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Authors' response

We thank the author for reading our article with great interest. We sincerely welcome the comments/ suggestion made by the author of this letter[1]. He has rightly mentioned that the kinetics of phages administered in animals and humans needs to be explored extensively. However, we have carried out a few studies earlier and have looked for the presence of phages in different tissues of the mouse model. The phages could be isolated from liver, spleen, peripheral blood, kidney, *etc.* beyond 72 h in good numbers (unpublished information). We have also raised antibody against phages in rabbit model to check the cross-antigenicity amongst the different phages specific for a particular bacteria (unpublished information). The author has mentioned about virulence factors harboured by the phages, which is quite natural because almost all the bacterial toxins have been found to be coded by the bacteriophages. The gene transfers including toxin genes are naturally occurring at very high frequency in the nature. In fact, we consume a variety of phages in huge amounts through food and water every day. Bacteriophage therapy is simply to exploit the natural process of bacterial lysis by phages if the bacteria are pathogenic. Designer phages (artificial phages) with lytic activity but without toxin genes might be the answer. The sole objective of our study was to see the efficacy of bacteriophages in chronic infections, *e.g.* chronic osteomyelitis which is difficult to treat with antibiotics. We found that high dosages of phages did not cause visible clinical morbidity and mortality[2]. As mentioned, a total of 44 phages isolated from different sources and sites were tested for their lytic activity on 100 clinical isolates of *Staphylococcus aureus*. We tested most virulent seven phages having highest spectrum of lytic activity but unique for each of them, on the 100 clinical *S. aureus* isolates. These seven phages were subjected to electron microscopy and also typing by molecular methods (RFLP, RAPD and also ERIC PCR at low melting temperature). Although electron microscopy could not differentiate each of the seven phages on morphological characters, but molecular methods showed that none of these seven phages had similar genotypic pattern. Therefore, we used cocktail of seven bacteriophages at the concentration of 10^{12} pfu/ml. However, we agree that detailed characterization (phenotypic, genotyic and functional) needs to be carried out. Detailed studies with regard to kinetics of phages which should include the entry of the phages into human cells and quantification of dosage (number and amount both) effective in clinical conditions need to be carried out. Group A rabbits were scarified to have the evidence of establishment of infection by means of culture, histopathology and radiological means at different time intervals, and group B rabbits were kept untreated up to six weeks duration and treatment response was observed up to eight weeks. These rabbits were kept beyond two months with one rabbit having sequel of infection as arthritic changes persisted even after cure of the infection. It was not possible to keep rabbits in pain for such a long time without intervention. Further, as per definition of chronic osteomyelitis, we considered six week period as it did not heal by itself.

We are conducting studies on bacteriophages against many of the clinically important bacteria. However, there is a need to facilitate the research in this upcoming area of bacteriophage therapy so that new therapeutic alternatives could be found.

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