Drug-Eluting Stents: Do We Know Enough About Safety?

To the Editor:

Recently, Lemos et al.1 and O’Neill and Leon2 provided a balanced overview about drug-eluting stents. The authors nicely addressed the various aspects of this new technology from the economical to the clinical side, including safety and side effects. We would like to supplement another important aspect of safety, the problem of drug interaction, which has not yet received sufficient consideration.

In the case of paclitaxel-coated stents, recent studies revealed the safety of this approach for the patients enrolled in the investigations.3,4 However, we have shown that the combination of paclitaxel and cyclosporine A induces a strong supra-additive, antiproliferative effect on vascular smooth muscle cells (SMC).5 Although the paclitaxel doses used for stent coating (given in μg/mm²) are not directly comparable with those used in cell cultures, the approaches can at least be compared on the basis of their biological effects. Whereas coated stents were designed to contain doses capable of suppressing SMC proliferation, our studies were performed with low doses of paclitaxel that had virtually no impact on SMC proliferation. This changed dramatically when SMC were treated with low-dose paclitaxel plus cyclosporine A at doses applicable for immunosuppressive purposes. This drug combination had a strong antiproliferative effect and with increasing doses also an apoptosis-inducing effect.5

These findings leave uncertainty whether paclitaxel-coated stents would be safe for use in patients treated with cyclosporine A. This question is of special interest because patients with a history of renal dysfunction plus renal transplantation or patients who have undergone heart transplantation are at increased risk of developing cardiovascular diseases. Would currently available paclitaxel-coated stents lead to adverse effects such as late malapposition due to apoptosis in the vessel wall? Would these patients be better treated by another regimen? Such questions about drug interaction, in this case exemplarily raised for paclitaxel-coated stents, will have to be evaluated to gain more knowledge about the safety of drug-eluting stents.

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