Reviewer's report

Title: Effect of Pre-Stroke Use of ACE Inhibitors On Ischemic Stroke Severity

Version: 1 Date: 7 March 2005

Reviewer: Joan Marti-Fabregas

Reviewer's report:

General

-----------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

This is an interesting study in which the authors suggest that patients with ischemic stroke pre-treated with any ACE inhibitor (ACEI) suffer less severe strokes, as measured by the NIHSS score. Patients were divided in 2 groups (ACEI vs non-ACEI) and their mean NIHSS scores were compared.

However, before accepting the results, there are some methodological problems that should be solved:

1) NIHSS scores should be provided as median values, and the authors should compare median NIHSS scores between groups (Mann Whitney U test) instead of mean values.
2) Some studies showed that people with less severe strokes are admitted later and patients with more severe strokes are admitted earlier at the Emergency Room. Therefore, the authors should provide and compare the time from stroke onset to admission NIHSS between both groups.
3) One explanation for the results is that lacunar infarcts are over-represented in the ACEI group. This is consistent with the idea that arterial hypertension is a risk factor for lacunar infarct and therefore more patients with lacunar infarct are treated with antihypertensive drugs. However, lacunar infarcts are a subtype of cerebral infarcts with a relative good prognosis, and lacunar infarcts will usually have a lower NIHSS score than total or partial non-lacunar cerebral infarcts. The authors should therefore re-analyze the results after controlling for stroke etiology.
4) All consecutive patients with a diagnosis of ischemic stroke must be included in calculations. There is no reason to exclude those patients in whom a MRI was not obtained or was of poor quality. If they had an ischemic stroke, they must be included. The MRI sub-study can be done with a subset of patients.
5) As it has been demonstrated that previous Transient Ischemic Attacks elicit ischemic tolerance of the brain and patients with previous TIA have less severe strokes than patients without previous TIA, it would be useful to know the frequency of TIA in this study, and to calculate this variable in the 2 group of patients (ACEI and non-ACEI).
6) The authors must explain whether they checked for compliance. It is frequent that patients with high blood pressure are non-compliant. Patients or their relatives should be asked about the last time that the patient received the treatment before the stroke.

-----------------------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The authors classified the stroke severity in mild, moderate and severe. This classification is arbitrary and not useful. Figure 1 is therefore unnecessary.

Although there were no differences in blood glucose and body temperature at admission, the values should be provided.
In Table 1, the p values of non-significant differences should be provided. It is conceivable that if ACEI have some effect in provoking less severe strokes, the higher the dose of the drug the higher this effect. Therefore, it would be useful to analyze if there is an inverse relationship between the ACEI dose and the NIHSS score. Such dose-effect would reinforce the results of the study. The abstract should state that the study is retrospective.

Discretionary Revisions (which the author can choose to ignore)

It would be interesting to analyze the results in patients admitted within the first 6 hours after the onset of symptoms. It would be interesting to have the 3-month follow-up of the patients included in the study. If patients pre-treated with ACEI have an increased probability of favourable outcomes, this would reinforce the suggested protective role of ACEI. However, as the authors state, this is not possible because some patients were treated with thrombolysis, endovascular treatments and neuroprotectants. Recent papers stress the effect of ACEI on cerebral autoregulation and cerebrovascular reactivity. This point should be included in the Discussion.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests