SCIENTIFIC LETTER

Diagnostic accuracy of a new shorter dobutamine infusion protocol in stress echocardiography

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Currently, a transthoracic echocardiographic examination is routinely included in the assessment of the majority of patients with cardiac disease. Other examinations are also demanded every day from the echocardiography laboratory. Of these, stress echocardiography is particularly time consuming. Shortening the time of infusion of a drug would increase the feasibility and the cost effectiveness of stress echocardiography,[1] provided of course that the diagnostic accuracy achieved using the classic drug infusion protocol is maintained.

An "accelerated" dipyridamole infusion protocol has been already used[2] and validated in a large study.[1] The standard protocol of dobutamine includes an initial dose of 10 μg/kg/min with increments of 10 μg/kg/min every three minutes up to 40 μg/kg/min which is maintained over six minutes and makes this procedure particularly long.

Keeping these considerations in perspective, we have tested the diagnostic accuracy of an "accelerated" dobutamine stress echocardiographic procedure in patients with suspected coronary artery disease.

METHODS

We prospectively enrolled 94 consecutive patients (mean (SD) age 61 (46) years; 67 male) who complained of chest pain, had no known history of coronary artery disease, and who underwent coronary angiography. Forty eight patients were receiving β blockers. Informed consent was obtained from all patients.

Dobutamine was administered intravenously at an initial dose of 20 μg/kg/min that was maintained over three minutes. Then, 40 μg/kg/min was infused over three minutes. At this point, 1 mg of atropine was given if the test was still negative and the patient had not reached 85% of the maximum predicted heart rate. Propranolol was infused after discontinuation of dobutamine. Intravenous glyceryl trinitrate was given when needed. Dobutamine infusion was prematurely stopped if one of the usual non-echocardiographic end points appeared.[2]

A 16 segment model was used and each ventricular segment was given a score according to its motion, as already described.[2] The wall motion score index was calculated from the sum of the segmental scores divided by the segments visualised. A positive response was defined as the increment of the score index by at least one grade.

Quantitative variables are expressed as mean (SD) and compared by Student's *t* test. Qualitative variables are expressed as percentages and compared with the χ^2 test. A probability value of $p < 0.05$ was considered significant.

RESULTS

Dobutamine infusion was not prematurely stopped in any patient. Eighty one patients received additional atropine. The overall test time (time from the patient being called from the waiting area to the time he/she leaves the echocardiography laboratory) was 41 (8) minutes. By comparison, the overall test time in our last 50 tests performed with the 15 minute protocol was 50 (11) minutes ($p < 0.05$).

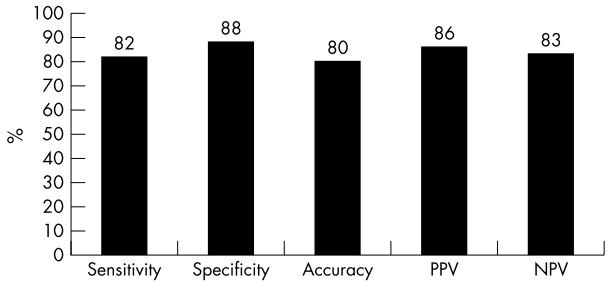

Figure 1 Diagnostic performance of the short protocol. NPV, negative predictive value; PPV, positive predictive value.

The diagnostic accuracy of the "accelerated" protocol is shown in fig 1. Dobutamine induced wall motion abnormalities appeared in 42 of 53 patients with coronary artery disease (sensitivity 82%) and in only five of 41 patients without disease (specificity 88%). The positive predictive value was 80%, the negative predictive value was 86%, and the diagnostic accuracy was 83%. The "accelerated" protocol was positive in 20 of 28 patients with one vessel disease (71%), in 15 of 17 with two vessel disease (88%), and in all eight patients with three vessel disease (100%).

