Correspondence

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Photoangioplasty Recount: Clear Punch or Dimpled Chad?

To the Editor:

The recent article by Rockson, et al1 presents the results of a phase I trial of photodynamic therapy in patients with peripheral arterial disease. This report seems to be based on preliminary data that do not provide convincing evidence to support its conclusion, ie, that photoangioplasty holds promise as an alternative intervention for flow-limiting atherosclerosis. The lack of a control group and limiting the intervention to a single lesion that is not necessarily a flow-limiting stenosis are especially problematic.

Smooth muscle cells constitute no more than 2% to 5% of the volume of the atherosclerotic plaque. Consequently, there is no basis for assuming that the cytotoxic effect of photodynamic therapy would reduce the plaque volume sufficiently to be hemodynamically significant. Even if these cells are killed and lysed, an explanation as to what happened afterward to the major extracellular components of the plaque (cholesterol deposits and fibrous and calcified material) seems necessary and important.

Because there are large differences in the diameter of iliac, common femoral, and superficial femoral arteries, the distance between the laser source and vessel wall and, consequently, the laser dosages were different and might also have affected the results.

The authors also need to address the issue of thermal injury, because the relatively high laser intensity that was used may cause thermal damage to the arterial wall and increase platelet aggregation with possible late thrombosis. Finally, modest clinical improvement in this study may also be due to the laser irradiation of blood. Several groups2,3 previously demonstrated a beneficial effect of low-intensity laser irradiation on local circulation.

It was previously demonstrated that endoluminal low-intensity laser irradiation decreases the volume of atherosclerotic plaques in humans.4 Histological examination and ultrastructural analysis of the material obtained from surgical specimens of previously illuminated segments revealed that this type of irradiation results in the destruction of smooth muscle cells in the surface layers of the atherosclerotic arterial segments. It is noteworthy that the necrotic alterations in cells caused by laser radiation were primarily due to damage to cytoplasmic structures. These observations were used to introduce a new method of treating atherosclerotic lesions: transluminal laser atherolysis (TLA). TLA alone in 37 patients with noncritical lesions and TLA as an adjunct to percutaneous transluminal angioplasty in 25 patients with advanced peripheral arterial disease demonstrated good short and long-term results.

Either TLA or photoangioplasty may have some value in the treatment of the early atheromatous plaque, but neither may be effective in treating advanced obstructive lesions. We think that these approaches should be used only as an adjunct to interventional procedures.

At present, photoangioplasty as solo therapy for peripheral arterial disease cannot pass “the Florida light test.” Therefore, additional experimental studies are needed before concluding that this treatment modality is clinically appropriate.

Nicholas Kipshidze, MD, PhD
Lenox Hill Heart and Vascular Institute and Cardiovascular Research Foundation
New York, NY

Harry Sahota, MD
Good Samaritan Hospital
Los Angeles, CA

Response

In their letter written in response to the published report of our phase I trial of motexafin lutetium photoangioplasty for human peripheral atherosclerosis,1 Drs Kipshidze and Sahota raise some thought-provoking questions.

The authors take exception to our suggestion, which was based on the observations published in the article, that photoangioplasty might hold promise as a future therapeutic intervention in human atherosclerosis. In response, we must reiterate that this is a report of a phase I study that examined the potential safety and tolerability of a therapeutic agent under investigation. Our data would seem to support the feasibility of further, phase II testing, because photoangioplasty with motexafin lutetium was well-tolerated by the patient population under scrutiny. Indeed, a phase II, randomized, double-blind multicenter study is under-way. Although we did not presume to draw mechanistic conclusions from our preliminary observations, we were gratified to see evidence in this small, nonrandomized, nonblinded study of a clinical response to the investigational drug and associated photodynamic therapy. These preliminary observations enhance our interest in exploring the potential mechanisms and therapeutic applications of this therapeutic approach.

Kipshidze and Sahota suggest, on theoretical grounds, that photoangioplasty could not exert its therapeutic effect through modulation of the smooth muscle cell population alone. Indeed, a phase II randomized, double-blind multicenter study is under-way. Although we did not presume to draw mechanistic conclusions from our preliminary observations, we were gratified to see evidence in this small, nonrandomized, nonblinded study of a clinical response to the investigational drug and associated photodynamic therapy. These preliminary observations enhance our interest in exploring the potential mechanisms and therapeutic applications of this therapeutic approach.

Decisions about the future applicability of ixazophyrin photoangioplasty will emanate from the results of ongoing and future clinical evaluations. We have not yet concluded that the modality is clinically appropriate. However, the available data at present, as published in our article, permit us to remain optimistic about a role for photoangioplasty within the therapeutic spectrum of interventional cardiology and radiology.
Correspondence

Stanley G. Rockson, MD
Mahmood Razavi, MD
Andrzej Szuba, MD, PhD
Steven Filardo, MD
Peter Fitzgerald, MD, PhD
John P. Cooke, MD, PhD
Shuja Yousuf, MD
Stanford University School of Medicine
Stanford, California

Arthur R. DeVault, PhD
Makus F. Renschler, MD
Daniel C. Adelman, MD
Pharmacyclics, Inc
Sunnyvale, California

Paul Kramer, MD
Mid-America Heart Institute
Kansas City, Missouri

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Nicholas Kipshidze and Harry Sahota

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