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Impact of Antibiotic Use in Patient Colonization with Multidrug-resistant Organisms

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Abstract

There are some variables associated with multidrug-resistant organisms (MDRO) establishment success in healthcare settings and infection outcomes such as long-time use of antibiotics, immunosuppression, medical devices, loss of skin integrity, time of permanence of patients in ICUs and microorganism virulence. Our aim was to review the impact of antimicrobial use in patients' colonization with MDRO. In fact, gene encoding resistance can be detected even in commensal microbiota. Some analysis using DNA sequencing to evaluate microbiomes has confirmed the impact of antibiotic use in microbiota leading to the emergence of potential pathogens. Conversely, the decreased use of a specific antibiotic can lead to loss of resistance.

Keywords: Bacterial drug resistance; Normal microbiota; Antimicrobial use; Inpatients

Background

Infections with multidrug-resistant microorganisms have increased significantly in recent years. Resistant microorganisms such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin resistant Enterococci (VRE), and multidrug-resistant Gram-negative bacteria are notable causes of health care-associated infections (HCAIs). The infected or colonised patients are the main source of multidrug-resistant microorganisms in healthcare settings. However, such an environment can be a reservoir and a source of dissemination, with even healthcare staff becoming carriers. In fact, there is a specific healthcare-associated ecosystem [1]. In this review we summarized and discussed the impact of antibiotic use in healthcare-associated ecosystems.

Antibiotic use and MDRO Colonization

In every context, the use of antibiotics impacts a microbial ecosystem and select resistant strains. The antibiotics eliminate or reduce the growth of pathogens as well as beneficial microbes, disrupting microbiota balance and reducing colonization resistance. This is an important step for patient colonization by MDRO in hospital settings. There are some variables associated with MDRO establishment success in healthcare settings and infection outcomes such as long-time use of antibiotics, immunosuppression, medical devices, loss of skin integrity, time of permanence of patients in ICUs and microorganism virulence [2,3].

Generally, patients are screened at units of major risk of infection acquisition such as Intensive Care Units (ICUs), but anatomic sites evaluated may differ among settings. The most common areas evaluated are anterior nares and rectum. Although, other areas may hide MDRO (such as groins). Furthermore, as routine surveillance usually targets inpatient with severe infections, it does not take into account patients discharged with colonization by MDRO, hospital environment contamination and community-acquired infections [4].

In an ecological evaluation of antibiotic use in long-term care facilities (LTCFs), a positive association of colonization with MDROs and antibiotic use was verified. Colonization status was evaluated by groin and perirectal swabs. An association of VRE acquisition with use of multiple antimicrobial classes such as aminoglycosides, cephalosporin and glycopeptides was also verified. It must be noted that a single antibiotic could be related to colonization with several MDRO species. Aminoglycosides increased the risk of MDRO acquisition; for example: VRE, *Acinetobacter bau-mannii, Escherichia coli, Proteus mirabilis*, and *Pseudomonas aeruginosa* (unadjusted HR>2 and P<0.05). Colonization with VRE, MRSA and *E. coli* in groins and perineum increased the risks of catheter-associated urinary tract infection [1]. Similarly, polymicrobial infection was an important factor to sepsis outcome among patients evaluated from 2008 to 2014 in a retrospective observational study [5].

Clindamycin and ciprofloxacin promoted changes to the Gram-negative component of the saliva and faecal human microbiota in an evaluation of the effects of the administration of these antibiotics. No change was registered in *E. coli* population immediately after ciprofloxacin administration, but within one-month *E. coli* levels significantly rose, although resistance to ciprofloxacin was low [6].

Some analysis using DNA sequencing to evaluate microbiome has confirmed the impact of antibiotic use in microbiota. It has highlighted dysbiosis with great emergence of potential pathogens [7-9]. In a microbiome evaluation by DNA sequencing before and after antibiotic use it was suggested that this exposition could improve the emergence of multi-resistant opportunistic pathogens, mainly in patients with reduced microbial diversity [7]. Similarly, the sequencing of intestinal microbiomes of Swedish students after exchange programs in other continent, where MDRO prevalence was high, showed increased acquisition of encoded genes resistant to widely used antibiotics of widely use [8].

Another study (with similar methods) reinforced these trends regarding antibiotic impact on normal microbiota, registering a raise of Enterobacteriaceae and rare resistance genes that were not detected before treatment. These genes encoding resistance were detected after seven days of anti-biotic administration [9]. Genes encoding resistance can be detected even in commensal microbiota. In fact, human microbiota is a great reservoir for antibiotic resistant genes and MDRO [10,11].

In a classical example, the use of oral vancomycin in gut microbiota of patients for two weeks altered the microbiota structure even 22 weeks after treatment and the microbial richness was decreased. The same study also verified the impact of vancomycin use in intestinal colonization by VRE in model mice. The resistance against VRE colonization was registered in mice untreated with vancomycin while mice treated with this antibiotic were highly susceptible to VRE colonization [12].

On the contrary, the decreased use of a specific antibiotic can lead to loss of resistance. A 14-year evaluation of trends in antibiotic susceptibility in *Staphylococcus aureus* in Boston revealed a decline in MRSA averages. It could be related to the declined use of some antibiotics such as oxacillin and penicillin since 2000 [13].

Our gut is a probable reservoir of the microbial resistance related genes including the extended spectrum beta-lactamase (ESBL)-producing strains. Several studies have evaluated antimicrobial resistant commensal *E. coli* isolated from not only inpatients, but also healthy children and adults in the community [14]. In a large data evaluation from a multicentre observational cohort in US, the prevalence of carbapenem-resistant Enterobacteriaceae (CRE) among patients admitted from the community with UTI, sepsis or pneumonia, more than 17% had infection caused by Enterobacteriaceae, and approximately 3% were CRE. The infections with CRE were associated with a four-fold increased risk of receiving inappropriate empiric treatment [15].

Considering all alterations in gut microbiota after antimicrobial use, some measures could be adopted to minimize the impact, such as antibiotic rotation to reduce long exposure to a given drug, and strategies to reconstitute microbiota such as probiotic use and faecal transplantation after long therapy with antibiotics [12,13].

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