

Correspondence

Efficacy of antibiotic-impregnated cement in total hip replacement

Sir—We have read with interest the systematic review on routine use of antibiotic-loaded cement in primary cemented hip arthroplasty by Dr. Parvizi et al. (2008), and would like to bring three issues to your attention.

Two randomized controlled trials (RCT, Pfarr and Burri 1979, Wannske and Tscherne 1979), six comparative cohort studies (Buchholz and Engelbrecht 1970, Buchholz and Gartmann 1972, Buchholz et al. 1977, 1984, Thierse 1978, Persson et al. 1999), the data of the Arthroplasty Register in Sweden, Canada and Finland, and the Cochrane Central Register of Controlled Trials, and other ongoing or unpublished relevant studies were not included in the article. In addition, McQueen et al. (1990) had published a follow-up report of their previous RCT (McQueen et al. 1987) with an expanded number of procedures; Engesaeter et al. (2003) had updated their previous observational study (Espeshaug et al. 1997) in the recent publication. If they only searched Medline, the authors would possibly miss 20%–70% of published RCTs (Dickersin 1994). All the above caused the selection bias which may overestimate the effectiveness of antibiotic cement.

Second, we wish to offer alternative views on several questionable points in the analysis. (i) As two sequential studies by Josefsson et al. (1990, 1993) shared the same patient group, the former should have been excluded. (ii) In the subgroup of McQueen et al. (1987), the 26 knee arthroplasties and 1 infected knee should have been excluded from 295 total joint arthroplasties and 3 infected joints, respectively. (iii) The reference by Lieberman was not indicated. (iv) In the report by Lynch et al. (1987), the infection rate of the plain cement group without previous hip surgery was 11/640. The authors had not given details about the calculation of 11/651. (v) Neither the results of the assessment of study quality nor the results

of the test for homogeneity were noted.

Finally, although the methodology for meta-analysis of non-randomized studies were immature yet, the paucity and the low Jadad score (never exceed 2) of the 4 RCTs forced the authors to include non-randomized studies. They tend to overestimate the effectiveness of the antibiotic cement (Schulz et al. 1995). Also, the trials were substantially different in their design; e.g. the data comparing antibiotic cement with no prophylaxis were combined with those comparing antibiotic cement with intravenous antibiotic, which might again exaggerate the effectiveness of antibiotic cement. Thus, subgroup or metaregression analysis may be preferable for the heterogeneity. While we understand the challenges inherent in performing this meta-analysis as the authors recognized, the above-mentioned drawbacks made it premature for any definite conclusion to be drawn, until a strictly-designed, multi-centered, large-sampled RCT is performed. Considering the dramatically lower preventive effect for the normal population than for the high-risk population (Jiranek et al. 2006) and the potential disadvantages associated with prophylactic antibiotic cement (Jiranek et al. 2006, Yan et al. 2007), it is difficult to accept the conclusion of the routine use of antibiotic cement based on the present evidence.

Xun-Zi Cai¹, Xian-Zhen Chen² and Shi-Gui Yan¹

¹Department of Orthopaedics,
Second Affiliated Hospital, School of Medicine,
Zhejiang University, 88 Jiefang Road,

²Department of Dermatology,
Sir Run Run Shaw Hospital, School of Medicine,
Zhejiang University,

³Qingchun East Road, PR China
Emilcai@hotmail.com

Sir—We would like to thank you Drs Cai, Chen and Yan for their insightful letter related to our article that was recently published in Acta (Parvizi 2008). We are grateful to the authors for raising some important issues related to our article.

Three main points were raised in the letter that will be addressed.

1) The authors of the letter have highlighted a list of articles that could have potentially been included in our meta-analysis. As they are aware, conducting meta-analyses requires adherence to strict and important rules. We had stated in our manuscript the strict criteria that included presentation of outcome data at specified follow-up times for study inclusion that were developed using accepted systematic literature techniques. Outcome data required for inclusion were the incidence of deep infection and the overall survival rate at the specified interval after surgery. Finally, each eligible study was assessed for scientific quality based on “Systems to rate the strength of scientific evidence” AHRQ Publication No. 02 E016, April 2002 (http://www.ahrq.gov/news/pubcat/c_evid.htm). This assessment was made by 2 of the authors who were blinded to the source institution, journal, and the authors for each included publication. Because of these strict rules some articles were not deemed to contain adequate data for inclusion. We agree with the authors of the letter that searching multiple databases is more comprehensive and likely to identify more published and non-published articles. In this particular study we had resorted to searching the Medline only in order to identify studies that had been subjected to strict peer-review scrutiny. Because of the latter we did not include data available in the Joint Registries in our final analysis. We did include published peer-reviewed data from the Norwegian Registry. Based on the extensive search of Chai, Chen and Yan, performed four years after our initial search, some articles are identified that could have potentially been included in our analyses. Some of these articles were not included in our analysis to prevent duplication as the presented data was a repeat analysis and representation of the same or similar cohort (McQueen 1990). Other articles were not included as they were on unrelated topic such as the article by Persson et al. (1999) that discusses economics of using antibiotic impregnated cement. The majority of the

articles that you cite Chai, Chen and Yan (Buchholz and Engelbrecht 1970, Buchholz and Gartmann 1972, Pfarr and Burri 1979, Wannske and Tscherne 1979) were not included as they were in German. Other articles not included were review articles such as the current concept reviews (Buchholz et al. 1984) which uniformly have little comparative / analyzable data. There were other studies that presented data related to the use of antibiotic cement during reimplantation surgery but their primary hypothesis did not focus on the intended topic of our study.

2) We respectfully disagree with the suggestion regarding exclusion of some of the potential subjects that could have been included in the study. We were fully cognizant of the potential that “publication bias” may have had on our analysis. This point had also been raised during the review process of this article prior to publication. We carefully addressed this point by having two reviewers as well as a biostatistician review our paper during the submission process. In order to prevent this we included funnel plots that show bias was not a factor here. The letter authors provide no basis for considering that exclusion of articles/subjects was a publication bias in this article. Even if such exclusion was to be considered, the sample size for our study is so large that exclusion of a few subjects should not have impacted the final results nor have changed our conclusions.

3) Some of these deficiencies that are outlined by the authors of the letter were in fact included in the Discussion. We agree with the authors that a large, multi-center, randomized study is the preferred study design to evaluate this issues. However, this is very difficult to undertake because of the size of the necessary study sample as well as the resources necessary to undertake such a large trial. The conclusions presented in the manuscript were based on the analyses performed on the available data in the literature and despite all the shortcomings of meta-analysis, we believe still stand.

Javad Parvizi, Khal Saleh, Michael Mont
Parvj@aol.com

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