

The Association between Prior Antibiotic Use and Subsequent Risk of Infectious Disease: A Systematic Review

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Abstract : Introduction: The microbiota lining epithelial surfaces is thought to play an important role in many human physiological functions including defense against pathogens and modulation of immune response. The microbiota is susceptible to disruption from external influences such as exposure to antibiotic medication. It is thought that antibiotic-induced disruption of the microbiota could predispose to pathogen overgrowth and invasion. We hypothesized that antibiotic use would be associated with increased risk of future infections. We carried out a systematic review of evidence of associations between antibiotic use and subsequent risk of community-acquired infections. Methods: We conducted a review of the literature for observational studies assessing the association between antibiotic use and subsequent community-acquired infection. Eligible studies were published before April 29th, 2016. We searched MEDLINE, EMBASE, and Web of Science and screened titles and abstracts using a predefined search strategy. Infections caused by *Clostridium difficile*, drug-resistant organisms and fungal organisms were excluded as their association with prior antibiotic use has been examined in previous systematic reviews. Results: Eighteen out of 21,518 retrieved studies met the inclusion criteria. The association between past antibiotic exposure and subsequent increased risk of infection was reported in 16 studies, including one study on *Campylobacter jejuni* infection (Odds Ratio [OR] 3.3), two on typhoid fever (ORs 5.7 and 12.2), one on *Staphylococcus aureus* skin infection (OR 2.9), one on invasive pneumococcal disease (OR 1.57), one on recurrent furunculosis (OR 16.6), one on recurrent boils and abscesses (Risk ratio 1.4), one on upper respiratory tract infection (OR 2.3) and urinary tract infection (OR 1.1), one on invasive *Haemophilus influenzae* type b (Hib) infection (OR 1.51), one on infectious mastitis (OR 5.38), one on meningitis (OR 2.04) and five on *Salmonella enteric* infection (ORs 1.4, 1.59, 1.9, 2.3 and 3.8). The effect size in three studies on *Salmonella enteric* infection was of marginal statistical significance. A further two studies on *Salmonella* infection did not demonstrate a statistically significant association between prior antibiotic exposure and subsequent infection. Conclusion: We have found an association between past antibiotic exposure and subsequent risk of a diverse range of infections in the community setting. Our findings provide evidence to support the hypothesis that prior antibiotic usage may predispose to future infection risk, possibly through antibiotic-induced alteration of the microbiota. The findings add further weight to calls to minimize inappropriate antibiotic prescriptions.

Keywords : antibiotic, infection, risk factor, side effect

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