Reviewer’s report

Title: The effect of high dose antibiotic impregnated cement on rate of Surgical Site Infection after hip hemiarthroplasty for fractured neck of femur: A protocol for a double-blind quasi randomised controlled trial.

Version: 2 Date: 26 May 2013

Reviewer: Olof Sköldenberg

Reviewer’s report:

The authors should be commended on performing a trial on this patient-group. True intervention studies on such large materials are few and far between and is really hard work as I am well aware of. I believe the protocol for the study is worthy of publication but I have a few remarks.

Major Compulsory Revisions:

EFFECT SIZE

On what basis do the authors think that the effect will be as large as removing 75% of all SSIs? A reduction from 4% to 1% is a very large effect size and since this is the basis for the sample size it should be elaborated upon. Are there any pre-clinical or clinical data that supports this large effect size? The only reference they have regarding this very foundation of the study is the Norwegian register study on revision surgery for total hip arthroplasty patients (not FNF-patients in this study [!]). The Norwegians had a 0.4% risk for revision due to infection in patients treated with both systemic and local antibiotics (in the cement) and 0.7% for patients only treated with systemic antibiotics. This 0.3% difference represents a 42% reduction in the occurrence of infection. Based on what will this new cementmix (in the current study) be much more effective?

The authors also state that a local application of gentamycin can only be applied by cement; there are of course other, perhaps even more efficient methods of doing this, for instance by using Gentaflecce or some other version of this (collagen pads with gentamycin).

Sample size calculation

The sample size calculation is mathematically correct but, in my opinion, still faulty since the effect size is overestimated.

CHANGE OF SYSTEMIC ANTIBIOTICS

The number of days or doses that prophylactic antibiotics is administered is not stated. In addition; Teicoplanin; a broad spectrum antibiotics with effect on multi-resistant strains of bacteria was added afet the first 1/3 of the study. This could have a profound effect on the primary outcome and the authors must elaborate on how they have controlled for this.
PRIMARY OUTCOME
The definition of a SSI is not in line with the current literature on periprosthetic joint infections (PJI). One could argue that a SSI is a different definition on an infection than a PJI. The implant itself and its biofilm-inducing properties are not considered in the 1992 definition of a deep SSI. In my opinion they should have used the current PJI definition as the primary outcome variable.

IF the authors still would like to have their (arguably older) definition of SSI instead of PJI the should argue for this in the discussion and why the general definition of SSI also is valid for prosthetic joints.


Defining PJI
A definite diagnosis of PJI can be made when the following conditions are met:
1. A sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from two separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. Four of the following six criteria exist:
   a. Elevated serum erythrocyte sedimentation rate (ESR) or serum C-reactive protein (CRP) concentration
   b. Elevated synovial white blood cell (WBC) count
   c. Elevated synovial neutrophil percentage (PMN%)
   d. Presence of purulence in the affected joint
   e. Isolation of a microorganism in one culture of periprosthetic tissue or fluid
   f. Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 400 times magnification

Minor essential revision

PARTICIPANT ALLOCATION
Having 2 different; premade; versions of bone cement as the primary intervention could, arguably, be a perfect tool for a true randomized controlled trial. The authors have not done this however and I think the main reason for this is lack of resources. Having a central randomization procedure is arguably easier than a local.

“… concerns about the impact on the credibility and fidelity of the study interventions were identified as problematic issues if individual participant randomisation.”
I am not sure what this means? Surgeons would protest if they were given cement with a new antibiotic mix if there was an individual randomization? but not, as now, if they were forced to use it every other month? Please elaborate on this.

The surgeons could easily have been blinded since the antibiotics (as I understand it from the paper) is already pre-prepared in the mixing system of the cement. The argument for NOT blinding this for the surgeons is very weak “….handling characteristics could potentially be different and the surgeon would need to be aware”.

This could, and should, of course have been investigated prior to the study. If the handling characteristics of the cement truly is different the surgeons have now for the last years learned that every other month the cement cures differently then the month before.

PARTICIPANT RECRUITMENT

Please describe the inclusion/exclusion criteria first and then how informed consent was acquired,

**Level of interest:** An article of importance in its field

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests