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Dipyridamole-induced adverse effects in myocardial perfusion scans: Dynamic evaluation

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ABSTRACT

Aim and Background: Dipyridamole-induced stress myocardial perfusion scans (MPS) has been widely used for management of coronary artery disease. The adverse effects of dipyridamole and other stress agents have been evaluated. The aim of this research is to confirm the dynamic data on dipyridamole side effects during MPS.
Methods: We collected data of 183 patients who underwent dipyridamole-induced stress MPS by retrospectively reviewing their clinical records, which included the severity of dipyridamole side effects in 3 min, 10 min, and 20 min after infusion. The incidence and severity at all three points, including the effect of age and gender, were obtained.
Results: Adverse effects occurred in 96 patients (69.6%). The most frequent symptoms were dizziness (42.8%), chest tightness (24.6%), abdominal pain (18.1%), and headache (15.2%). Most symptoms were Grade 1 to 2, according to the grading system for common terminology criteria. The median duration of symptom persistence was 36 min, not significantly different among age and gender.
Conclusion: This study demonstrates that the adverse effects of dipyridamole were generally minimal and its duration was acceptable for clinical usage.

1. Introduction

Cardiovascular disease has been the second most common mortality since 2000 in Taiwan [1]. Myocardial perfusion imaging (MPI) is a useful tool in diagnosing and follow up care for coronary artery disease [2]. According to current clinical guidelines for better sensitivity and specificity, the exam is performed with a stress test [2–4]. Dipyrdamole, a vasodilator, is one of the most widely used agents in stress tests in Taiwan. According to prior literature, up to 70% of patients undergoing dipyridamole stress suffer from adverse effects such as flush, chest pain, headache, dizziness, hypotension, abdominal pain, or diarrhea [5–9]. However, severity and duration of adverse effects have not been analyzed. As stated, the aim of this study is to examine dynamic data of dipyridamole side effects during MPS.

2. Materials and methods

2.1. Patients and data collection

In our institute, symptoms of patients receiving dipyridamole-stress MPI for 3 min, 10 min, and 20 min were recorded, according to the Common Terminology Criteria of Adverse Effects v4.0 (CTCAE) [10]. Records were written and maintained by physicians and technicians. Symptoms recorded included: chest tightness, palpitation, abdominal pain, diarrhea, nausea, headache, dizziness, neck pain, dyspnea, weakness, and flush. If symptoms persisted for more than 20 min after administration, we recorded timing of recovery. In the case of aminophylline use to relieve adverse effects, we also recorded administration timing.

From July 2nd 2013 to July 19th 2013, there were 183 patients receiving MPI. There were 138 complete records of symptoms after delivery of dipyridamole. For an evaluation of confounding factors, we collected the following parameters: age, gender, and frequency of regular exercise. These comorbidities were recorded in the clinical chart review: hypertension, diabetes, dyslipidemia, prior myocardial infarction (MI), documented coronary artery disease (CAD), and congestive

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heart failure. The laboratory data over 3 months were also recorded: creatinine level, lipid profile, and hepatic enzyme glutamate pyruvate transaminase (GPT).

These methods were approved by our institutional review board.

2.2. Stress protocol

All patients underwent the Thallium-201 (Tl-201) stress and early-redistribution MPI with the dipyridamole stress test, on the recommendation of the Society of Nuclear Medicine and Molecular Imaging (SNMMI and EANM). Heart rate, blood pressure, and ECG monitoring were performed throughout the stress test.

2.3. Statistics

R project version 3.1.2 was used for statistical analysis. The continuous parameters were expressed in terms of mean and standard deviation (SD). The categorical variables were expressed as count and percentage. Severity of each symptom at 3 min, 10 min, and 20 min were also expressed as count and percentage.

The Kaplan-Meier curve was used to highlight persistent symptoms.

Patients were in two groups according to age (age >65). For an evaluation of confounding factors, e.g., gender and age, the Kaplan-Meier curve and Cox regression test were used for comparison between males and females, the age groups, and the exercise groups.

3. Results

Data from 138 patients were analyzed and listed in Table 1. The average age was 66.1 ± 13.4 years (range 32–90). Seventy-five were male (54.3%) and 60 study subjects exercised more than 3 times per week (43.5%). There were 96 patients (69.6%) suffering from symptoms of drug side effects during observation. Between the symptomatic and asymptomatic group, the incidence of comorbidities and lab data were not statistically different, except that the serum creatinine level was higher in the asymtomatic group. However, in the symptomatic group, the ratio of female patients was significantly higher than in the asymptomatic group ($p = 0.002141$), while the age was significantly younger ($p = 0.009262$).

