
Antibiotics in Older Adults

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Antibiotics are frequently prescribed in the older person, the dosification needs special care, since the pharmacokinetic parameters changes with aging and the side effects can be different in the older person. The creatinine clearance changes and we must modify the way we prescribe such antibiotics to the elderly, calculating. The variety of antibiotics now available led us to consider this paper in which we have presented the antimicrobial agents that can be considered in the treatment of the older person. We present several groups: the penicillins, cephalosporins, monobactams,

carbapenems and betalactamase inhibitors or the great betalactam group. Other trimetoprim-sulfamethoxazole, the newer macrolides (azithromycin and clarithromycin) as well as the aminoglycosides, vancomycin, clindamycin, metroridazole. The indications and contraindications are presented and reviewed.

Key words: Antibiotics, Aging, Pharmacokinetics, Betalactamic antibodies, Quinolones, Aminoglycosides, Macrolides

Antibiotic use in the older people is important because of the serious consequences of mistreated infections in this particular group. The demographics are changing in the beginning of the 20th century, for the first time in the United States and Puerto Rico, people older than 60 years outnumbered children aged 14 years and younger. By the year 2050, the number of people living in the USA older than 65 years of age will double to reach nearly 80 million (1). In spite of the many advances that have occurred in the prevention, diagnosis, and treatment of infectious diseases, infections still cause 30% of deaths in the elderly and are the most frequent cause of hospitalization in this population.

Managing infections in the elderly is a challenge. Diagnosis of infections can be problematic, because elderly patients frequently lack classic signs and symptoms of infection such as fever and leukocytosis. When infection occurs, the elderly often present with unusual symptoms such as poor appetite, nausea, vomiting, and changes in

mental status. Physical findings and laboratory results are often difficult to interpret as many of the elderly have baseline pulmonary and urinary tract abnormalities (e.g., rales, bacteriuria, pyuria). Therapy is problematic because of the increased potential for toxicity of antimicrobial agents in the elderly.

The approach to antibiotic use in elderly patients is a unique and challenging problem. Older patients often suffer more serious complications of infection. Approximately one third of persons older than age 80 and a higher percentage of elderly disabled persons reside in long-term care facilities; bacterial flora in such institutions remain intermediate between the relatively antibiotic resistant hospital flora and the flora typical of community-acquired infections. The rapid emergence of resistant microorganisms and the development of new classes of antimicrobial agents present potential diagnostic dilemmas and therapeutic challenges to treating clinicians (2).

Although less than 10% of the entire population older than the age of 65 years resides in nursing homes the challenges of managing infections in this population are great (3).

Special considerations in the older adult. Infectious diseases in older persons compared with younger individuals are relatively more frequent and severe (4). The elderly also suffer greater complications of these

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infections, which eventually contribute to a higher mortality. Infections in aging adults that are associated with increased morbidity include urinary tract infection, which often is associated with bacteremia and persistence or recurrence of infection, pneumonia, often complicated by bacteremia, extrapulmonary sites of infection, delayed resolution, and pulmonary function compromise; tuberculosis infection and disease, which is prone to dissemination and consequent development of extrapulmonary and miliary forms of this disease; and intraabdominal infections (i.e., cholecystitis, appendicitis, and diverticulitis), which are more likely to progress to abscess formation, perforation, and gangrene (5-6).

The higher death rates in older patients are the result of many factors, including diminished host defenses, presence of underlying diseases (e.g., diabetes mellitus, malignancy, cerebrovascular accidents, and alcoholism), nosocomial infections, and complications from diagnostic and therapeutic procedures, and delays in diagnosis and treatment as well as adverse reactions to antibiotics. Rapid diagnosis and prompt institution of appropriate antibiotics are essential for improved survival from infectious diseases in this population.

Pharmacokinetics and pharmacodynamics. The selection and dosing of antibiotics in the older person necessitates a clear comprehension of the physiologic changes (e.g., the decline in renal function and consequently the clearance of these agents) and the higher frequency of adverse drug reactions commonly encountered in this vulnerable population (7-8). The relationship of age and antibiotic pharmacodynamics and pharmacokinetics is discussed (9). Although it is unclear whether drug absorption, hepatic metabolism, and drug response vary significantly with old age, it is evident that drug clearance from the body, particularly through renal mechanisms, is altered in aging persons.

Oral absorption. With aging there is a reduction in the rate of gastric acid output with a concomitant rise in gastric pH. There is a reduced rate of gastric emptying, a decline in blood flow to the small intestine and an increased incidence of duodenal diverticula (10). In spite of these changes, orally administered drugs are generally absorbed well with only a modest slowing of absorption rate (11). Information is lacking on how drug absorption may be altered in the elderly who are receiving histamine receptor 2 (H-2) blockers or proton pump inhibitors or in those with a gastrostomy or jejunostomy feeding tube.

Compliance. Older patients have been perceived as being noncompliant drug regimens. While there are no good data to support this perception (12), there are many reasons for noncompliance in this population (13). Compliance can be improved by improving communication

between patient and caregiver (e.g., providing the patient with written as well as oral instructions), relying on assistance from relatives who can help administer medications, and by keeping the regimen as simple as possible (e.g., single daily doses) (14-16).

Side effects. Side effects from drugs are more common in the older than in a younger population. Some of this excess toxicity is related to decreased renal function and related to the greater potential for drug-drug interactions.

Susceptibility of the end organ to drugs. For example, the older person have fewer functional nephrons and cochlear hair cells than younger individuals. Therefore, deafness or renal insufficiency from aminoglycosides may be observed at a much earlier point during therapy than in a younger individual.

Cost efficiency. The cost of antimicrobial therapy for the older person is an important consideration in the overall management of infections. Although the acquisition costs of antibiotics contribute significantly to the overall expense of antimicrobial therapy, other costs must be taken into account when making valid cost comparisons among different drugs (17). Examples of other costs are preparation and administration costs (drug reconstitution, intravenous administration material, pharmacy labor) and costs of monitoring of drug levels and adverse reactions. An often-overlooked cost, which should be considered in the overall expense of antimicrobial therapy, is the cost of additional medical care required because of adverse reactions to antibiotics.

Renal function. Age related decline in renal function predominately underlies the decreased drug clearance (7). Because several antibiotics are excreted largely of reduced muscle mass with age, levels may be necessary for certain drugs in older patients. As a result of reduced muscle mass with age, the creatinine clearance is a more accurate estimate of renal function than the serum creatinine (18).

The number of intact nephrons and hence renal function declines with normal aging (10). In addition, chronic illnesses common in the older person such as diabetes mellitus, congestive heart failure, and hypertension contribute to a decrease in renal function. The Cockcroft-Gault equation, based on age, body weight, and a single serum creatinine value (Cr), closely correlates with creatinine clearance (CL_{Cr}) measured by a 24-hour urine collection (10).

$$CL_{Cr} = \frac{[140 - \text{age (yr)}] \times \text{weight (kg)}}{\text{Cr (mg/dL)} \times 72} \times 0.85 \text{ in women}$$

The major drawback to using this equation is that it requires using the patient's ideal body weight. This may be difficult to determine especially in morbidly obese or edematous patients. Furthermore, the serum creatinine

value may be spuriously low in the elderly because of malnutrition and decreased muscle mass. Often creatinine values within “normal” limits indicate varying degrees of renal insufficiency. For example a serum creatinine of 1.0 in a frail 85-year-old woman weighing 86 pounds may represent a creatinine clearance as low as 25 mL/min.

Drug-drug interactions. Older patients frequently are taking a number of medications such as anticoagulants, antiarrhythmics, antihypertensives, antidepressants, and antiseizure agents. Certain antibiotics are associated with an increased side effect profile in older patients, including aminoglycosides (renal and auditory nerve dysfunction), β -lactam antibiotic (seizures, skin rash), macrolides (nauseas, abdominal cramps), vancomycin (renal dysfunction), and quinolones (seizures, hallucination) (8). Drug interactions in the older person are increased as a consequence of greater numbers of medications taken concomitantly than as a consequence of age per se (19).

Clinical aspects of infections. The most common infections in the older person involve the respiratory, urinary, and gastrointestinal systems and the skin and soft tissues (20-21). The bacterial causes of infections in the older are somewhat varied. Gram-negative bacilli (aerobic or facultative anaerobic) generally are implicated in infections in this population. Mixed infections, as a result of polymicrobial isolates including anaerobic bacteria, often are encountered in older person. The diagnostic precision is crucial in the elderly patient, and it is more difficult to achieve (18). Diagnostic specimens that require patient cooperation (e.g., sputum samples; body fluids, including pleural fluid or cerebrospinal fluid; and tissue samples, including liver biopsy, may be difficult to obtain in the frail, debilitated, cognitively impaired, or severely ill patient.

Clinical manifestations of infection in aging patients may be unusual, nonspecific, or absent. Patients may present with weakness, malaise, confusion, and loss of appetite, falls, or urinary incontinence as the initial manifestation of infection (18). Fever, a hallmark of infection, can be blunted or absent in infected older patients (4,22). Although body temperature elevation (hyperthermia or fever) in elderly persons is an indicator for the presence of serious infection, decreased body temperature (hypothermia) is a more ominous sign.

Principles of Antibiotic Therapy

When selecting antibiotics for a specific infection in the older person, the unique problems and issues mentioned earlier must be taken into consideration. Because of the high risk of complications and death resulting from infections, the diverse infectious causes,

and the difficulty in obtaining diagnostic - specimens, initial empiric antibiotic therapy selection for specific infections is a valid and practical option (23).

Antibiotic Groups and Their Use

Table 1. Empiric Antibiotic Therapy for Urinary Tract Infection (UTI) in the Elderly

Type of UTI	Organism	Parenteral Antibiotics
Uncomplicated	<i>E. coli</i> , Proteus spp., Klebsiella spp.	Quinolones Trimetoprim-sulfamethoxazole; oral cephalosporins
Complicated	As above plus Enterobacter spp., <i>P. aeruginosa</i> , <i>Serratia marcescens</i>	Quinolones, Third-fourth generation cephalosporins; Aztreonam; piperacillin-tazobactam; ticarcillin-clavulanate; \pm aminoglycosides
Chronic catheter	Same as complicated UTI plus Enterococcus spp.	As above but consider adding ampicillin (or vancomycin)

Table 2. Empiric Antibiotic Therapy for Skin and Soft Tissue Infections

Infection	Organism	Parenteral Antibiotics
Simple cellulitis Nonimmunocompromised	<i>S. pyogenes</i> , <i>S. aureus</i>	Nafcillin or oxacillin; \pm penicillin; first generation cephalosporin (cefazolin) (cephalexin)
Immunocompromised	As above plus gram-negative bacilli, including <i>P. aeruginosa</i>	As above, plus aztreonam; quinolones; cefepime, ceftazidime piperacillin-tazobactam \pm aminoglycosides
Diabetic lesions	As above plus gram-negative bacilli, including <i>P. aeruginosa</i>	Piperacillin-tazobactam, ticarcillin-clavulanate; ampicillin-sulbactam; ertapenem, cefoxitin; cefotetan; clindamycin (or metronidazole) + third-fourth generation cephalosporins (or quinolones, aztreonam)
Pressure ulcer: Early, superficial	Streptococci, staphylococci, <i>E. coli</i>	Second- or third-generation cephalosporins
Chronic, deep	As above plus other gram-negative bacilli, anaerobes	Same regimen as diabetic lesions, must cover anaerobes. Quinolone plus clindamycin or metronidazole

Beta-lactams. (β -lactams, which include the penicillins, cephalosporins, carbapenems, and monobactams as well as the (β -Lactams/ β -Lactamases inhibitor combination agents, are especially useful in treating infections in older patients because of their favorable pharmacokinetics, relative safety, and broad spectrum of activity (24).

Table 3. Empiric Therapy for Lower Respiratory Tract Infections in the Aging Person

Infection	Organism	Parenteral Antibiotics
Community acquired pneumonia	<i>S. pneumoniae</i> , <i>H. influenzae</i>	New fluoroquinolones or Amoxicillin-clavulanate or ampicillin-sulbactam ± macrolide or third generation cephalosporin
	Atypical agents- Legionella, Mycoplasma, Chlamidia	
Hospital-acquired	<i>S. aureus</i> (MSSA)	Nafcillin/oxacillin/cefazolin Third of fourth generation cephalosporin;
	Gram negative bacilli	aztreonam; quinolone ± aminoglycoside
Nursing home-acquired	Gram-negative bacilli, <i>S. aureus</i> , <i>S. pneumoniae</i> , anaerobes	Third of fourth generation cephalosporins ± clindamycin; ticarcillin-clavulanate; piperacillin-tazobactam; imipinem; meropenem ± aminoglycoside; quinolone; Add vancomycin for methicillin-resistance
	<i>S. pneumoniae</i> , gram-negative bacilli, anaerobes	Third or Fourth generation cephalosporins ± clindamycin, ± quinolones or aztreonam or aminoglycoside

Table 4. Empiric Therapy for Bacterial Meningitis Infective Endocarditis, and Intra-abdominal Infections in Aging Person

Infection	Organism	Parenteral Antibiotics
Infective endocarditis		Ampicillin (or penicillin) + Nafcillin (or oxacillin) + Gentamicin or streptomycin
Native valve	Streptococci, <i>S. aureus</i>	
Prosthetic valve	Streptococci, staphylococci, gram-negative bacilli	Vancomycin + gentamicin ± rifampin
Intra-abdominal infections Cholecystitis, appendicitis, diverticulitis	<i>E. coli</i> , Klebsiella spp., Enterococcus spp., anaerobes, other gram negative bacilli	Third/Fourth generation cephalosporin; ampicillin-sulbactam; ticarcillin-clavulanate; piperacillin-tazobactam; ampicillin + clindamycin (or metronidazole) + quinolones (or aminoglycosides)

Penicillins. All penicillins in general may be selected for the treatment of susceptible pathogens that infect the lungs, urinary tract, skin and soft tissue, bones and joints, gastrointestinal tract, and inflamed meninges (27). Dose reduction of approximately 50% for penicillins is necessary when the creatinine clearance is less than 30 mL/min

because the drug clearance occurs primarily by renal excretion. Natural penicillins (penicillin G) and the semisynthetic aminopenicillins (ampicillin and amoxicillin) are prescribed for infections caused by *Streptococcus pneumoniae* (penicillin-susceptible strains), other penicillin-sensitive streptococci (i.e., *Streptococcus pyogenes*, *viridans* group streptococci, and *Streptococcus bovis*), *Listeria monocytogenes*, and *Neisseria meningitidis*. Because of the increasing frequency of penicillin-resistant *S. pneumoniae* isolated in the elderly, penicillin is no longer recommended as the initial therapy of choice for serious infections with this organism, pending results of susceptibility data (26).

Penicillin G remains the primary treatment option for *Treponema pallidum* infection and actinomycosis and still is effective against many anaerobic bacteria. The aminopenicillins also are prescribed for infections caused by Enterococcus and susceptible *Escherichia coli* and *Proteus mirabilis*; clinicians should be aware of the emerging resistance of common bacteria to ampicillin (e.g., *E. coli*) when prescribing these drugs (27). The semisynthetic antistaphylococcal penicillins (nafcillin, oxacillin, methicillin, cloxacillin, and dicloxacillin) are the antibiotics of choice for susceptible *Staphylococcus aureus* infection. The increasing emergence of methicillin-resistant *S. aureus* (MRSA) infection in the elderly, particularly in hospitalized patients and residents of long-term care facilities, has limited the use of the antistaphylococcal penicillins (28).

The extended-spectrum and semisynthetic antipseudomonal penicillins, which include the older carboxypenicillins (carbenicillin and ticarcillin) and the newer ureidopenicillins (azlocillin, mezlocillin, - and piperacillin), have spectra similar to the aminopenicillins but with expanded activity toward gram-negative bacilli, including *Pseudomonas aeruginosa* (29). These agents are ideally prescribed in combination with another antibiotic (or a β -lactamase inhibitor) for the treatment of mixed infections or to enhance synergistic activity; monotherapy with these broad-spectrum agents should be avoided because of the rapid and increasing emergence of antibacterial resistance.

Cephalosporins. Because of their favorable pharmacokinetics, relative safety and efficacy, and broad antimicrobial spectrum, the cephalosporins frequently are recommended for the treatment of infections in the elderly (29-32). Similar to penicillins, these agents are excreted primarily by renal mechanisms; some cephalosporins are metabolized and excreted by the biliary route. Cross-reacting hypersensitivity reactions to cephalosporins in penicillin-allergic individuals have been documented in approximately 5% to 10% of cases.

