Drug-induced Torsade de Pointes:
Review of the National Adverse Drug Reactions Reporting System in Taiwan

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Background

Torsade de Pointes (TdP) is a rapid form of polymorphic ventricular tachycardia which is related to evidence of delayed ventricular repolarization with long QT interval or prominent U waves showed on electrocardiogram (ECG). Although the prevalence of drug-induced TdP remains unknown, associated risk factors and potential risky drugs have already been well studied. However, discrepancies of prescribing patterns, lifestyles, and prevalence of cardiovascular diseases between Taiwan and other countries may result in different patterns of relevant drugs and risk factors of TdP. The main purpose of this study was to review the patterns of drug-induced TdP in Taiwan.

Method

The data of this study was derived from the database of National ADR Reporting System and Standardised MedDRA Queries (SMQs, MedDra: Medical Dictionary for Regulatory Activities) were used to define drug-induced TdP when retrieving the associated adverse drug reaction (ADR) cases up until February, 2013.

Result

Table 1. Patient Characteristics

	patient number (%)
Gender	
Female	77 (57.0)
Male	58 (43.0)
Age (Mean±S.D.)	60.6±18.6
≦30	9 (6.7)
31–54	36 (26.7)
55–74	46 (34.1)
≧75	37 (27.4)
Unknown	7 (5.2)

A total of 135 TdP cases were identified under the definition of Standardised MedDRA Queries. Most of the cases were female (57.0%). 110 cases (81%) were considered as serious. The average age was 60.6 ± 18.6 years old and 83 cases (61.5%) were greater than 55 years old.

Amiodarone, moxifloxacin and digoxin were most frequently reported. The onset of drug-induced TdP was within 2 weeks in most cases (56.3%).

Table 2. Case Characteristics

Outcome	Case number (%)	Relationship	Case number (%)
		certain	2 (1.5)
		probable	60 (44.4)
recovered/resolved	20 (14.8)	possible	65 (48.1)
recovering/resolving	61 (45.2)	unlikely	5 (3.7)
Not recovered/not resolved	1 (0.7)	conditional	2 (1.5)
fatal	6 (4.4)	unassessable	1 (0.7)
unknown	47 (34.8)	**Onset time**	**Case number (%)**
Seriousness	**Case number (%)**	≦1 day	31 (23.0)
death	8 (5.9)	2–14 days	45 (33.3)
life-threatening	45 (33.3)	15–30 days	10 (7.4)
(prolonged) hospitalization	20 (14.8)	31–100 days	9 (6.7)
other serious ADRs	37 (27.4)	≧101 days	16 (11.9)
non-serious ADRs	25 (18.5)	unknown	24 (17.8)

61 cases (45.2%) were recovering or resolving from the ADR. As for the outcome of the ADR, 81% (110 cases) were defined as serious per reporter. Left ventricular ejection fraction (4.4%), serum magnesium (17.8%), heart rate (21.5%), and QTc interval (27.4%) were seldom recorded in the case report.

Table 3. Most Frequently Reported Drugs

	Torsade de pointes	Ventricular tachycardia	ECG QT prolonged	ECG QT abnormal	Case number (%)
amiodarone	11	5	7		23(11.4)
moxifloxacin	3	2	9		14(7)
levofloxacin	4	4	3		11(5.5)
digoxin	1	8	1		10(5)
cisapride	6				6(3)
methadone			5		5(2.5)
fluconazole	4		1		5(2.5)
cimetidine	1	1	3		5(2.5)
clozapine			5		5(2.5)
quinidine		3	2		5(2.5)
erythromycin	2	1	2		5(2.5)
fentanyl		2	2		4(2)
haloperidol	1	1	2		4(2)
zotepine			4		4(2)
sulpiride	2		1		3(1.5)
ciprofloxacin		1	2		3(1.5)
thioridazine	1	1	1		3(1.5)
astemizole		1	2		3(1.5)
rocuronium bromide		1	2		3(1.5)
olanzapine			3		3(1.5)
terfenadine	2		1		3(1.5)
propafenone	1	2			3(1.5)
ziprasidone			2	1	3(1.5)
escitalopram		1	2		3(1.5)
imipramine	1	1	1		3(1.5)
總計	**42**	**35**	**64**	**1**	**142(70.6)**

Conclusion

Female and elderly counts for majority of the cases analyzed which was in consistency with the risk factors being well-studied. Prescribers should consider the risk of QT prolongation which can be fatal when weighing the risks and benefits for at-risk groups upon prescribing drugs with known TdP risk. Parameters of risk factor including left ventricular ejection fraction, serum magnesium, heart rate, QTc interval, and etc. should be assessed and recorded for better case evaluation.

Reference

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