Title: Effect of paracetamol (acetaminophen) and ibuprofen on body temperature in acute ischemic stroke. PISA, a phase II double blind randomized placebo-controlled trial. ISRCTN 98608690

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Reviewer: Prof Jose Ferro

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

GENERAL REVIEW

This is an important phase II study demonstrating that high doses of paracetamol can decrease body temperature in acute stroke patients and that indobufen did not have such effect.

My main criticism is ethical: it is not the usual practice to randomise to placebo patients with temperature as high as 39o. Such temperatures cause at least discomfort and should be treated.

SPECIFIC COMMENTS AND SUGGESTIONS

Background. Limit this section to the evidence supporting the rational of the study: harmful effect of high body temperatures in acute stroke, choice of drugs and dosages.

Study power. In previous studies the dose of 6000 mg of paracetamol decreased body temperature by 0.4oC. wasn't 0.5oC too optimistic?

In a acute stroke trial the no of subjects under observation will decrease after day 1 due to deaths, early discharges, etc. The no of subjects was calculated for the main outcome that was measured at 24 hours. Such no is insufficient for later measurements.

Confounding factors. How were stroke type and severity categorised for the logistic regression?

Side effects. There is no information on concomitant medication that may be responsible for some of the gastric and liver side effects.

Competing interests:

None declared.