

Cilostazol Uses in Contraindicated conditions: A review from Taiwan

Adverse Drug Reporting System and Health Insurance Database

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Declaration

The Taiwan National Adverse Drug Reaction Reporting Center, operated under Taiwan Drug Relief Foundation, is designated and funded by Taiwan Food and Drug Administration, Department of Health, Taiwan.

Background

Taiwan National Adverse Drug Reaction Reporting System was put in place to collect and analyze spontaneous reports to ensure safety of drugs since 2003.

In March 2013, European Medicines Agency (EMA) has announced that cilostazol should not be given to patients who have unstable angina or who have had severe tachyarrhythmia, myocardial infarction or a recent coronary intervention nor to those receiving two or more antiplatelets or anticoagulants.

Objective

To identify potential safety concerns about cilostazol in Taiwan.

Methods

- (1) We reviewed all cilostazol-associated reports collected by Taiwan National Adverse Drug Reaction (ADR) Reporting System from 2003 to 2013. Cases with above contraindicated conditions were further analyzed.
- (2) We searched 2009 Taiwan National Longitudinal Health Insurance Database (LHID) for patients who received cilostazol prescriptions for over 30 days and further analyzed the risks mentioned above.

Results

- (1) We identified 100 cilostazol associated ADR reports and of which, 12 (12.0%) were contraindicated with a mean age of 67. Congestive heart failure (25.0%), combination therapies and bypass surgery (16.7%) accounted for the top three contraindications.
- (2) In addition to antiplatelets or anticoagulants, ginkgo biloba is also the most common combination therapy in Taiwan database.
- (3) In LHID, we identified 1943 cases combination antiplatelets therapies (2.93%), severe tachyarrhythmia (2.68%), and congestive heart failure (1.54%) represent the top three contraindications.

Conclusions

Our findings suggest that cilostazol were commonly prescribed in patients with above contraindications in clinical practice in Taiwan. Cautions should be addressed to health care professionals and further domestic regulatory actions should be taken for this potential risk.

Table 1. Demographics of 12 contraindicated cases

No.	Gender	Age	Adverse reaction	Patient outcome	Contraindication
Any cardiovascular disease					
1	F	62	Palpitation, headache	Non serious adverse reaction	Congestive heart failure
2	M	80	Pancytopenia	Prolonged hospitalization	1. Congestive heart failure, NYHA Fc II 2. Coronary artery disease
3	M	87	Congestive heart failure worsen	Hospitalization	1. Congestive heart failure 2. Atrial fibrillation with RVR
Concomitant medication					
1	M	62	Coagulopathy, Gastrointestinal bleeding	Prolonged hospitalization	Warfarin+clopidogrel +enoxaparin
2	M	61	Leg edema	Non serious adverse reaction	Aspirin+ dipyridamole
3	M	57	INR increased, gastrointestinal bleeding	Non serious adverse reaction	Warfarin
4	M	65	INR increased	Require intervention to prevent permanent impairment or damage	Warfarin
5	M	36	Headache	Non serious adverse reaction	Ginkgo biloba
6	M	68	Epistaxis	Hospitalization	Ginkgo biloba
7	F	41	Vertigo	Require intervention to prevent permanent impairment or damage	Ginkgo biloba
PCI/CABG					
1	M	62	Intracranial hemorrhage	Life-threatening	PCI within 6 months
2	M	61	skin rash	Non serious adverse reaction	PCI within 6 months

Abbreviation: F, Female; M, Male; RVR, rapid ventricular response; PCI, Percutaneous coronary intervention; CABG, coronary artery bypass graft

Table 2. The number and percentage of cilostazol use in contraindicated conditions in LHID

Contraindication	Million sampling number (N=1943)	Estimated number of people exposed to risk*	Percentage(%)
Cardiovascular disease/angioplasty			
Severe tachyarrhythmia	52	1196	2.68
Unstable angina	8	184	0.41
Myocardial infarction	21	483	1.08
Congestive Heart Failure	30	690	1.54
PCI/CABG	43	989	2.21
Any cardiovascular disease	102	2346	5.25
Bleeding disorders			
Intracranial hemorrhage	1	23	0.05
Gastrointestinal bleeding	0	0	0
Dual antiplatelet therapy/Anticoagulants			
Aspirin+ Clopidogrel	57	1311	2.93
Aspirin+ Ticlopidine	9	207	0.46
Warfarin	83	1909	4.27

* The estimated number is about 23 times for Taiwan whole population.