The Effect of Mild-to-Moderate Mental Stress on Coronary Hemodynamics in Patients with Coronary Artery Disease

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SUMMARY Eleven men with coronary artery disease were studied to determine whether they would manifest inappropriate coronary vasoconstriction in response to mental stress. Mental stress was induced by having the patient perform difficult mental arithmetic in time with a clicking metronome. Aortic blood pressure and thermodilution coronary sinus blood flow were recorded continuously before and during the mental arithmetic. For the group, heart rate rose from 70 to 82 beats/min, systolic blood pressure rose from 161 to 181 mm Hg and diastolic blood pressure rose from 71 to 78 mm Hg. Coronary resistance decreased by 16%. The index of myocardial oxygen consumption rose by 40%, and there was an equivalent rise in coronary sinus blood flow of 41%, with no change in coronary arteriovenous oxygen difference.

Because the increase in myocardial oxygen consumption was accompanied by a proportional increase in coronary sinus blood flow, a decrease in coronary resistance and no change in myocardial oxygen extraction, we conclude that the response of patients with coronary artery disease to at least moderately severe mental stress is not characterized by abnormal coronary vasoconstriction.

THE PRESENT STUDY was carried out in men with ischemic heart disease to define the response of the human coronary vasculature to mental stress. In particular, we were seeking evidence for the existence of an abnormal vasomotor response (inappropriate coronary vasoconstriction) to mental stress. Mudge et al. reported inappropriate coronary vasoconstriction in patients with coronary artery disease during exposure to cutaneous cold. The present study was designed to determine whether a similar response occurred with mental stress.

Methods

Eleven men ages 40–62 years who were undergoing cardiac catheterization and coronary arteriography as potential candidates for coronary bypass surgery were studied without prior sedation. All medication was discontinued 48 hours before the catheterization. Appropriate informed consent was obtained from each patient before the study. After standard right-heart catheterization, a #7 thermistor catheter (Wilton Webster Laboratories) was inserted into the coronary sinus for measurement of coronary sinus blood flow by the continuous thermodilution technique. The catheter was positioned under fluoroscopic guidance so that the external thermistor lay 5–10 mm inside the coronary sinus ostium as visualized by injection of 2–3 ml of contrast medium. The recording of the coronary sinus temperature by the thermistor showed a steady temperature, reflecting an absence of contamination by right atrial blood. The stability of the catheter's position was checked before and immediately after the stress period. Five percent dextrose at room temperature was injected at a rate of 38.5 ml/min. The mental arithmetic was initiated 15–20 seconds after the temperature of the injectate-blood mixture reached a steady level. Details of the method have been published.

Arterial blood pressure was recorded continuously by means of a #20 Teflon cannula in a radial or femoral artery.

The procedure for inducing mild-to-moderate mental stress was carried out as follows. The investigator advised the patient that important measurements were about to be made during which time the patient would be required to perform some "simple" mental calculations. The importance of giving correct answers in time with a clicking metronome was emphasized. The patient was then instructed to subtract the number 17 serially from 1013, and the metronome was set in motion behind his head at a rate of one click every 2 seconds. As the patient tried to perform this nearly impossible task, the investigator began calling out the correct answers every 2 seconds. At the same time, other physicians present implied to the patient that his poor performance was due to lack of effort, which would invalidate the test results.

The period of stress lasted approximately 2–2.5 minutes, and upon its conclusion it was explained to the patient that he had been given a difficult task designed to measure his response to mental stress. He was reassured that he had done well, and no patient suffered ill effects from the procedure.

Samples were drawn for arterial and coronary sinus oxygen tension and saturation before the stress procedure and immediately before its conclusion. Blood oxygen content (ml/100 ml) was calculated as hemoglobin (g/100 ml) × 1.34 × percent hemoglobin oxygen saturation/100 + 0.0031 × oxygen tension (mm Hg). Oxygen tension was determined with an Instrumentation Laboratory model 113 pH/gas an-
alyzer; hemoglobin oxygen saturation and hemoglobin concentrations were measured with an Instrumentation Laboratory model 182 Co-oximeter. Coronary sinus blood flow was recorded continuously from immediately before the period of stress until shortly before its conclusion. After the stress procedure, left ventricular catheterization and coronary arteriography were performed.

Left ventricular coronary resistance was calculated as the quotient of mean arterial blood pressure (mm Hg) and coronary sinus blood flow (ml/min). The index of left ventricular myocardial oxygen consumption was calculated as the product of coronary arteriovenous oxygen content difference (ml/100 ml) and coronary sinus blood flow (ml/min) × 10⁻².

