Dobutamine Stress Test. Specificity and Sensitivity of Continuous ST-Segment Monitoring in 12 Simultaneous Standard ECG Leads

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Introduction and objectives. This study was designed to evaluate the specificity and sensitivity of the dobutamine stress test with continuous ST-segment monitoring in 12 standard leads.

Patients and method. We analyzed 75 patients, 36 with unstable angina, 22 post-myocardial infarction angina, 3 after successful angioplasty, 6 chronic stable angina, and 8 atypical chest pain (with normal coronary arteries). All of them underwent coronary angiography (coronary lesions were considering significant with > 70%). Beta-blocking agents, calcium antagonists, and nitrates were discontinued for 48 h before the test. A 12-lead ECG was acquired automatically and ST-segment changes were monitored. Dobutamine infusion started at 5 g/kg/min and was increased at 3-minute intervals to 10 g, 20 g, and a maximum of 40 g/kg/min. If heart rate did not reach 85% of the theoretical maximum, 0.5-1 mg atropine was given without discontinuing dobutamine infusion.

Results. Fifty patients (67%) had abnormal coronary arteries (excluding vessels with 100% obstruction) and 25 patients (33%) had normal arteries. In the group of patients with coronary lesions, the test was abnormal in 90% and normal in 10%. In the group of patients with normal arteries, the test was abnormal in 16% and normal in 84%. Consequently, the test had 90% sensitivity, 84% specificity, and 10% false negative and 16% false positive results.

Conclusions. Our results showed that the dobutamine/ECG test was a simple, effective, and safe bedside tool for diagnosing the severity of coronary disease.

Key words: *Unstable angina. Electrocardiography. Test. Acute myocardial infarction.*

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Prueba de estrés con dobutamina. Especificidad y sensibilidad de la monitorización continua y en tiempo real del segmento ST en 12 derivaciones simultáneas

Introducción y objetivos. Estudio diseñado para evaluar la especificidad y sensibilidad del test con dobutamina bajo monitorización continua y en tiempo real del segmento ST en 12 derivaciones simultáneas, en pacientes con enfermedad coronaria.

Pacientes y método. Se estudió a 75 pacientes, 36 con angina inestable, 22 con angina postinfarto, tres post-angioplastia coronaria exitosa, seis con angina crónica y ocho bajo estudio por precordialgia atípica (con arterias angiográficamente normales). Todos los pacientes fueron evaluados con coronariografía. Dos días antes del test se suspendieron los fármacos bloqueadores beta, antagonistas del calcio y nitritos. La monitorización del segmento ST fue continua, sobre 12 derivaciones simultáneas. La infusión intravenosa de dobutamina se comenzó con 5 g/kg/min. Con 3 min de intervalo, se aumentó a 10, 20 y hasta un máximo de 40 g/kg/min. Si la frecuencia cardíaca no alcanzaba el 85% del máximo teórico, se agregaba atropina i.v. a dosis de 0,5-1 mg sin discontinuar la dobutamina.

Resultados. Excluyendo casos con arterias con obstrucciones del 100%, 50 pacientes (67%) tuvieron lesiones significativas y 25 enfermos (33%) no. En el grupo con lesiones coronarias, el test fue anormal en el 90% y normal en el 10%, mientras que en el grupo sin lesiones el test fue normal en el 84% y anormal en el 16%. Esto implica una sensibilidad del 90% y una especificidad del 84%, con un 10% de falsos negativos y un 16% de falsos positivos. No hubo efectos colaterales significativos.

Conclusiones. Los resultados nos permiten afirmar que este test es un método sencillo, eficaz y seguro en pacientes con enfermedad coronaria, especialmente en la búsqueda de isquemia residual.

