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Antibiotics by bolus or infusion for bacterial meningitis? : pö [A u t h o r s r e p l y]

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lower doses (10–15 mg/kg) to safeguard against hepatotoxicity.⁴ Practically, use of infusions in resource-constraint settings is less feasible than bolus administration and can potentially delay initiation of timely antimicrobial treatment in such serious illnesses.

We declare that we have no conflicts of interest.

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Authors' reply

We were pleased to learn how meticulously Bhavneet Bharti and Sahul Bharti had read our Article on slow initial β -lactam infusion and oral paracetamol in bacterial meningitis of children.¹ They pay specific attention to data from children with pneumococcal meningitis who were not receiving concomitant oral paracetamol. Here, our intention-to-treat analysis for the predefined

secondary outcome comprising death or any sequelae (including severe and less severe neurological and hearing sequelae) favoured infusion therapy over boluses, with an odds ratio (OR) of 0.18 (95% CI 0.03–0.90; $p=0.04$). Bharti and Bharti propose relative risk (RR) instead of OR less than 0.50 as a “statistically better measure of effect size”. Calculation of RR in our study was possible, but we chose to use ORs for all our analyses. The RR for the secondary outcome of death or any sequelae is 0.48 (95% CI 0.31–0.77; $p=0.027$ by Fisher's exact test). Bharti and Bharti have calculated RR for a composite endpoint, which we did not have at all in our protocol: death, or severe neurological sequelae, or deafness. If done so, neither OR nor RR would have a suggested significant benefit.

Regarding paracetamol, we intentionally used higher than usual doses to maximise its likely beneficial effects. By contrast with use of paracetamol in adult patients, its use is safe in children beyond the neonatal age, and there is no evidence to suggest that a daily dose lower than 100 mg/kg for a few days would be substantially hepatotoxic or otherwise harmful;^{2,3} our anaesthesiologists have used higher doses for many years without problems.

We agree that in a resource-poor setting infusion is not equal in ease of use to the traditional bolus administration. However, this fact should be put into perspective. Mortality associated with bacterial meningitis has not decreased substantially since the advent of chloramphenicol and

ampicillin half a century ago. In some African countries, the case fatality rate of bacterial meningitis still exceeds 50%.^{4,5} If we could mitigate this disease by such a simple way as investing in a small infusion pump that administers cefotaxime (or perhaps any other β -lactam) slowly, while giving concomitantly the inexpensive, safe, and readily available paracetamol orally, many children in those resource-poor settings could benefit. This approach was and is our motive for these complicated trials.

HP is a clinical scientific consultant for the Serum Institute of India. The other authors declare that they have no conflicts of interest.

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