Communications to the Editor

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The Loss of Endothelium-Dependent Vascular Tone Control in Systemic Sclerosis

To the Editor:

Systemic sclerosis (SSc) is characterized by the widespread involvement of the microvasculature and by severe damage to the endothelium as well as by the modification of vascular tone control. The endothelium-dependent control of vascular tone is one of the main functions that is jeopardized during endothelial injury.

The work of Cailes et al is a precious report showing the impairment of the endothelium-dependent control of the vascular tone in the lungs of SSc patients. Actually, our group was the first to report in 1990 such a result in the acral circulation of patients with SSc. We demonstrated that during the evolution of the disease, the endothelium-dependent vasodilation was impaired either when the level of von Willebrand factor, the marker of endothelial injury, was normal in the early phase of the disease or when it was greatly raised in the advanced phase of the disease. The failure of endothelial-dependent regulation of vasodilation then was confirmed in the acral circulation by Bedarida et al and in the skin circulation by La Civita et al.

Recent data indirectly also demonstrate a defective vasodilatation ability in the renal vasculature of SSc patients who have no sign of kidney involvement during standard clinical evaluations. In fact, we have found that the renal functional reserve, or the ability of the kidney to increase its glomerular filtration rate (GFR) and effective plasma flow (ERPF) when challenged with a protein or an amino acid load is blunted in patients with SSc. During the amino acid load test, GFR, ERPF, and total renal vascular resistance (TRVR) remained substantially unchanged in 20 SSc patients ([mean ± SD] GFR, −2 ± 13.1 mL/min; ERPF, −4.1 ± 62.5 mL/min; and TRVR, 662 ± 2,215 dyne·s·cm⁻⁵), whereas 10 healthy control subjects showed the expected significant changes in these parameters (GFR, 30.0 ± 13.3 mL/min [p < 0.001]; ERPF, 111.6 ± 39.6 mL/min [p < 0.001]; TRVR, −1,659 ± 559 dyne·s·cm⁻⁵ [p < 0.004]). Only five of 20 SSc patients had a GFR increase comparable to that of the control subjects (≥ 10%). The defective response was not dependent on the duration or the clinical subset of the disease, and it could be observed early in the course of the illness (median time interval from diagnosis, 18 months).

There is general agreement that the activation of the renal functional reserve depends on preglomerular vasodilation, and nitric oxide has been indicated as a major mediator of the phenomenon. Thus, the defective renal functional response to the protein load reflects an impaired endothelial-dependent vasodilation in the renal vasculature.

In conclusion, the analysis of the literature of the last decade shows that in SSc, the endothelium-dependent control of the vascular tone is profoundly deranged in different organs. This evidence strongly suggests that the pivotal aim of the physician, in particular in the early phase of the disease, is the protection of the endothelium in order to keep its function at a steady level. This might allow an adequate blood flow, thus avoiding the damage due to ischemia and reperfusion, as well as the further breakdown of vessel patency.

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REFERENCES

2. Which or how many appliances required additional advancement beyond the position determined by the patient (“The final protrusion of the jaw was not recorded because the patients were instructed how to change the amount of protrusion depending on symptoms and did so regularly at home”).

3. Whether the mandibular position was less effective for the appliances advanced at the time of PSG with the specific intent of improving snoring and apnea/hypopnea index, cannot constitute an evaluation of the effectiveness of the appliance as positioned by the patient or dentist. Rather, the second PSG must be viewed as an experimental process that looks at the titratability of this MAA. If the PSG purporting to assess outcome was in fact experimental, the accuracy of the study must remain in question until another therapeutic follow-up PSG is conducted on all patients whose MAAs were retracted by the patient to a more comfortable (and possibly less effective) position after the experimental PSG.

The adjustment of the MAA at the time of the second PSG, with the specific intent of improving snoring and apnea/hypopnea index, cannot constitute an evaluation of the effectiveness of the appliance as positioned by the patient or dentist. Rather, the second PSG must be viewed as an experimental process that looks at the titratability of this MAA. If the PSG purporting to assess outcome was in fact experimental, the accuracy of the study must remain in question until another therapeutic follow-up PSG is conducted on all patients whose MAAs were retracted by the patient to a more comfortable (and possibly less effective) position after the experimental PSG.

To clarify any possible confusion in either the dental or medical sleep fields, and to clarify further data summarized in this study, I request that this letter be published in CHEST at your earliest convenience.

B. Gail Denko, DMD
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Reference