Palabras clave: *Angina inestable. Electrocardiografía. Test. Infarto agudo de miocardio.*

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INTRODUCTION

The pharmacologic stress test, especially with echocardiography or radioisotope monitoring, is a tool that is frequently used for patients who are recuperating from an acute coronary event. The substances most

ABBREVIATIONS

ECG: electrocardiogram.
AMI: acute myocardial infarction.
DB: dobutamine.
CU: coronary unit.
mm Hg: millimeters of mercury.
mm/s: millimeters/second.
μg/kg/min: microgram/kilogram/minute.
ms: milliseconds.
IV: intravenous.

frequently used are dobutamine, dipiridamol, and, more recently, arbutamine.[1-3] For this test to provide satisfactory results, expensive equipment and experienced operators are required.[4]

The possibility of continuously monitoring the behavior of the ST segment with 12 electrocardiographic (ECG) leads simultaneously could provide a new, simple, and less expensive method of evaluating the consequences of a dobutamine infusion. Until now, few studies have been published in which ECG control is achieved with recordings every 3 minutes[5] and with echocardiography monitoring.[6] In 1991, Coma-Canella reported 95% sensitivity and 78% specificity by adding ECG monitoring to stress echocardiography with dobutamine.[1] In 1994, Mairesse et al[2] described the necessity of new criteria for pharmacological stress tests, but stated that diagnostic images are still required to predict the existence of coronary pathology with any certainty. In 1997, Martínez-Martínez et al[3] proposed the use of dobutamine stress testing under standard ECG control in place of ergometry. In 1998, Coletta et al[4] and De Felice et al[5] studied standard ECG modifications with an intravenous (IV) dobutamine infusion and the possible impact of spontaneous contractile recuperation after an acute myocardial infarction. In 1999, Rambaldi et al[6] investigated the T-wave modifications as a marker for myocardial viability, while Witchitz el al[7] studied the sensitivity of this method. In our study we used for the first time the usual protocol of dobutamine with continuous real-time monitoring of the ST segment with 12 simultaneous ECG leads. Our objective was to evaluate the specificity and sensitivity of a dobutamine stress test with continuous real time monitoring of the ST segment with 12 simultaneous ECG leads in patients with heart disease.

PATIENTS AND METHODS

Patients

None of the patients in our study had a history of interventricular communication, valvulopathy, or myo-

cardiopathy, or a known history of hypersensitivity to dobutamine or atropine, or both. Exclusion criteria were severe arterial hypertension, severe ventricular arrhythmia, or a clinical coronary status that would not allow temporary suspension of treatment.

Acute coronary events were produced in 36 patients (30 men and 6 women; average age 62±2 years) admitted to the coronary unit with a diagnosis of unstable angina within 10 days of the procedure. In all cases, total clinical and echocardiography stability were required during the 3 days preceding the test.

There were a total of 22 patients (20 men and 2 women, average age 64±4 years) with post-infarct angina who were also asymptomatic and stable 3 days prior to the test.

Three patients recuperated immediately (in less than 3 days) from successful transluminal angioplasty (3 men with an average age of 56±4 years).

A total of 6 patients presented with chronic stable heart disease (5 men and 1 woman; average age 66±6 years).

Eight individuals admitted for thoracic pain did not have a pathologic enzymatic curve or clear electrocardiographic evidence of acute heart disease (6 men and 2 women; average age 61±3 years).

Prior medication

Two days before the test, beta blockers, calcium antagonists, and long-acting nitrites were discontinued, with only sublingual nitrites being permitted on demand.

ST-segment monitoring

A Spacelab monitor was used, with simultaneous and continuous recording of 12 real time leads for the automatic quantification of the ST-segment levels. In addition to visualization on the screen and storage of all data, a paper recording at the rate of 25 mm/s was obtained, using 0.05 to 109 Hz filters.

An ischemic response was defined as the new appearance or worsening of an ST-segment depression greater than 1 mm horizontal or descending measured at 60 ms from point J in at least 2 leads in the same topographic area (anterior, inferior, or lateral).[8]

The same equipment allowed us to automatically control arterial pressure every 3 minutes.

Dobutamine/atropine protocol

All patients were studied in the coronary unit (CU), with all necessary emergency equipment available at all times.

The modified Ohio State University protocol[9] was used. The intravenous (IV) dobutamine infusion was begun at a dose of 5 μg/kg/min. At 3-minute intervals

the dose was increased to 10, 20, and a maximum of 40 μg/kg/min. If the cardiac frequency did not reach a minimum of 85% of the theoretical level for the sex and body surface of the patient, 0.5 to 1 mg of IV atropine was added, without discontinuing the dobutamine infusion.

