Stroke preventive treatment using perindopril and indapamid in the context of Indian primary care

PROGRESS, the “Perindopril Protection against Recurrent Stroke Study”,[1] has had a major influence on clinical practice and treatment guidelines for the prevention of recurrent stroke. Nevertheless, the trialists’
use of the phrase “perindopril-based” treatment is misleading, since perindopril without indapamide showed no benefit for stroke prevention.[2-4]

In PROGRESS, patients randomized to receive treatment could receive either of two different antihypertensive regimens: (a) perindopril (4 mg/day) or, (b) perindopril (4 mg/day) plus indapamide (2.5 mg/day). Compared to placebo, perindopril alone showed no benefit (Chi-square = 0.235, P=0.63). Perindopril plus indapamide, however, showed a highly significant benefit (Chi-square = 30.468, P<0.0001).

The two treatment regimens in PROGRESS were amalgamated and presented as the effects of “perindopril-based” antihypertensive therapy.[1] The amalgamated results showed a significant benefit of treatment compared to placebo (Chi-square = 19.812, P<0.0001) despite the lack of effect of perindopril monotherapy due to the highly significant benefit of treatment with perindopril plus indapamide.

In this issue of Neurology India, the results of an observational, multicenter study performed in the setting of primary care throughout India are presented.[5] The aim was to assess whether the preventive benefits described in the PROGRESS trial would be reflected in primary care practice, in a population with different demographics and clinical characteristics.

The incidence of recurrent stroke in this primary care setting was similar to that seen with the amalgamated results of the PROGRESS trial, which is interpreted to suggest that treatment using perindopril with or without indapamide may be effective to prevent recurrent stroke in the Indian primary care setting.[6] There was no control group however, and so the study does not provide direct evidence of a preventive treatment benefit, as acknowledged in the paper.[8]

The authors of the Indian study[8] are to be commended for appending the words “with or without indapamide” to the ubiquitous “perindopril-based” terminology found throughout the recent literature and derived from the original PROGRESS publication.[1] This is a first step towards a more balanced presentation of PROGRESS-related material.

However, the authors do not report separately the results of their subgroups of perindopril with or without indapamide. If the results are similar to those of the PROGRESS trial, as the authors claim, then it is possible that only the group treated with perindopril plus indapamide benefited in terms of stroke prevention.

The curious practice of having a “flexible” regimen where a known stroke protective drug (indapamide)[6] may or may not be added to one which is not yet proven (perindopril) - and then amalgamating the results so that it is unclear which drug is responsible for the benefit - is misleading and should not be repeated. Future studies should either remove indapamide from the protocol (if perindopril is truly the drug of interest) or include indapamide monotherapy as a treatment option. Only then will we be able to truly differentiate the active component(s) of “PROGRESS-based” treatment and make the best possible medical and economic decisions for the widespread prevention of recurrent stroke.

R. A. Wennberg, C. Zimmermann
Department of Medicine, University of Toronto, University Health Network, 399 Bathurst Street, Toronto, ON, M5T 2S8, Canada.
E-mail: richard.wennberg@uhn.on.ca

References

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