Antibiotic Resistance, Part 2: Gram-negative Pathogens

Catherine M. Oliphant, PharmD, and Kathryn Eroschenko, PharmD

ABSTRACT

Antimicrobial resistance is rapidly increasing among gram-negative bacteria. Gram-negative bacteria are common causes of community- and nosocomial-acquired infections. Common mechanisms of resistance in gram-negative pathogens include altered target sites, β-lactamase production, decreased antibiotic penetration, and efflux pumps. The mechanisms of resistance and treatment options for *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* will be discussed in this article. Antimicrobial resistance presents challenges to clinicians in choosing appropriate and effective regimens. Prudent use of antimicrobial agents may reduce the emergence of further resistance in these important gram-negative bacteria.

Keywords: antibiotic, antimicrobial, gram negative, resistance, treatment

© *2015 Elsevier, Inc. All rights reserved.*

The widespread use of antibiotics has resulted in the emergence of multidrug-resistant bacterial pathogens. The prevalence and rate of antimicrobial resistance among important gram-negative pathogens are increasing. β-lactamase production is a common resistance mechanism in gram-negative bacteria. Other mechanisms of resistance include decreased antimicrobial agent penetration, altered target sites, and efflux pumps. Because of the increased frequency of resistant gram-negative pathogens, the selection of appropriate antimicrobial therapy is becoming more challenging to clinicians.

Gram-negative bacteria are commonly implicated in both community- and nosocomial-acquired infections. *Haemophilus influenzae* and *Moraxella catarrhalis* both produce β-lactamases and are resistant to commonly used β-lactam antibiotics. Recommended antimicrobial therapy for *Neisseria gonorrhoeae* is now limited to a single regimen of combination therapy. Nosocomial gram-negative pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* are also becoming increasingly resistant to commonly used antimicrobial agents.

Important mechanisms of resistance are emerging and are severely limiting antimicrobial choices for patients with these resistant gram-negative pathogens. Extended-spectrum β-lactamases and carbapenemases have emerged and have negatively impacted morbidity and mortality. Multidrug-resistant gram-negative pathogens are increasingly encountered in nosocomial settings. Antimicrobial resistance among gram-negative pathogens has developed to all currently available antimicrobial agents. Knowledge of resistance mechanisms, susceptibility trends, and gram-negative pathogen resistance is imperative for appropriate prescribing of antimicrobial therapy.

ANTIBIOTIC MECHANISM OF ACTION

Antimicrobial mechanisms of action were briefly reviewed in part 1 of the antibiotic resistance article (see table 1 in the Antibiotic Resistance, Part 1: Gram-positive Pathogens article).

GRAM-NEGATIVE RESISTANCE MECHANISMS

Mechanisms of resistance were reviewed in the Antibiotic Resistance, Part 1: Gram-positive

Readers who are members of the American Association of Nurse Practitioners (AANP) may receive 1.0 continuing education contact hours and 0.8 pharmacology hours, approved by AANP, by reading this article and competing the online posttest and evaluation at https://cecenter.aanp.org/program?area=JNP.

Table 1. Mechanisms of resistance by organism and antibiotics to avoid[2,6,12,19,22,24,26,30]

Bacteria	Mechanisms of Resistance	Antibiotics to Generally Avoid
Enterobacteriaceae (ie, *E coli*, *Klebsiella* spp, *Enterobacter* spp)	ESBL producing	Penicillins, 1st-/2nd-/3rd-/4th-generation cephalosporins, aztreonam, TMP-SMX, fluoroquinolones, aminoglycosides
	AmpC producing	Penicillins, 1st-/2nd-/3rd-generation cephalosporins, aztreonam, TMP-SMX, fluoroquinolones, aminoglycosides
	Carbapenemase producing	Carbapenems, penicillins, 1st-/2nd-/3rd-/4th-generation cephalosporins, aztreonam, TMP-SMX, fluoroquinolones, aminoglycosides
	Mutations in DNA gyrase/ topoisomerase	Fluoroquinolones
P aeruginosa	ESBL producing	Penicillins, 3rd-/4th-generation cephalosporins, aztreonam, fluoroquinolones, aminoglycosides
	AmpC producing	Penicillins, 3rd-generation cephalosporins, aztreonam, fluoroquinolones, aminoglycosides
	Carbapenemase producing	Carbapenems, penicillins, 3rd-/4th-generation cephalosporins, aztreonam, fluoroquinolones, aminoglycosides
	Efflux pumps	β-lactams
	Alteration of outer membrane porin channels	β-lactams
	Mutations in DNA gyrase/ topoisomerase	Fluoroquinolones
H influenzae and *M catarrhalis*	β-lactamase production	Non–β-lactamase containing penicillins (ie, ampicillin, amoxicillin)
N gonorrhoeae	β-lactamase production	Penicillins
	Plasmid and chromosomal-mediated	Cephalosporins[a]
	Target site alterations in gyrA and parC	Fluoroquinolones

[a] Exception is ceftriaxone (and in certain situations, cefixime).

Pathogens article. In addition, resistance mechanisms will be discussed further within each featured bacterial section and are further summarized in Table 1 (which also identifies antibiotics to avoid with each resistance mechanism).

RISK FACTORS

Table 2 provides a list of risk factors.

GRAM-NEGATIVE PATHOGENS

Infections secondary to gram-negative pathogens occur most commonly in the urinary, gastrointestinal, and respiratory tract systems; however, infections may occur in any body system. Infections range from mild, community-acquired to more severe infections occurring in institutionalized patients (hospital or long-term care facilities) or in those with recent health care exposure. Table 3 identifies therapeutic options for resistant gram-negative pathogens.

Escherichia coli

Escherichia coli are a member of the family Enterobacteriaceae, a group of gram-negative bacteria often referred to as enterics because they reside in the gastrointestinal tract. Pathogenic strains differ from nonpathogenic or commensal strains in that they produce virulence factors. *E coli* is responsible for a wide range of diseases including cystitis, pyelonephritis, intra-abdominal infections, bacteremia, and sepsis. *E coli* is a common health care–acquired or nosocomial pathogen. However, there is an increasing prevalence of extended-spectrum β-lactamase (ESBL)-producing and quinolone-resistant *E coli* in

Download English Version:

https://daneshyari.com/en/article/2663424

Download Persian Version:

https://daneshyari.com/article/2663424

Daneshyari.com