Criteria for interrupting the dobutamine infusion were: *a)* reaching 85% of the maximum cardiac frequency for the age and size of the patient; *b)* the appearance of angina; *c)* severe arterial hypertension (more than 220/120 mm Hg); *d)* decrease in systolic arterial pressure greater than 30 mm Hg; *e)* the appearance of severe ventricular or supraventricular arrhythmias; *f)* appearance of a significant ST-segment depression in 2 leads from the same area or worsening of pre-existing changes, and *g)* the end of the protocol.

The test was not considered diagnostic when:[10] due to early interruption due to the appearance of *c, d,* and *g* in the preceding list, or a combination thereof; when collateral limiting side-effects were seen; when the protocol resulted in a normal test without having achieved 85% of the theoretical maximum cardiac frequency.

Coronary angiography

Coronary angiography was performed by interventionist cardiologists who did not participate in the investigations in all patients within 10 days of the dobutamine test. Lesions were estimated visually, with those greater than 70% considered significant.

Statistical evaluation

Our first objective was to answer the following questions:
– If an ischemic condition existed, what would be the probability that the test would be positive?
– If heart disease was not present, what would the probability be that the test would be negative?

If the ST-segment changes really constituted a continuous variable,[9] for the purposes of our investigation we classified the results as positive or negative according to whether or not they were produced in accordance with the above-mentioned definitions. As a template or gold standard, coronary angiography was used.

Collateral side-effects

We defined as minor collateral side-effects that could not cause potential situations which compromised the life of the patient, were auto limited, or could be well controlled pharmacologically. On the other hand, we considered major collateral side-effects those situations that could potentially cause a clinical picture that compromised the patient´s life or prolonged hospitalization of the patient.

RESULTS

Seventy-five consecutive patients were analyzed prospectively. Table 1 lists the demographic and baseline clinical characteristics of these patients; the distribution by sex and age were similar in the 5 subgroups, and there were not very significant differences related to cardiovascular risk factors, with the exception of a minor prevalence of diabetes mellitus in the patients in with precordial pain under study.

The coronary angiography results are given in Table 2 (the clinicians did not know the results of the test being studied. The lesions were estimated visually, and those of more than 70% were considered significant. Obstructions of 100% were not included.

With the logical exception of the successful post-angioplasty patients, the 3 clinical forms of heart disease (unstable, chronic stable, and post-AMI angina) showed a significantly greater number of cases with arterial lesions.

TABLE 1. **Demographic and baseline clinical aspects**

	Unstable angina	Post AIM angina	Post coronary angioplasty	Chronic stable angina	Precordial under study
N (%)	M: 29 (80.5) W: 7 (19.5)	M: 14 (63.6) W: 8 (10.6)	M: 3 (100)	M: 4 (66.7) W: 2 (33.3)	M: 6 (75) W: 2 (25)
N total	36	22	3	6	8
Age (average year±SD)	63 (6.7)	61 (7.9)	59 (5.8)	64 (8.1)	63 (5.8)
Smoking					
Current	18 (50%)	18 (81.8%)	3 (100%)	3 (50%)	4 (50%)
Past	10 (27.8%)	2 (9.1%)		3 (50%)	2 (25%)
Never	8 (22.2%)	2 (9.1%)			2 (25%)
Hipertensión	14 (38.9%)	7 (31.8%)	1 (33%)	2 (33%)	2 (25%)
Dyslipidemia	16 (44.4%)	4 (18.2%)	2 (67%)	2 (33%)	3 (37.5%)
Diabetes mellitus	4 (11.1%)	2 (9.1%)	0	1 (16.7%)	0
History of previous infarct	3 (8.3%)	1 (4.5%)	0	4 (66%)	0

M indicates men; W, women; SD, standard deviation.

