LETTER TO THE EDITOR

Revisiting Screening for Autonomic Neuropathy

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Dear Editor,

First of all, I must say that the article, *Necessity of Baseline Diabetic Autonomic Neuropathy Screening to start Cardiovascular Safety Outcome Trials: A Focus on Antidiabetic Agents and Autonomic Neurointegrity,*[1] dealt by the authors, is a very important and at the same time, often neglected issue, in the management of diabetes mellitus (DM). Although autonomic neuropathy increases the mortality in patient with diabetes by 1.5–3-fold (after adjusting for other cardiovascular risk factors),[2] screening for cardiovascular autonomic neuropathy (CAN) has not been focused as part of baseline measures in many of the major cardiovascular outcome trials (CVOTs)—as rightly pointed out by the authors. Considering the fact that there are patients who have specifically suffered cardiac arrest due to autonomic neuropathy,[2] screening for autonomic dysfunction is extremely important for diabetic patients, presenting with unexplained tachycardia, orthostatic hypotension, erectile dysfunction or sexual dysfunction (in case of female patients), etc.

However, the article has raised an important question, that is, whether the microvascular and macrovascular complications of DM are in continuum or they are running simultaneously, hand in hand, accelerating the complications of DM as experiments in animal models of diabetic neuropathy suggest that the multi-factorial metabolic changes of diabetes affect neurons and vasa nervorum endothelium, compromising vascular supply of nerves.[3] Again, though United Kingdom Prospective Diabetes Study (UKPDS) trial, it has been showed that a strict control of blood pressure reduced microvascular and macrovascular complications of DM, the action to control cardiovascular risk in diabetes (ACCORD) and the action in diabetes and vascular disease: preterax and diamicron MR controlled evaluation (ADVANCE) trials showed that an improved glycemic control reduced microvascular complications.[4] Again, in both diabetes control and complications trial (DCCT) and UKPDS, it had been shown that cardiovascular events were reduced, probably also due to "legacy effect" or metabolic memory. So, where is the missing link?

In this context, it is worth mentioning that the authors have discussed the effects of different kinds of antidiabetic agents on autonomic nervous system in a very elaborate way in this article and they have aptly pointed out that there is a paucity of literature, regarding clinical studies related to this complex interaction of insulin resistance, antidiabetic agents, and the challenge posed by recurrent attacks of hypoglycemia; as glycemic control is extremely important to prevent autonomic neuropathy.

The authors are very much justified in raising concerns about the hypoglycemic episodes of insulin therapy, gastrointestinal side effects of metformin therapy or hypotensive effects of SGLT-2 inhibitors.

At the end, the authors have rightly concluded that screening for autonomic neuropathy should be done for subjects, while recruiting them for cardiovascular (CV) safety trials.

Thank you.

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