The frequency and severity of adverse effects are listed in Table 2 and Fig. 1. Adverse effects occurred in 96 patients (69.6%), with the most frequent symptoms being dizziness (42.8%), chest tightness (24.6%), abdominal pain (18.1%), and headache (15.2%). These effects accompany dyspnea (8.7%), nausea (8.0%), neck pain (7.2%), weakness (5.1%), palpitation (3.6%), and flush (2.9%). No patients had diarrhea in our study population, while most symptoms were Grade 1 and 2. Seven patients had Grade 3 symptoms as shown in Table 6. There were 18 patients receiving aminophylline treatment due to adverse effects. For patients with symptoms at 3 min, the persistent symptoms can be seen in the Kaplan-Meier curve (Fig. 2). The median duration of persistent symptoms was 36 min (95% confidence interval [CI]: 30–46 min). Fifty-six patients (40.6%) did not recover from side effects at 20 min, while 32 of them were female.

Table 2
Number and percentage of symptoms at 3, 10, and 20 min.

	3rd minute	10th minute	20th minute	Any time
Chest tightness	26 (18.8%)	24 (17.4%)	17 (12.3%)	34 (24.6%)
Palpitation	4 (2.9%)	2 (1.4%)	2 (1.4%)	5 (3.6%)
Abdominal pain	13 (9.4%)	19 (13.8%)	7 (5.1%)	25 (18.1%)
Dyspnea	10 (7.3%)	7 (5.1%)	4 (2.9%)	12 (8.7%)
Diarrhea	0	0	0	0
Nausea	5 (3.6%)	7 (5.1%)	7 (5.1%)	11 (8.0%)
Headache	16 (11.6%)	13 (9.4%)	11 (8.0%)	21 (15.2%)
Dizziness	52 (37.7%)	45 (32.6%)	30 (21.7%)	59 (42.8%)
Neck pain	5 (3.6%)	5 (3.6%)	8 (5.8%)	10 (7.2%)
Weakness	3 (2.2%)	6 (4.3%)	7 (5.1%)	7 (5.1%)
Flush	3 (2.2%)	1 (0.7%)	1 (0.7%)	4 (2.9%)
Overall	84(60.9%)	79 (57.2%)	56 (40.6%)	96 (69.6%)

Table 1
Patient background information.

	Total	Symptomatic	Asymptomatic	P-value
Number	138	96	42	
Gender				0.002141
Male	75 (54.3%)	41 (42.7%)	33 (78.6%)	
Female	63 (45.7%)	55 (57.3%)	9 (21.4%)	
Age (years old)	66.1 ± 13.4 (32-90)	64.2 ± 13.24 (32-90)	70.6 ± 12.88 (41-90)	0.009262
Frequency of exercise (times per week)				
Range	0-7			
Median	1			
Mean	2.8	2.9	2.5	0.4626
≥3	60 (43.5%)			
Using aminophylline	18			
Timing (min)	22.2 ± 8.5			
Comorbidity				
Hypertension	85 (61.6%)	56 (58.3%)	29 (69.0%)	0.317
Diabetes	37 (26.8%)	24 (25.0%)	13 (31.0%)	0.6048
Dyslipidemia	51 (37.0%)	34 (35.4%)	17 (40.5%)	0.7077
Prior MI	22 (15.9%)	14 (14.6%)	8 (19.0%)	0.6844
Documented CAD	39 (28.3%)	23 (24.0%)	16 (38.1%)	0.1358
Congestive heart failure	10 (7.2%)	7 (7.3%)	3 (7.1%)	1
Creatinine (n = 125)	1.37 ± 1.07 (0.57–6.87)	1.19 ± 0.77 (0.57–6.69)	1.79 ± 1.49 (0.81–6.06)	0.02368
HDL (n = 111)	40.31 ± 10.52 (19–77)	40.83 ± 10.83 (22–77)	39.17 ± 9.88 (19–59)	0.4284
LDL (n = 111)	97.52 ± 29.16 (41–218)	97.17 ± 27.07 (41–195)	98.29 ± 33.69 (48–218)	0.8642
TG (n = 106)	155.95 ± 113.54 (35–769)	162.07 ± 108.49 (42–69)	142.42 ± 124.68 (35–552)	0.438
GPT (n = 119)	29.77 ± 26.98 (4–261)	29.66 ± 17.7 (6–101)	30.03 ± 41.48 (4–261)	0.9597
Pretest SBP	150.95 ± 22 (101–214)	150.25 ± 23.32 (101–214)	152.57 ± 18.82 (110–183)	0.5392
Pretest DBP	86.88 ± 12.3 (57–126)	86.87 ± 13.43 (57–126)	86.90 ± 9.40 (71–106)	0.9876
Post test SBP	130.8 ± 18.27 (94–188)	132.02 ± 19.37 (94–188)	128.02 ± 15.29 (94–164)	0.1971
Post test DBP	75.21 ± 11.87 (49–113)	75.8 ± 12.37 (52–113)	73.86 ± 110.65 (49–95)	0.3505