Is endothelial-independent vascular reactivity compromised in obese subjects with metabolic syndrome?

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TO THE EDITOR: Schinzari et al. (4) compared the endothelial-dependent and -independent vasodilatory responses in controls and subjects with metabolic syndrome (MetSyn). The primary objective was to explore the integrity of the nitric oxide (NO) pathway and evaluate the effects of hyperinsulinemia on blood flow in subjects with different insulin sensitivity.

The authors found that vascular responses to acetylcholine, sodium nitroprussate, and verapamil during hyperinsulinemia were lower in the MetSyn group than in controls. The authors interpreted these results to suggest that endothelial-dependent and -independent pathways regulating vascular resistance were equally affected in subjects with MetSyn (4). However, the title and the interpretation of the results could be misleading, as the data do not entirely reflect these results. Indeed, the authors did not compare vascular responses between the control and MetSyn groups before and during hyperinsulinemia. This comparison is critical to understanding the grade of impairment in subjects with MetSyn. It is also necessary to confirm whether the impairment is either exclusively limited to the endothelium or also affects subendothelial vasodilatory mechanisms.

A crude analysis based on the data presented in the manuscript’s graphs and results is shown in Fig. 1. The two graphs suggest that in basal conditions the endothelial-dependent response was impaired in subjects with MetSyn, whereas the endothelial-independent vascular response was preserved. A more robust statistical analysis could have been conducted by entering both the diagnostic (control vs. MetSyn) and the insulin level group (basal vs. high) in the model as fixed factors and building an interaction term to compare the time-related vascular responses for each pharmacological agent. This would have shown whether there was any difference in vascular reactivity between the diagnostic and the insulin level groups.

Why are vascular responses to hyperinsulinemia different between groups? Insulin stimulates endothelial NO production via an Akt-dependent activation of the endothelial NO synthase (3). Compromised insulin signaling, therefore, reduces NO synthesis and impairs vasodilatation, which is probably contributing to the differences in vascular reactivity seen during hyperinsulinemia (2). The authors also suggest that insulin could have local vasodilatory effects on the vascular smooth muscle cells via modifications of calcium influx (4). However, the transcapillary (or transendothelial) transfer of insulin in the interstitium was not taken into account in this hypothesis. As the process is rate limiting (1), it still depends on the integrity of the endothelial cells, and it is delayed in obese insulin-resistant subjects (5). Therefore, it could be speculated that the rate and amount of insulin delivered into the interstitial space...
may be coresponsible for the lack of vasodilatory effects of insulin in subjects with MetSyn.

A between-group comparison of the vascular responses in the basal and hyperinsulinemic states should be conducted to confirm the generalized impairment in vascular reactivity in the obese group with MetSyn.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES