Safety of Pharmacological (Intravenous Dipyridamole) Stress for Thallium-201 Perfusion Imaging in Patients with Coronary Artery Disease Unable to Exercise

Pages with reference to book, From 237 To 239

Maseeh-uz-Zaman, Rashid Hashmi, Khalid Niaz, Akhtar Ahmad, Shahid Kamal (Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

Exercise Thallium-201 myocardial perfusion imaging is a sensitive technique for detection of CAD, However, in patients unable to perform exercise pharmacological stress with intravenous dipyridamole can be used to dilate coronaries. Out of 123 patients (21 men and 104 women; mean age 52.03 years) evaluated, 110 were considered tobe unable toperform adequatestressby theirphysicianwhile remaining 15 had LBBB. One hundred and seven patients had chest pain with or without a remote MI while 18 individuals were clinically asymptomatic but had ECG abnormalities. Intravenous dipyridamole was administered at a rate of 0.142 mg/kg/min for 4 min. After 3 min an i.v. bolus of T1-201 was given. Diffuse or occipital headache of mild to moderate intensity occurred in 50 (40%) cases; 39 patients experienced chest pain and had either a positive thallium scan (26 cases) suggestive of CAD ora normal thallium study (15 cases). Complete relief from dipyridamole induced symptoms was brought by i.v. aminophylline and sublingual nitrate in 51 of 54 cases (94%) and 11 of 18 (61%) respectively. We, therefore, conclude: 1) i.v. dipyridainole-thallium scintigraphy offers a safe, effective and reliable method for evaluating CAD in those who are unable to perform adequate exercise and 2) parenteral aminophylline is very effective antidote to dipyridamole (JPMA 44:237,1994).

Introduction

Thallium-201 myocardial scintigraphy is a sensitive technique for detecting coronary artery disease (CAD). Standard exercise testing with either treadmill or ergometer is commonly developed to induce myocardial stress for T1-201 imaging. Unfortunately a significant number of patients are unable to perform an adequate exercise test due to musculoskeletal problems or sedentary life style. In these patients pharmacological vasodilatation induced by intravenous or oral dipyridamole in combination with standard T1-20l scintigraphy is a safe, efficacious and reliable alternative for the non-invasive diagnosis of CAD[1,2]. In this study, we assess the safety of using pharmacological (dipyridamole) stress during thallium imaging evaluating CAD inpatients in whom standard exercise was not feasible.

Patients and Method

Patients Selection

One hundred and twenty-five patients (21 men and 104 women; mean age 52.03. years) were evaluated in this study. All patients gave signed informed consent One hundred and ten patients were considered by their physicians to be physically unable to perform adequate exercise test (18 had musculoskeletal problems) while 15 had left bundle branch block (LBBB). One hundred and seven patients had either chest pain (n=90), a remote MI more than 3 months before the study (n=4), or both angina and remote MI (n=13). The remaining 18 patients were clinically asymptomatic but had significant ECG abnormalities. Exclusion criteria for the protocol were hfo asthma or severe COPD on bronchodilator or steroids, presence of wheezing during physical examination, severe CCF (NYHA class III or IV) or

recent MI (within 5 weeks of study).

Dipyridamole Infusion Protocol

All studies were performed after about 12 hours of fasting. Patients who were using dipyridamole had this drug discontinued atleast 24 hours before the test. Caffeine ingestion was not allowed for 12 hours preceding the study. With the patient in the supine position baseline heart rate, blood pressure and 12 lead ECO were recorded. Dipyridamole was infused through a peripheral antecubital vein at a rate of 0.142 mg/kg/min for 4 minutes with continuous monitoring of vital signs and ECG recorded every minute. Three minutes after the completion of infusion, a bolus of 2.5 mCi (92 MBq) of Thallium-201 was given intravenously[3]. This was followed by acquisition of planar images under a large field of view gamma camera interfaced to a sophisticated computer in the anterior, LAO 45 and LAO 70 degree views. After4 hours myocardial imaging was repeated to see redistribution of Thallium-201. In the event of clinical signs or symptoms suggesting ischaemia, sublingual nitroglycerine (1-3 tablets) or/and aminophylline (50-200 mg)was infused i.v. slowly (not more than 25 mg/mm) about 1 minute after Thallium-201 bolus.

Results

On the 125 patients evaluated in this study, none had any major adverse event like fatal or non-fatal MI or acute bronchospasm. However, 78(68.4%) had some form of minor adverse reactions. Minor adverse events experienced by the patients, in descending order of incidence, are listed in Table.

Table. Adverse events experienced by patients underwent intravenous dipyridamole-Thallium-201 perfusion imaging.

