Angiotensin-receptor blockade in acute stroke

Sir,
The debate on angiotensin converting inhibitors/receptor blockers made interesting reading.[1-3]

Professor Padma brought about the important results of ACCESS trial[4] in putting forth her argument. However, the contrary argument by Rohit Bhatia and the commentary by Professor Subhash Kaul did not touch this important trial.

The ACCESS trial is important in the context of the debate because it is the clinical trial that most closely examines the debate question whether angiotensin axis blockade is beneficial in acute stroke setting, and whether its benefits is due to its effects that is beyond its antihypertensive effect.

The result of ACCESS trial is interesting both in terms of its effect size and with respect to the nature of effect. The ACCESS trial found that the absolute risk reduction (ARR) of cumulative mortality is 4.3% and that of vascular events was 8.9% at the end of 12-months period after giving candesartan for a period of 7-days from onset of stroke. The study was unblinded at the end of 7 days and both group received candesartan according to the necessity of lowering BP. There was no significant difference in the BP between the both groups whether at the onset of stroke or during the study period. The results in both the groups (onset course candesartan and onset course placebo) differed mainly in terms of myocardial events. In other words, a 7-day stroke-onset course of candesartan reduced the myocardial events at the end of 12 months!

While the physiological plausibility of this is debated on, the effect size of the results looks incredible. It translates to a number needed to treat of 23.5 for 12-months mortality and 11.3 for 12-months vascular events. In comparison, HOPE trial, described to be the landmark trial on ACEI, had an absolute risk reduction of 3.6% and NNT of 27 for composite vascular events at the end of 5 years follow-up.[5] This would be an ARR of 0.72 and NNT of 139 on a 12-months scale. In fact, the survival curve of HOPE trial started to diverge only after 200 days of follow-up.

If we give credence to ACCESS trial, the debate is sealed with at least level-2 evidence in favor of both acute stroke angiotensin axis blockade and the extra-antihypertensive effect of candesartan.

But is it that straight forward? Was the result of ACCESS too good to be true? Hopefully, the ongoing Scandinavian Candesartan Acute Stroke Trial would be answering this question.[6]

Srijithesh P. Rajendran

Department of Neurology, Jawaharlal Institute of

Postgraduate Medical Education and Research, Pondicherry, India

For correspondence:
Dr. Srijithesh P. Rajendran, Department of Neurology, SS Block, Jawaharlal Institute of Postgraduate Medical Education and Research, Dhanvanthri Nagar, Pondicherry 6, India. E-mail: srijitheshpr@rediffmail.com

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