Bone & Joint Research

Morgenstern M, Vallejo A, McNally MA, et al. The effect of local antibiotic prophylaxis when treating open limb fractures: a systematic review and meta-analysis. *Bone Joint Res* 2018;7:447-456.

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Authors' reply:

10 October 2018

Sir,

We thank Professor Stengel for his positive comments about the presentation of our work on the impact of systemic and local antibiotic therapy in fracture-related infection (FRI) at The European Bone & Joint Infection Society (EBJIS) meeting, and our article in *Bone & Joint Research*.[1]

We fully understand and appreciate his important comment. In fact, we addressed this point in the discussion section of our published work since we considered that the studies of Henry et al,[2] Ostermann et al[3] and Ostermann et al[4] (references 13, 14 and 15, respectively, in our paper) could be cumulative reports of the same patient cohort, increasing over time. Despite careful review of each of the mentioned manuscripts, the authors of these references did not state or indicate that they included the same cohort of patients in all studies. However, we were unable to contact the corresponding author of the latest references (P. Ostermann). Therefore, in the absence of any substantive evidence, and a lack of any published statement, we decided to leave these three references in our systematic review. In order to satisfy the concerns, we have already performed a separate calculation of the meta-analysis by excluding the first two references[2,3] and have already added the following text to the discussion section:

"Another limitation of this systematic review may be that Henry et al[13] and Ostermann et al[14,15] might have used a cumulative cohort since the same group of authors, from the same centre, using a similar technique, described their results in three different studies. However, since they did not mention having used the same cohort of patients, all three studies were included in this meta-analysis. Assuming a cumulative cohort was used, and excluding their first two studies (Henry et al[13] and Ostermann et al[14]) from our meta-analysis, the recalculation of pooled data would show similar results with a significant risk reduction if local antibiotics were given prophylactically (4.9%) compared with the control group receiving standard systemic prophylaxis alone (15.8%) ($p < 0.001$)."

With regard to Prof. Stengel's query about the difference between the randomized controlled trial (RCT) and the cohort studies, we added the following to our discussion:

"Conversely, the only RCT in this meta-analysis did not find any beneficial effect in preventing FRI with the use of tobramycin-loaded PMMA beads. Moehring et al[17] reported an increased risk of FRI with the use of antibiotic-loaded PMMA depots (8.3% vs 5.3%). However, this study is associated with a

considerable risk of bias due to patient prognostic factors not being reported, inadequate case-matching with regard to Gustilo–Anderson grade, and the absence of a clearly defined primary outcome (Table I). The somewhat greater infection rate in the intervention group may be explained by the smaller group size and by the fact that this cohort received just a single-dose systemic antimicrobial prophylaxis, whereas in the control group, systemic antibiotics were continued until wound coverage.[17]"

Concerning the use of the term 'case-control-study', we agree with Prof. Stengel's comment and, in fact, this was an oversight missed in our proof checks, and not an intentional use of the term. We regret the error and thank you for providing an opportunity to disclose it.

*"Table I provides an overview of the primary studies included for quantitative analysis (supplementary material): one RCT[17] and seven retrospective **case-control studies**,[13-16,18-20]".*

We hope that these comments address Professor Stengel's questions to his satisfaction.

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1. **Morgenstern M, Vallejo A, McNally MA, et al.** The effect of local antibiotic prophylaxis when treating open limb fractures: a systematic review and meta-analysis. *Bone Joint Res* 2018;7:447-456.
2. **Henry SL, Ostermann PA, Seligson D.** The prophylactic use of antibiotic impregnated beads in open fractures. *J Trauma* 1990;30:1231-1238.
3. **Ostermann PA, Henry SL, Seligson D.** The role of local antibiotic therapy in the management of compound fractures. *Clin Orthop Relat Res* 1993;295:102-111.
4. **Ostermann PA, Seligson D, Henry SL.** Local antibiotic therapy for severe open fractures. A review of 1085 consecutive cases. *J Bone Joint Surg [Br]* 1995;77-B:93-97.