What does antibiotic history tell you about antibiotic resistance? – the relationship between prior macrolide and fluoroquinolone use and resistance in S. pneumoniae

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Abstract

Background: Prior exposure to antibiotics (ABs) is an important predictor of resistance (AR) for many pathogens. We explored the relationship between the timing and duration of prior AB use and resistance in pneumococci.

Methods: TIBDN has performed population-based surveillance for invasive pneumococcal disease (IPD) in Toronto/Peel since 1995, and for surveillance from SPN from spumolBAC since 2002. AB histories are obtained by chart review, patient and MD interview.

Results: Between 2000-2010, TIBDN identified 4440 episodes of IPD, and collected 3875 sputum/BAL isolates. 7388 (68%) of these were adults, 907 (12%) were newborns. 323 (4.5%) were macrolide non-susceptible and 7198 isolates were available. 185 (2.5%) were R (MIC>4) to cipro (FQR), 137 (2.2) to levofloxacin (LVT), 1444 (20%) to erythromycin (ERY). FQR is associated with respiratory isolates vs IPD (P<.001), nosocomial (P<.002) & LTC acquired cases (P>.001), older age (P<.001). The relationship between the category of prior use of antibiotics and pneumococcal resistance to FQs and macrolides (MLs) is shown below. Relationships were independent of other FQR risk factors.

Results cont.

Patients who were failing therapy with macrolides or fluoroquinolones were much more likely than other patients to have pneumococcal isolates resistant to the class of antibiotics they were failing (Figure 3). Resistance rates were substantial even in patients who had received only one or two doses of the antibiotic (i.e. <24 hours of therapy).

Conclusion: Antibiotic histories may be more useful if they include a longer period of time than 3 months.

Introduction

Antibiotic use is the primary cause of antimicrobial resistance and individual antibiotic use has shown to increase the risk of resistance to antibiotics in subsequent infections.

We have previously shown that, in patients presenting with invasive pneumococcal disease, use of fluoroquinolones and macrolides in the previous three months is associated with substantial increases in the rate of resistance to fluoroquinolones and macrolides in the infecting isolate (VanderKolk, CID 2005).

In this study, we asked how the timing of prior fluoroquinolone and macrolide therapy affected the risk of resistance in infecting pneumococci.

Methods

The Toronto Invasive Bacterial Diseases Network (TIBDN) has performed population-based surveillance for invasive pneumococcal disease in metropolitan Toronto and Peel region (pop. 4M) since January 1, 1995. From 2002 to 2009, all respiratory site isolates from hospital laboratories were also collected. Broth microdilution antimicrobial susceptibility tests were performed according to CLSI standards.

Demographic and clinical data are collected from review of health records and interviews with patients and attending physicians. Details of previous antibiotic treatment have been collected since 2000. Patients are asked if they had received any antibiotics in the previous 3 months and if they had received treatment for the current infection prior to the diagnostic specimen that was positive for S. pneumoniae.

Definitions

Failure: patients currently on antimicrobials or within 48 hours of completion of a course of antibiotics when the culture yielding pneumococci was obtained.

Relapse: patients who were treated for the current infection and completed a course of antibiotics from 3-14 days before the culture yielding pneumococci was obtained.

Prior therapy: patient was treated for an unrelated episode of infection in the previous three months

Antibiotic histories were available for 5806 (70%) of episodes of disease: 1067 patients (18%) had been exposed to fluoroquinolones in the previous three months, while 762 patients (13%) had been exposed to macrolide antibiotics. Patients exposed to macrolide antibiotics were more likely to be failing therapy at presentation (Figure 2).

Fluoroquinolone and macrolide resistance in patients with previous exposure to the same class of antibiotics, by time from last dose of prior antibiotics to pneumococcal infection

The time course of return to baseline resistance after exposure to antibiotics varied depending on the antibiotic. At 3 months after the last dose of a fluoroquinolon e, patients were still significantly more likely to have a fluoroquinolone resistant isolate than other patients. (Rates of fluoroquinolone resistance are too low to identify whether different fluoroquinolone antibiotics are different). At two months after clarithromycin therapy, resistance rates were close to baseline (22% vs. 17% for patients never exposed). In contrast, resistance rates after azithromycin therapy remained significantly elevated at 3 months (Figure 4).

Conclusions

• Recent exposure to antibiotics in the same class is an important predictor of macrolide and fluoroquinolone resistance in pneumococci.

• Pneumococci isolated from patients who are failing therapy with an oral macrolide or fluoroquinolone when they are admitted to the hospital are likely to be resistant to the class of antibiotics that they are failing.

• This is true even if they have taken only 1 or 2 doses of the antibiotic.

• Antibiotic histories may be more useful if they include a longer period of time than 3 months.

• At 2 months after last exposure to clarithromycin, macrolide resistance has returned to close to baseline.

• At 3 months, resistance to fluoroquinolones persists.

Acknowledgements:
We are grateful to the infection control practitioners, microbiology technologists, public health staff and our tireless TIBDN staff for their ongoing contributions to this surveillance. This work has been supported in part by an unrestricted grant from Bayer Healthcare AG.

Figure 1. Fluoroquinolone and erythromycin resistance in patients with and without recent exposure to antibiotics of the same class, TIBDN, 2000-2009.

Figure 2. Differences in the distribution of prior use of fluoroquinolones and macrolides in patients presenting with pneumococcal infection, TIBDN, 2000-2009

Figure 3. Fluoroquinolone and macrolide resistance in pneumococcal isolates from patients with different types of exposure to the same class of antibiotics.

Figure 4. Fluoroquinolone and macrolide resistance in patients with previous exposure to the same class of antibiotics, by time from last dose of prior antibiotics to pneumococcal infection.