TABLE 2. Coronary angiography results

	Without arterial lesions greater than 70%	With arterial lesions greater than 70%
Unstable angina (36 patients)	1 (2.8%)	35 (97.2%)
Post-AMI angina (22 patients)	8 (36.36%)	14 (63.6%)
Post-angioplasty (3 patients)	0	0
Chronic stable angina (6 patients)	1 (16.6%)	5 (83.4%)
Precordalgia under study (8 patients)	8 (100%)	0

100% lesions were not included.

TABLE 4. Specificity and sensitivity of tests

	Coronary angiography (+)	Coronary angiography (-)	Totals
ECG/dobutamine (+)	45 (91.83%)	4 (8.17%)	49 (65.3%)
ECG/dobutamine (−)	5 (19.23%)	21 (80.77%)	26 (34.7%)
Totals	50 (66.66%)	25 (33.34%)	75 (100%)

Test sensitivity: 45/(45+5)=0.9 (90%).
Test specificity: 21/(4+21)=0.84 (84%).
False negatives: 100−specificity=100−84=16%.
False positives: 100−sensitivity=100−90=10%.

Table 3 shows a comparison of the coronary angiography results with those with ECG/dobutamine tests; in the study population, 60% had abnormal coronary angiography and ECG/dobutamine test. This percentage increased to 80% with in the unstable angina group and decreased to 9% in the group with precordial pain of non-coronary origin (precordalgia under study), which we called the control group.

On the other hand, in 28% of the study population both tests were normal, which in the precordalgia group the percentage was 87.% (*P*<.001).

Table 4 shows the values that resulted from the calculation of the sensitivity and specificity of this method. Of the 49 patients with a positive ECG/dobutamine test, 45 (91.8%) also had significant lesions on angiography, while of the 26 patients with normal (or negative) ECG/dobutamine test, only 5 patients had significant angiographic lesions.

Table 5 demonstrates the clinical and hemodynamic response to the infusion of dobutamine and the eventual addition of atropine: the average length of the test was approximately 11 minutes, with a double product peak between 17 600 and 18 200, without any important differences between the 5 patient subgroups.

Atropine was needed in 83% of the patients with unstable angina, 73% who presented with post-AMI angina, in the 3 post-angioplasty patients, in 67% of the patients with chronic angina, and in 87% of the precordalgia group.

Of the 49 patients with a positive ECG/dobutamine test, 30 had typical angina. The presence of this symptoms did not change the specificity or sensitivity of the test (91% and 86%, respectively).

The recovery time for 50% of the ST segment was significantly shorter in the post-angioplasty patients (0.8 vs 2.9 minutes in the unstable angina group).

The peak of depression of the ST segment was 1.8 mV in 91.7% of patients with unstable angina, 1.6 mV in nearly 50% of patients with post-AMI angina and 1 of the 3 patients with angioplasty, 1.3 mV in 66% of the chronic patients, and 0.8 mV in 1 of the 8 individuals with precordial pain.

Side-effects

Following the definitions given in the Patients and methods section, during the dobutamine infusion (with the eventual addition of atropine) 75% of patients experienced minor side-effects: facial pain, nausea, and headache, principally). The test did not have to be suspended in any of these cases.

We did not record any cases of severe arterial hypotension (decrease in systolic arterial pressure greater than 20 mm Hg) and there was a 6% occurrence of supraventricular arrhythmias that did not require specific treatment or the suspension of the test.

DISCUSSION

This study is, at the moment, the first prospective clinical investigation to evaluate the specificity and sensitivity of continuous real-time ST segment monitoring with 12 simultaneous leads with dobutamine infusion.

TABLE 3. Comparison of the coronary angiography results with the ECG/dobutamine

	ECG/DB (+) CAG (+), n=45 (60%)	ECG/DB (+) CAG (−), n=4 (5.33%)	ECG/DB (−) CAG (+), n=5 (6.67%)	ECG/DB (−) CAG (−), n=21 (28%)	Totals, n=75
Unstable angina	31 (86.11%)	2 (5.56%)	3 (8.,33%)	0	36
Post-AMI angina	9 (40,9%)	1 (4,55%)	1 (4,55%)	11 (50%)	22
Post-angioplasty	1 (33%)	0	0	2 (77%)	3
Chronic angina	4 (66.66%)	0	1 (16.67%)	1 (16.67%)	6
Precordalgia under study	0	1 (12.5%)	0	7 (87.5%)	8

CAG indicates coronary angiography; ECG/DB, ECG/dobutamine test.

