Selective Serotonin Reuptake Inhibitors and Myocardial Infarction

To the Editor:

Sauer et al\textsuperscript{1} reported a protective role in myocardial infarction of selective serotonin reuptake inhibitors (SSRIs) with high affinity for the serotonin transporter, such as paroxetine and sertraline. The rationale for this study was that depletion of platelet serotonin storage by serotonin reuptake inhibition may lead to attenuation of platelet activity and therefore decrease the risk of myocardial infarction. Discussing the lack of positive impact on cardiovascular outcome of the non-SSRI antidepressants with serotonin reuptake activity, the authors considered a balance between beneficial effects and deleterious effects, with the beneficial effects being negated by deleterious effects.

We believe that such a combination of positive and negative effects also exists for SSRIs with high affinity for the serotonin transporter, even though the ultimate balance gears toward a beneficial effect. For example, paroxetine and likely sertraline substantially increase serum levels of low-density lipoprotein cholesterol,\textsuperscript{2,3} a conventional cardiovascular risk factor. Interestingly, in the Sauer et al\textsuperscript{1} report, the percentage of hypercholesterolemia appears to be greater in the group of patients taking antidepressants than in the group of subjects not using antidepressants. In the study by Serebruany et al\textsuperscript{4} quoted by the authors, more patients on SSRIs were taking lipid-lowering agents. Endothelium-derived nitric oxide (NO) is not only the major effector of vasodilatation but also inhibits platelet aggregation and adhesion. Increased endothelium NO production is usually considered to be positive from a cardiovascular point of view, whereas decreased endothelium NO production is considered to be negative. The metabolic end products of nitric oxide (NOx) are often used as a marker for endothelial NO production. We have shown that paroxetine administration increases plasma levels of NOx and normalizes initially decreased plasma levels of NOx in depressed patients (Lara et al\textsuperscript{5}; W. Chrapko et al, unpublished data, 2002), which would suggest a positive cardiovascular impact of paroxetine on endothelium and platelet function.

Although they did not directly measure platelet activity in their investigation, Sauer et al\textsuperscript{1} are to be commended for assessing the impact of a specific biological effect of SSRIs on cardiovascular outcome. Such studies, ideally associated with concomitant biological measurements, should lead to greater understanding of the impact of antidepressants on cardiovascular outcomes than studies without clear mechanistic hypotheses. However, on the basis of our data and those of others, the cardiovascular impact of SSRIs likely extends beyond the activity of SSRIs at the platelet serotonin transporter and includes a combination of positive and negative effects susceptible to interindividual variability.

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