: 930-2.
- Dingli K, Morgan R, Leen C. Acute dystonic reaction caused by metoclopramide, versus tetanus. *BMJ* 2007; 334: 899-900.
- Fahn S. Systemic therapy of dystonia. *Can J Neurol Sci* 1987; 14: 528-32.
- JAEM 2013; 12: 80-4 Işıkay et al. Metoclopramide-Induced Acute Dystonic Reaction
- Gal P, Reed MD. Medications. In Behrman RE, Kliegman RM, Jenson HB,



Editors. Nelson Textbook of Pediatrics. 17th ed.
Philadelphia: WB, Saunders
Company; 2004. p. 2432-2501.
HealthCentral. "Side Oral Reglan Efecte."
<http://www.healthcentral.com/acid-reflux/find-drug-50680-73.html?ic=4031>
Low LC, Goel KM. Metoclopramide poisoning
in children. *Arch Dis Child*
1980; 55: 310-2.

Yis U, Ozdemir D, Duman M, Unal N.
Metoclopramide induced dystonia in
children: two case reports. *Eur J Emerg Med*
2005; 12: 117-9.
Ponte CD, Nappi JM. Review of a new
gastrointestinal drug-metoclopramide.
Am J Hosp Pharm 1981; 38: 829-33.
RxList. "Reglan.: Efecte secundare"
<http://www.rxlist.com/reglan-drug.htm>

