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In vivo activity of co-trimoxazole combined with colistin against *Acinetobacter baumannii* producing OXA-23 in a *Galleria mellonella* model

By

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Abstract

Objectives. *Acinetobacter baumannii* is a critical nosocomial pathogen. *A. baumannii* infections have become a grave challenge due to their ability to develop resistance to different antimicrobial agents. The current study aimed to evaluate the potential synergism and bactericidal activity of a combination of colistin and cotrimoxazole against carbapenem-resistant *A. baumannii* (CRAB) in a *Galleria mellonella* model. **Methods.** Four clinical *A. baumannii* isolates were biochemically and molecularly identified. Their antimicrobial susceptibility levels were established and the molecular characterization of the carbapenemase-encoding genes was performed. The synergism and bactericidal effect of the colistin/cotrimoxazole combination was assessed using the checkerboard assay and time–kill experiments. An in vivo evaluation of the activity of the combination was performed using the *Galleria mellonella* model. **Results.** A fractional inhibitory concentration index (FICI) of 0.5 was found for all strains, indicating that the colistin/cotrimoxazole combination exhibited powerful synergistic activity. The combination displayed both synergistic and bactericidal activity at sub-breakpoint concentrations for all strains. Cotrimoxazole monotherapy showed the least protective activity in the *G. mellonella* model. The survival rate ranged from 66.7–79.2 % at 24 h and was 29.2–60.4 % at 96 h for the tested isolates. Colistin monotherapy performed better than cotrimoxazole monotherapy; the *G. mellonella* survival rate ranged from 77.1–97.9 %, at 24 h and from 64.5–72. % at 96 h. The colistin/cotrimoxazole combination improved *G. mellonella*'s survival rate at 96 h remarkably in comparison to colistin or cotrimoxazole monotherapy. **Conclusions.** Finally, the combination of colistin and cotrimoxazole appears to be a promising therapeutic option for the management of CRAB-associated infections. It is essential to assess the clinical application and the dose–response relationships of combinations such as colistin plus cotrimoxazole.