A change in coronary vasomotor tone was deemed appropriate if the associated change in myocardial oxygen consumption was accompanied by a proportional change in coronary blood flow with no change in coronary arteriovenous oxygen difference.³

Statistical significance of the differences was determined using the paired t-test.

Results

All 11 patients were found to have at least one high-grade (≥75% of luminal diameter) occlusive lesion of the left coronary arterial tree, and eight also had high-grade lesions of the right coronary artery (table 1).

The stress-induced changes in heart rate, blood pressure, and coronary sinus blood flow began soon after initiation of the stress and usually peaked at 30–60 seconds. Table 1 presents the control values and the values of the monitored variables during the stress period and at the time of peak coronary sinus blood flow. Heart rate rose by 6–24 beats/min, from a mean of 70 to 82 beats/min (p < 0.001) for the group, systolic blood pressure by 4–38 mm Hg, or from 141–161 mm Hg on the average (p < 0.001), and diastolic pressure by 2–15 mm Hg, or from 71 to 78 mm Hg for the group (p < 0.001). The index of left ventricular myocardial oxygen consumption rose by 40%, from 18.6 to 26.1 ml/min (p = 0.006). These changes were accompanied by a 41% increase in coronary sinus blood flow, from a mean of 128 to 180 ml/min (p = 0.005). Coronary resistance fell by a mean of 16% (p = 0.008). There was no change in coronary arteriovenous oxygen difference.

No patient complained of anginal pain during or after the mental stress. There were no ST-T changes in lead V₅ during or immediately after the mental stress.

Discussion

The increases in heart rate and systemic blood pressure in our patients were similar to the cardiovascular changes reported by others in normal subjects undergoing various types of emotional stress.⁴,⁵ Animal studies have shown that excitement also causes marked increases in myocardial oxygen consumption and coronary blood flow and decreases in coronary resistance.⁶-⁸

Because the venous system of the right coronary bed drains into the right atrium or into the coronary sinus close to its orifice,⁹ coronary sinus blood flow measured by the thermodilution technique principally

<table>
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<tr>
<th>Age (Pt)</th>
<th>Coronary sinus blood flow (ml/min)</th>
<th>Arteriovenous O₂ difference (ml/100 ml)</th>
<th>Myocardial O₂ consumption (ml/min)</th>
<th>Coronary resistance (mm Hg/ml/min)</th>
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<th>Heart rate (beats/min)</th>
<th>Site of occlusive lesions (≥75%)</th>
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Abbreviations: C = control, before onset of mental stress; S = during peak effect of mental stress; LCA = left main coronary artery; LAD = left anterior descending coronary artery; LCx = left circumflex artery; RCA = right coronary artery.

Table 1: Coronary Hemodynamic and Metabolic Effects of Mental Stress
reflects the left coronary blood flow.10 Because all of the patients had high-grade lesions in their left coronary artery system (table 1), we assumed that the effect of mental stress on diseased coronary arteries would be reflected by the measured changes in coronary sinus flow. Thus, it is of interest that an appropriate relationship between coronary blood flow and myocardial oxygen demand was maintained in the presence of moderate-to-severe coronary artery disease under the influence of mental stress sufficient to elicit a marked cardiovascular response. Not only was there no absolute coronary vasoconstriction, as indicated by the fall in coronary resistance, but also, the increase in coronary blood flow could be deemed fully appropriate to the increase in myocardial oxygen consumption, because the latter was achieved with no increase in myocardial oxygen extraction. Myocardial oxygen extraction is a more sensitive indicator of the adequacy of change in coronary blood flow in response to a given stimulus than the direction and magnitude of change in coronary resistance.11–15 Mohrman and Feigl15 observed coronary vasodilation in response to intracoronary injection of norepinephrine or carotid sinus reflex, as expected. However, a simultaneous decrease in the coronary sinus oxygen saturation indicated that the decrease in coronary resistance was not enough to permit the coronary blood flow to increase commensurate with the rise in myocardial oxygen demand.

It cannot be ruled out that coronary constrictive stimuli accompany mental stress and that they are effectively blocked by metabolic autoregulatory vasodilation. Some authors used β-receptor blockade to unmask coronary constrictive stimuli in experimental animals16–21 or pacing-controlled tachycardia in human subjects.1–22 Robinson23 reported that angina pectoris was induced by mental stress at the same level of systemic pressure–heart rate product, an index of myocardial oxygen consumption,24 as by exertion. This suggests the absence of effective coronary constrictive stimuli during mental stress. It is possible that pacing-induced tachycardia or β-receptor blockade could unmask the presence of coronary constrictive stimuli during mental stress or that such stimuli may become apparent if more severe degrees of mental stress are induced.

References
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