Reviewer's report

Title: Peak plasma interleukin-6 and other peripheral markers of inflammation in the first week of ischaemic stroke correlate with brain infarct volume, stroke severity and long-term outcome.

Version: 4 Date: 15 September 2003

Reviewer: José Castillo

Reviewer's report:

General
The authors present a study carried out with 37 patients in which they discover an association, already demonstrated by other authors, between plasmatic levels of IL-6, the volume of the infarct and the residual neurological deficit. The subject is of great interest owing to its physiopathological, prognostic and therapeutic implications.

Discretionary Revisions (which the author can choose to ignore)
1. The authors justify the need for an up-to-date work like the one they present, with bibliographic citations dating from 7, 5 and 2 years ago. There is a much more recent bibliography which continues to justify the need for studies such as that presented by the authors.

2. It would be helpful for the authors to clarify the statistical tests used to determine the univariate relationships. The Pearson coefficient is useful for comparing continuous variables, but for the clinical scales the use of a test such as the Spearman would be more suitable.

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

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. The work suffers from limitations, fundamentally owing to the small number of cases, despite being a study conducted on patients admitted consecutively during a period of 9 months. In the opinion of the revisor, the impossibility of developing multivariate models prevents the demonstration of an independent association between levels of IL-6, the volume of the infarct and the neurological sequelae. Similarly, the authors should attempt to explain other variables, clearly associated with the volume and the neurological deficit, such as glycemia and fibrinogen.

2. The method described by the authors does not provide an assurance that the last sample of plasma obtained for the determination of the IL-6 is not 48 hours prior to the CT utilized for the determination of the volume of the infarct.

3. The authors should specify the inter-observer variability involved in determination of the volume of the infarct, in order to justify the need for 5 different measurements.

4. One fifth of the patients included in the study have experienced prior infarctions. The authors need to specify whether these were ipsilateral or contralateral to the present case. The presence of prior ipsilateral infarcts could complicate the measurement of the volume of the present infarct. For the same reason, the authors need to clarify the scoring of the prior mRS, in order to adequately assess the relationship between the mRS at 3 or 12 months and the concentration of IL-6.
5. The authors state that some biological variable, such as temperature, was determined at all visits. Which of these was used to compare with levels of IL-6? Did the time of maximum temperature coincide with the peak of IL-6?

6. Twenty-two per cent of the patients have auricular fibrillation, but only half receive anticoagulants. The authors should justify this apparent discrepancy.

7. The relationship between the averages of the various clinical scales is difficult to understand. At three months, an NIHSS of 5 (minimum sequelae) coincides with an mRS of 3 (dependent patients); similarly, the maximum score of the NIHSS 17, does not appear to be related to a score of 5 in the mRS. At 12 months, 90 points in the Barthel Index corresponds with a score of 3 in the mRS (?).

**Advice on publication:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** A paper of limited interest

**Quality of written English:** Acceptable

**Declaration of competing interests:**

None