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The Impact of Carbapenem-Sparing Interventions on the Evolution of Resistance in Pseudomonas aeruginosa in the USA

Author(s)

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1. Jeffrey Townsend, PhD (Role: Co-Author)
2. Abhishek Pandey, PhD. (Role: Co-Author)
3. Amber B. Tang, B.S. (Role: Co-Author)
4. Yiziying Chen, Master's in Biostatistics (Role: Presenting Author)
5. Eric M. Foster (Role: Co-Author)
6. Dilip Nathwani, MB (Role: Co-Author)
7. Sanjay Merchant, PhD (Role: Co-Author)
8. Eric Sarpong, PhD (Role: Co-Author)
9. Meagan C. Fitzpatrick, PhD (Role: Co-Author)
10. Alison Galvani, PhD (Role: Co-Author)

Abstract Text

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Background

Carbapenem resistance (CR) among *Pseudomonas aeruginosa* infections is a pressing public health concern in the United States. Therapeutic alternatives for CR infections are limited. Implementation of a key antimicrobial stewardship intervention such as formulary restriction, which is one of the many stewardship strategies, can minimize selection pressure for resistance. We evaluate the consequent impact of this intervention on bacteremia patients infected with *P. aeruginosa* in the US.

Methods

We developed a population-genetic model of selection for CR. Increases in CR were modeled as a consequence of inappropriate prescription. Inappropriate empiric therapy, i.e. antibiotic, did not cover the organism or appropriate coverage not started within 2-days, was estimated from a published study and future projections were based on historical resistance frequencies and yearly carbapenem consumption associated with *P. aeruginosa* bacteremia. We projected peak *P. aeruginosa* CR frequencies and cumulative CR cases from 2020–2040. We compared scenarios without carbapenem restriction to usage decreased linearly by an amount demonstrated in a previous hospital study (51.7%) over 5 years of implementation starting in 2020 (early implementation) or 2030 (late implementation).

Results

Early and late implementation of carbapenem restriction leads to CR frequencies that ascend as high as 42% and 74% respectively eventually mitigating those frequencies by bringing them down to 23% and 37% respectively. By 2045, early carbapenem restriction

could prevent 29,600 CR cases of *P. aeruginosa* bacteremia, compared to 15,200 prevented by late implementation.

Conclusion

We demonstrate that early restriction of carbapenem consumption could markedly reduce future CR in *P. aeruginosa* bacteremia patients. Implementing early carbapenem restriction should be expected to result in a lower ultimate frequency of CR and a lower number of cumulative cases of resistant infections, thereby decreasing the overall burden of CR cases that will be encountered in the future.

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