Cardiac Society of Australia and New Zealand, 47th Conference, 1998, Auckland, New Zealand. Abstract.

BETEL NUT CAUSES PARADOXICAL VASOCONSTRICTION IN PATIENTS WITH CORONARY ARTERY DISEASE - AN EXCITING NEW DISCOVERY IN PAPUA NEW GUINEA WITH IMPORTANT CLINICAL IMPLICATIONS

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The chewing of betel nut with pepper and shell lime has been a habit of PNG people because of its euphoric effects. Betel nut contains an alkaloid, Arecoline, which is a parasymphatomimetic agent similar to Acetylcholine (Ach). Ach causes vasodilatation in a normal coronary artery due to the release of Endothelium Derived Relaxing Factor (Nitric Oxide). However, in atherosclerotic vessels, it causes paradoxical vasoconstriction and the mechanism is thought to be a defect in endothelial vasodilator function, causing the release of histamine and serotonin (Ludmer et al, 1986).

The aim of this study was to determine whether betel nut causes myocardial ischaemia in patients with positive stress test. Eight patients with angina pectoris and positive stress test on treadmill were studied. In each subject, a 12-lead ECG was performed at baseline, every 5 minutes for 20 minutes. Heart rate (HR), systolic and diastolic BP were also recorded. The ECGs were read by 2 cardiologists in a blinded manner. Ten normal volunteers were also studied as controls.

In the normal subjects, apart from increased HR and a variable BP response, there were no ischaemic changes on ECG with betel nut chewing. In 5 out of 8 patients, the ECGs at rest were either normal or with minor ST-T wave changes. From 5 to 15 minutes of betel nut chewing, there were significant ST segment depression (>2mm) similar to the change during the stress test, indicating acute myocardial ischaemia; the changes were gone by 20 minutes.

The results suggest that betel nut containing Arecoline causes myocardial ischaemia in patients with coronary artery disease as indicated by a positive stress test. The mechanism is postulated to be similar to Ach (Ludmer et al, 1986). These findings may have several clinical implications in PNG, but further studies are required.

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Paradoxical vasoconstriction induced by acetylcholine in atherosclerotic coronary arteries.

Ludmer PL, Selwyn AP, Shook TL, Wayne RR, Mudge GH, Alexander RW, Ganz P.

Abstract

Acetylcholine is believed to dilate normal blood vessels by promoting the release of a vasorelaxant substance from the endothelium (endothelium-derived relaxing factor). By contrast, if the endothelium is removed experimentally, acetylcholine constricts blood vessels. We tested the hypothesis that muscarinic cholinergic vasodilation is impaired in coronary atherosclerosis. Graded concentrations of acetylcholine and, for comparison, the nonendothelial-dependent vasodilator nitroglycerin were infused into the left anterior descending artery of eight patients with advanced coronary stenoses (greater than 50 percent narrowing), four subjects with angiographically normal coronary arteries, and six patients with mild coronary atherosclerosis (less than 20 percent narrowing). Vascular responses were evaluated by quantitative angiography. In several segments each of four normal coronary arteries, acetylcholine caused a dose-dependent dilation from a control diameter of 1.94 +/- 0.16 mm to 2.16 +/- 0.15 mm with the maximal acetylcholine dose (P less than 0.01). In contrast, all eight of the arteries with advanced stenoses showed dose-dependent constriction, from 1.05 +/- 0.05 to 0.32 +/- 0.16 mm at the highest concentration of acetylcholine (P less than 0.01), with temporary occlusion in five. Five of six vessels with minimal disease also constricted in response to acetylcholine. All vessels dilated in response to nitroglycerin, however. We conclude that paradoxical vasoconstriction induced by acetylcholine occurs early as well as late in the course of coronary atherosclerosis. Our preliminary findings suggest that the abnormal vascular response to acetylcholine may represent a defect in endothelial vasodilator function, and may be important in the pathogenesis of coronary vasospasm.