Metoclopramide-Associated Extrapyramidal Syndrome (EPS) in Patients under 18 years: Results from Taiwan National Adverse Drug Reaction Reporting System

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Background

Metoclopramide (MTC) is a benzamide derivative which acts on D2-dopamin receptor and serotonin 5-HT3 receptor as antagonist. It is usually used as an anti-emetic or prokinetic drug which extrapyramidal syndrome (EPS) is the most frequently mentioned adverse drug reaction.

In November 2011, Swissmedic announced that the specially developed pharmaceutical forms of MTC for pediatric was withdrawn from the market because of the higher risk of EPS. In the same time, MTC is contraindicated in children less than 1 year-old and not recommended using in patients between 1 and 18 years in Swiss.

Objectives

The objective was to study metoclopramide-associated extrapyramidal syndrome reported to Taiwan ADR reporting system in patients under 18 year-old for further measurements regulatory.

Table 1. Characteristics of cases with MTC-associated EPS less than 18 years

Item	Less than 18 years	Less than 1 year
No. of case	59	6
Gender (%)		
Male	32(46)	5(83)
Female	27(54)	1(27)
Age (yr, mean±SD)	10.3±5.7	0.53±0.28
Onset time (day)*		
<1	20	6
<2	8	0
<3	13	0
Over 3 days	6	0
Metoclopramide pharmaceutical forms		
Injection	33	3
Oral tablet	15	1
Oral solution	3	2
Outcome (%)		
Death	0	0
Life-threatening	1(1.6)	0
Porlonged hospitalization	2(3.4)	0
Hospitalization	6(10.3)	0
Require intervention to prevent permanent impairment or damage	21(35.6)	3(50)
Others	29(49.1)	3(50)
Severity (%)**		
Mild	12(20)	2(33)
Medium	45(76)	4(67)
Severe	0	0
Unassessable	3(4)	0

*__Onset time__: Time to onset of adverse reactions after drug administration.

**__Mild__: Discontinue use/dose reduced without additional treatment. __Medium__: With additional treatment/hospitalization. __Severe__: life-threatening/hospitalized over 7 days

Methods

Data had been collected from 2002 to 2012 by Taiwan National Adverse Drug Reaction (ADR) Reporting System. All Suspected metoclopramide-associated cases were included.

Extrapyramidal syndrome was defined as Preferred Term (PT) level under Extrapyramidal Syndrome of Standardised MedDRA Query (SMQ) version 14.0. The proportion of EPS of all MPC-reported ADRs and baseline characteristics were analyzed.

Results

A total of 565 reported cases which corresponds to 75% of all MTC-associated ADRs were extracted. The average age was 46.6±21.9 years and 60% were female.

In children less than 18 years, 59 cases were reported as MTC-related EPS corresponding to 88% of all types of ADRs reported in this subgroup. In children less than 1 year, there were 6 MTC-associated EPS cases which count 85% of all types of ADRs reported in this subgroup.

There were no death case in our database and most cases recovered with proper management except 3 cases without enough information to assess. The onset time of EPS in 90% of patients less than 18 year-old was within 72 hours.

Pediatric dose regimen was over the recommendation dosage by micromedex in 13 out of 59 pediatric cases and the pediatric dosage listed in the package inserts was not well-informed in most products in Taiwan.

Conclusions

On our review of MTC-associated EPS, there was no severe case reported in all age group from our database and the proportion of EPS to the other ADRs of MPC was slightly higher in children less than 18 years.

However, no other latest evidences could be found to prove this risk further, and the need of clinical use should be taken into consideration when it comes to the indication and contraindication of metclopramide. Simultaneously, the contents of package inserts should be modified to provide enough information to prescribers.

Reference

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