Adverse events	No. of patients	%
Headache	50	40
Chest pain	39	31
ST-T change	36	29
Hypotension	19	15
Flushing	14	11
Dyspnea	12	10
Nausea	8	6
Hypertension	5	4
Vomiting	4	3
Arrythmia	1	0.8

The most common adverse event was headache which occurred in 50 (40%) cases. It was either diffuse or occipital varying from mild to moderate in intensity in majority of cases. Chest pain or discomfort was experienced by 39 (31%) cases. This was associated with ST-T changes in ECO and a positive thallium scan in 26 patients. In the remaining 13 patients no dipyridamole induced ST-T change or perfusion defect on thallium scan was noted. In 54 patients, parenteral aminophylline alone was administered to treat dipyridamole induced events. Complete recovery from chest pain/discomfort,

headache, nausea and vomiting was noted in 51(94%) cases. In 2 (4%) patients partial recovery was seen. In one patient, a female, 10 mg of intravenous metoclopromide was administered to control severe nausea and vomiting. Sublingual nitroglycerin (1-3 tablets) was used in 18 patients with minor adverse events (nausea, palpitation and dyspnea). Almost complete recovery was noted in 11(61%) individuals while remaining 7 (3 1%) responded to i.v. aminophylline. In this study 59 patients (47%) had ETT before thallium study, of which 32 (55%) were negative for ischaemia. In 12 (20%) patients ETT was positive while remaining 15 (25%) cases had an inconclusive study. In 22 patients with negative ETT, thallium scan was positive for mild to moderate ischaemia, mostly reversible. In the sub-group of patients with positive ETT, 7 patients had a positive thallium scan while in remaining 5 no perfusion abnormality was noted (false positive ETT). In patients with an inconclusive Efl, thallium scan was positive for ischaemia, mostly reversible, in 7 cases while in remaining 8 cases scan was negative for ischaemia.

Discussion

Pharmacological vasodilatation with intravenous dipyridamole in combination with standard Thallium-201 is a recently developed innovative approach to the non-invasive diagnosis of coronary artery disease[4]. The mechanism by which dipyridamole induces coronary vasodilatation is thought to be through the blockade of cellular adenosine uptake, leading to a subsequent increase in both myocardial and arterial wall adenosine content. Adenosine acts predominantly on the small resistance vessels with little effort on vascular resistance in ischaemic coronary zones where small vessels are already maximally dilated. This may cause ischaemia by two mechanism: an increase in myocardial oxygen consumption or the "coronary steal" phenomenon[5]. Recently, adenosine, a direct mediator of coronary dilatation, has beenused with T1-201 to assess CAD inpatients unable to perform an exercise test[7]. In this study 68.4% of the participants experienced minor side effects. Headache (diffuse or occipital) was the commonest side effect occurred in 50 (40%) cases followed by chest pain in 39 (31%) and ischaemic changes in ECG in 36 (29%) cases. These are significantly higher than whose reported in other studies[6] but comparable with side effects associated with adenosine infusion[7]. High incidence of headache may be due to the female dominated sample (42 females and only 8 males complained of headache), low threshold for headache at standard dose of dipyridamole in our population and finally inclusion of feeling of heaviness of head as “headache” in this study. Similarly high incidence of chest pain is probably due to patient selection. In 26 patients with chest pain and positive thallium study pain was due to underlying CAD while in remaining 13 patients with normal thallium scans the cause of chest painis not known[7]. Headache in majority of individuals was moderate in severity and relieved either spontaneously after sometime or after i.v. aniinophylline. In26 patients with chest pain, positive thallium scan suggests coronary artery disease. In 13 clinically asymptomatic patients with ECO abnormalities but normal thallium scan, probability of CAD is low and cause of chest painin these “normal” individuals is yet not known[7]. In nearly all patients who experienced dipyridamole induced side effects, use of i.v. aminophylline was found very effective in relieving symptoms. Sublingual nitroglycerin was found less effective. We, therefore, conclude: 1) i.v: dipyrithmole-thallium scintigraphy offers a sale, effective and reliable method for evaluating CAD in those who are unable to achieve maximal stress with standard exercise-thallium testing and 2) parenteral antinophylline is very effective antidote to dipyridamole.

References

1. Gould, K.L., Westcott, R.J., Aibro, P.C. et al. Non invasive assessment of coronary stenosis by

myocardial imaging during pharmacologic coronary vasodilatation: II. Clinical methodology and feasibility. Am. J. Cardiol., 1978;41:279-87.
2. Gould, K.L., Sorenson, S.G., Albro, P. et. al. Thallium-201 myocardiaal imaging during coronary vasodilatation induced by oral dipyridamole. J. Noel. Med., 1986;27:31-36.
3. Gill, J.B., Millder, D.D., Bonchu, C.A. et al. Clinical desicion making: dipyridamole thallium imaging.J. Nucl. Med., 1986;27:132-37.
4. Homma, S., Gilliand, Y., Guiney, TB. et al. Safety of intravenous dipyridamole for stress testing with Thallium imaging. Am. J. Cardiol., 1906;59: 152-54.
5. Walker, R., Jane, M.A. and Wilder, R.P.H. Dipyridamole combination with exercise for Ti -201 myocardial imaging. Br. Heart S., 1986;55:321-29.
6. Ranhosky, A. and Kempthorne, JR. Intravenous Dipyridamole 11-201 Imaging Study Group: Safety of i.v Dipyridamole 11-201 myocardial perfusion imaging. Circulation, 1 990;81:1205-9.
7. Verani, S.V., Mahmarian, J.J., Hixaon, J.B. et al. Diagnosis of CAD by controlled coronary vasodilatation with adenosine andT 1- 201 aeintigraphy in patients unable to exercias. Circulation, 1990;52:80-87.