TABLE 5. **Clinical and hemodynamic response to the infusion of dobutamine**

	Unstable angina	Post AIM angina	Post coronary angioplasty	Chronic stable angina	Precordial under study
N	36	22	3	6	8
Test duration, min. (mean±SD)	11±2.3	10.8±2.9	11.4±3.0	11.8±4.1	11.9±4.1
Double prod. Peak	17 820±3850	17 660±2,977	18 059±3121	17 825±2850	18 221±2327
Atropine given, %	30 (83)	16 (73)	3 (100)	4 (67)	7 (87)
Angina, n (%)	27 (75)	19 (86)	0	2 (33)	0
Time at 50% ST recuperation	2.9±1.6	2.7±2.1	0.8	1.1±2.7	–
ST depression n (%) relative to baseline ST	33(91.7%) 1.8 mV	10 (45.4%) 1.6 mV	1 (33%) 1.6 mV	4 (66%) 1.3 mV	1 (12.5%) 0.8
T wave (–)	3	2	– 2	–	
Final FVE	4	1	1	–	1
SV arrit.	2	1	–	–	1

Double prod. indicates double product (systolic arterial T. cardiac F.); FVE, frequent ventricular extrasystoles; SV arrit., significant supraventricular arrhythmias.

It was not our intention to compare the efficacy of this diagnostic method with other well-proven tests, such as stress echocardiography and the various radioisotope resources, but to investigate the efficacy of a method that, because of its simplicity and cost to benefit ratio, could be a special tool that would useful in hospitals with limited technological resources.

The results obtained from a population with different forms of heart disease and a group of individuals admitted with precordial pain (with normal arteries on angiography) showed that the ECG/dobutamine test has a 90% sensitivity and 84% specificity, with 10% false negatives and 16% false positives. These results suggest the use of coronary angiography as a valuable diagnostic gold standard.

A decisive element at the time of evaluating the patient was the fact that the test was performed in the coronary unit, without the need to transfer the patient, with equipment that was easy to use and that provide objective results, eliminating the factor of personal interpretation.

As was expected due to the considerable international experience accumulated regarding diagnostic IV infusion of dobutamine/atropine under echocardiography or radioisotope control, there were no significant side-effects, giving the these a high level of safety.

Perhaps the percentage of false positive was somewhat higher than was expected (16%); nevertheless, it must be kept in mind that being a diagnostic development without antecedents, many doubtful recordings were considered negative in order not to negatively influence the protocol.

This can be confirmed with new experiences that involve a greater number of patients.

The ECG/dobutamine test, which is habitually used to investigate residual ischemia, is an evaluation that produces serious complications in less than 1% of patients.[11] The test has a sensitivity of 80% and a specificity of 84%, the first varying between 74%, 86%, and 92% for lesions of 1, 2, and 3 vessels, respectively.[10] Nevertheless, it is not an evaluation that is easy to perform, especially if experienced operators are not available.

Another limiting factor of the stress echocardiogram with dobutamine is that the subendocardial resolution is not always adequate, which is an indispensable requirement for an adequate interpretation of the changes in the regional parietal dynamic.[12]

Finally, it must be remembered that approximately 5% of patients do not have an adequate ultrasonic window.[18,13-15]

It is just as important to clearly specify the admission criteria for the CU as it is the discharge criteria. Possessing a simple diagnostic strategy that is available 24 hours a day allows good categorization of the patient´s discharge risk, as well as the correct selection of the immediate diagnostic-therapeutic strategy to follow.

CONCLUSIONS

With the specificity and sensitivity obtained and the simplicity and security of the procedure,[16,17] the ECG/dobutamine test appears to have an important diagnostic and prognostic value in patients who recover from acute coronary events. If we add to this the simplicity and cost to benefit ratio[18-21] (both for the patient and for the institution where they are admitted), the tendency that has been observed justifies new studies in larger study populations to prove definitively prove this hypothesis and establish this method as a

new and useful diagnostic resource for heart disease.

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