Sildenafil/Nitrate Interaction

To the Editor:

The ACC/AHA consensus document on sildenafil (Viagra)\textsuperscript{1} takes a very cautious approach to interaction between organic nitrates and sildenafil, suggesting that neither should be used within 24 hours of the other in any dose and by any route of administration. While justifiable on the basis of current information (Pfizer studies 148/230 and 148/231, which show approximate doubling of maximal blood pressure reduction by nitrate after sildenafil), this approach could result in the withholding of nitrates for conditions in which their own effects may be lifesaving and when administration may be safe in an appropriately low dose.

The document refers to nitrate action and interaction with sildenafil only on the basis of change in arterial pressure (and for a very small group, in pulmonary pressure and cardiac output). The powerful beneficial effects of organic nitrate on conduit arteries, wave reflection, and aortic impedance\textsuperscript{2,3} are not mentioned in the report. Effects of nitrates on arterial wave reflection cause characteristic changes in the radial (as well as the aortic) pressure waveform\textsuperscript{2,3} and were illustrated in Murrell’s initial description of nitroglycerine as an antianginal agent in 1879.\textsuperscript{4} These effects can be quantified as a reduction in augmentation of the ascending aortic systolic pressure, as generated from the radial artery pressure pulse waveform by applanation tonometry.\textsuperscript{2,3}

Using this method, we have been able to show in a limited study that sildenafil 50 mg approximately doubles the effect of a small dose of glyceryl trinitrate administered by dermal patch, that this effect begins within 1 hour and persists for up to 8 hours after sildenafil administration, and that it occurs independently of any blood pressure alteration. Such results are in accordance with the known pharmacological action and metabolism of sildenafil and with the maximal blood pressure-lowering effect of sublingual and oral nitrates after sildenafil administration. If confirmed, this information should permit nitrates to be used with sildenafil in appropriately low doses and with appropriate titration, at least by the intravenous or transdermal route.

Uncertainty about nitrate/sildenafil interaction results from almost complete reliance on sphygmomanometric blood pressure recordings. Use of pulse wave analysis provides new information on nitrate action and interaction between nitrate and sildenafil.

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