Reviewer’s report

Title: Performance of Interleukin-6 and Interleukin-8 serum levels in pediatric oncology patients with neutropenia and fever for the assessment of low-risk

Version: 1 Date: 24 April 2007

Reviewer: Eveline de Bont

Reviewer’s report:

General
This paper addresses an important topic. The aim of the study was to determine the value of serum levels of IL-6, IL-8 and CRP as predictors for sepsis or prolonged fever in children with fever and chemotherapy induced neutropenia at the start of a febrile episode. Furthermore Diepold et al aimed to analyze whether IL-6 and IL-8 could define a group at low risk of septicaemia. In the results IL-6 and IL-8 are presented as useful to define a group at low risk for sepsis, with IL-6 as the best predictor bacteremia or severe bacterial infection.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The presentation of the study aim seems to be inconsequent; the aims of the study imply that the lower limit of the high risk group is the higher limit of the low risk group, but isn’t there a grey area. In the Method section the definitions of neutropenia, low risk, and high risk for sepsis are missing. Furthermore it is unclear at which time points the blood samples are taken. The division in febrile episodes up to three days and of five days or more was not seen before; we would like to see the reasoning that led to this division. The results should start with the amount of patients and episodes that were included at the beginning and the amount of patients that were finally analysed. Where the analysis similar when only the first episodes per patient were included? This should be mentioned either here or in the discussion, as inclusion of one patient several times can introduce bias. We would also like to see the absolute values of the different parameters and groups. The sensitivity, specificity and positive predictive value for the group which will develop a sepsis or a longer period of fever is given. However the key question is what the sensitivity, specificity and positive predictive value for the group at low risk for a bacterial infection or serious infectious complications is, as this can have treatment consequences. “Patients with IL-6 values below 42 pg/ml on the first day of fever have a high chance to belong to the group of patients with a short episode of fever” is too vague. The total groups of patients with low-grade fever and a documented gram positive or gram negative blood culture are small (28 and 14 patients respectively), one can imagine that a larger group would e.g. reveal IL-8 to be the most accurate parameter.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
In the discussion it is mentioned that “factors used so far to define a low risk group were determined at day 3 after admission”, this is not true; there are studies, e.g. by Santolaya, Aquino and Oude Nijhuis which determine low risk groups before day 3 after admission. The most important indicators, mentioned next, might be updated too. In the conclusion IL-6 and IL-8 are stated to define a group with short duration of fever, we think this is too strong as no sensitivity, specificity and positive predictive value are mentioned for this patient group.

Discretionary Revisions (which the author can choose to ignore)

What next?: Reject because scientifically unsound
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests