Reviewer's report

Title: Epoetin administrated after cardiac surgery: effects on renal function and inflammation in a randomized controlled study

Version: 2 Date: 31 May 2012

Reviewer: Anja Haase-Fielitz

Reviewer's report:

Major

“We used uNGAL as a surrogate of renal function as it has been described to be an earlier and more sensitive marker of AKI than creatinine.”

- In this study urine NGAL (biomarker of tubular injury) was measured late in the course (48 and 96hrs after ICU admission). There are meanwhile data from >10.000 patients admitted to the intensive care unit showing that NGAL peaks about 6 hours after the renal injurious event with a rapid decline following this episode.

=> Can the authors comment on timing of NGAL measurement and their hypothesis about expected NGAL peak/rise.

“We expected to observe a decrease in uNGAL levels, which are associated with decreasing mortality and shorter hospital stay.”

-Considering the dynamic of NGAL after cardiac surgery, the expected decrease in uNGAL two to four days after Erythropoietin administration was - given the above considerations - difficult if not impossible to observe.

-The provided power calculation however based on changes in uNGAL from ICU admission to 48 hours postoperatively. No real baseline value (preoperative) was available with NGAL most likely being already increased in patients subsequently developing AKIN at the time of randomization (ICU admission).

-In the registry the study is described as open label whereas in the manuscript the authors provide the following information: “…The envelopes were opened by a nurse from the Nephrology Unit who prepared the syringes for injection. Investigators and patients were blinded to the treatment.” Please explain.

-Intraoperative characteristics per treatment group are missing including length of cardiopulmonary bypass, urgency of operation, fluid balance, hemodynamic variables, inotropes, vasopressor and transfusions administered. Please provide these data in a separate Table.

-At which day after ICU admission was AKI diagnosed?

-Were patients with established AKI (according to AKIN) at enrolment excluded?
“... we calculated that 35 patients treated by EPO and 35 controls were necessary to obtain a 95% power with # <0.05, assuming a between group difference of one standard deviation in our primary endpoint. Predicting a drop out of 10 patients (5 in both groups), we decided to include 80 patients: 40 would be treated by EPO and 40 by placebo.”

-Please be more concise in the power calculation and include numbers for expected and clinically meaningful uNGAL differences as well as expected standard deviation. This will enable readers to reproduce the calculation.

Minor

-Please add serum creatinine in Table 3.

-As the authors used the CONSORT checklist (Supplement), the flow diagram should be filled in according to CONSORT including reasons for exclusion.

-Please add the year of study enrolment under methods.


-Abstract: “…EPO treatment did not significantly modify urinary NGAL levels compared to placebo [2.5ng/ml (-17.3;22.5) vs 0.7ng/ml (-31.77;25.15) , p=0.77] . Please add the timing of NGAL measurements.

-“Markers of renal function such as urinary NGAL, cystatin C and creatinine...” NGAL is generally recognized to be a tubular injury/damage biomarker whereas creatinine and cystatin C constitute glomerular filtration/function markers.

“In addition no patients received nephrotoxic agents such as aminoglycosides or contrast media.” Were contrast media administered before cardiac surgery (e.g. PCI)?

-Please provide the postoperative haemoglobin level in all 3 groups within the first 2 weeks of Erythropoietin application.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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