There were 11 patients with resting wall motion abnormalities (12%). Wall motion score index at baseline was slightly higher for patients with three vessel disease (three vessel 1.56 (0.41); two vessel 1.18 (0.28); one vessel 1.08 (0.29); p = ns in all comparisons). Increment of wall motion score index (that at rest minus that at peak stress) was 0.38 (0.19) in patients with one vessel disease and 0.53 (0.29) in patients with multivessel disease ($p = 0.05$). Ischaemia-free time was shorter in patients with three vessel disease (4.5 (1.4) mins) than in those with two and one vessel disease (5.1 (1.5) mins and 5.2 (3.1) mins, respectively; $p<0.05$ in both comparisons).

Minor side effects presented in 45 patients (46%) and included headache, dizziness, palpitations, dyspnoea, and nausea. Systemic hypertension (systolic blood pressure > 200 mm Hg, diastolic blood pressure > 120 mm Hg) was detected in four patients. Non-sustained ventricular tachychardia occurred in two patients and terminated spontaneously. No patient had sustained ventricular tachychardia, myocardial infarction, ventricular fibrillation or death.

DISCUSSION

In our clinical practice, echocardiography is a mainstay in the assessment of patients with almost any type of cardiac disease. As a consequence, echocardiography laboratories have to face an overload of work and long waiting lists. Of the techniques performed in the laboratory, stress echocardiography is particularly time consuming. Theoretically, shortening the infusion time of a drug would improve the cost effectiveness of

the test and reduce the waiting lists. Recently, an "accelerated" dipyridamole infusion protocol, long used by our group,[2] was validated in a large study.[1] On the other hand, we have noticed in our routine practice that, when the test is done for diagnostic purposes, a positive response to dobutamine rarely appears during the first stage (10 μg/kg/min). Bearing these considerations in mind, we designed an "accelerated" dobutamine infusion protocol, which shortens the infusion time from 15 minutes to six minutes.

Other attempts have been made to implement an "accelerated" dobutamine infusion protocol.[3 4] Both groups used a continuous high dose dobutamine infusion over 10 minutes. It can be presumed this protocol had a low capability for grading the positive response and a low correlation with disease severity since the dose was not gradually incremented. More importantly, patients did not undergo coronary angiography; thus, diagnostic accuracy and stratification of positive responses were not performed.

To enter the clinical arena, this protocol must show a favourable comparison with the older protocol. In other words, the new protocol must fulfil four requirements: high diagnostic accuracy, capability of grading the severity of the ischaemic response, prognostic power, and comparable safety profile. The first two requirements have been addressed by the current study. The diagnostic accuracy reported here is similar to that obtained previously by us[2] and others[5] using the standard protocol. Regarding the stratification of the test, wall motion score index and ischaemia-free time were useful parameters to stratify a positive response and to identify patients with different severity of coronary artery disease.

Obviously, this study does not have the capability to assess the prognostic power. If the protocol is implemented, further investigations will be necessary to elucidate it. Given that the maximal dose of dobutamine is the same in both protocols, it seems reasonable to assume that the predictive power will be similar.

As this pilot study involved only 94 patients, we cannot affirm that this protocol is safe. Although the same safety profile for the "accelerated" protocol may be claimed because the maximal dose is the same, the administration of high doses of dobutamine in a short period of time may favour arrhythmias and hypertensive responses. Moreover, our population can be considered low risk, because patients with previous myocardial infarction were excluded.

This protocol cannot be universally accepted in the echocardiography laboratory. Viability cannot be assessed when the initial dose is 20 μg/kg/min. If the stress technique is aimed at testing viability, the starting dose should be 5 μg/kg/min and increments of 5 or 10 μg/kg/min must be used.

In conclusion, the "accelerated" dobutamine infusion protocol has a high diagnostic accuracy for coronary artery disease. It identifies different grades of severity and has good correlation with the morphology of the stenosis. Further studies are needed to assess its safety profile and prognostic power.

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