Based on their antimicrobial spectra, four generations of cephalosporins have been described. The first generation cephalosporins are effective in treating pulmonary, urinary, skin and soft tissue, and bone infections caused by susceptible *S. aureus* and nonenterococcal streptococci, *E. coli*, *Klebsiella*, and *P. mirabilis*. Parenteral cefazolin and the oral agent cephalexin are frequently used first-generation cephalosporins that may be considered for use in older patients. Second-generation cephalosporins include the parenteral cefonicid, cefoxitin, cefotetan, and cefuroxime; cefprozil is an oral agent, and cefuroxime axetil is available as an oral preparation. These agents have greater activity against enteric gram-negative bacilli, including *E. coli*, *P. mirabilis*, and *Klebsiella*, and less gram-positive antibacterial activity than the first-generation cephalosporins. Within this group, several agents have unique advantages; for example, cefoxitin and cefotetan have excellent activity against anaerobes, including the *B. fragilis* group; cefuroxime is resistant to (-lactamases, enters the cerebrospinal fluid well, and is available in an oral form (not recommended for CNS infections); cefonicid's extended serum half-life permits once-daily or twice-daily dosing regimens. Cefuroxime and cefonicid may be useful in treating community-acquired pneumonia caused by *S. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*, *Klebsiella*, and *S. aureus* (31).

Mixed infections associated with aerobic and anaerobic bacteria, such as diabetic and pressure ulcers, and intra-abdominal infections (e.g., cholecystitis, diverticulitis, appendicitis) have been treated effectively with cefoxitin or cefotetan (32). Cefotetan and other cephalosporin antibiotics in this class often are used for perioperative prophylaxis for intra-abdominal surgery (33). Cefuroxime can be prescribed for older persons with bacterial bronchitis, skin and soft tissue infections, and urinary tract infection caused by susceptible pathogens.

Third-generation cephalosporins are most useful in the therapeutic armamentarium for older persons with nosocomial gram-negative bacillary pneumonia, complicated urinary tract infections, gram-negative meningitis, intra-abdominal infections, nosocomial soft tissue and wound infections, and sepsis of undetermined origin. Frequently used third generation cephalosporins include the parenteral agents cefotaxime and ceftriaxone and the oral agent cefixime. Ceftazidime also is a commonly used parenteral antipseudomonal cephalosporin in this class (34). The new fourth-generation cephalosporin cefepime is currently the only commercially available agent in this class. The unique difference in the antibacterial spectrum of cefepime in comparison with the third-generation antipseudomonal cephalosporin ceftazidime is its enhanced gram-positive spectrum, including

susceptible *S. aureus*; this agent also has a U.S. Food and Drug Administration (FDA) approved indication for the treatment of febrile neutropenia.

Monobactams. Aztreonam is the only commercially available monobactam (35-37). The gram-negative antibacterial spectrum is comparable to that of the antipseudomonal cephalosporin, ceftazidime; this drug has no activity against anaerobes or gram-positive bacteria. Indications in the older person include parenteral therapy for urinary tract infections, pneumonias, intra-abdominal infections (in combination with an anti anaerobic agent), and sepsis caused by susceptible organisms (38-39). In contrast to cephalosporins and carbapenems, monobactams do not cross-react with penicillin and may be used safely in penicillin- allergic patients. For older patients with a creatinine clearance less than 30 mL/min but greater than 10 mL/min, the dose should be lowered by 50% after the initial standard dose.

Carbapenems. Carbapenems are a class of broad-spectrum (-lactam agents that includes imipenem-cilastatin, ertapenem and meropenem (38-40). The antibacterial spectrum includes most gram-positive cocci, gram-negative bacilli, and anaerobes, with notable exceptions: most isolates of MRSA, resistant *Enterococcus faecium*, and *Stenotrophomonas maltophilia*. Imipenem is associated with lowering of seizure threshold, and dose adjustment according to the creatinine clearance is essential in the elderly. Meropenem, in contrast, does not enhance seizure potential and may be used in infections of the nervous system (38,41). Ertapenem activity is lacking for *Pseudomonas aeruginosa* and less active for enterococci (40).

β -Lactamase inhibitors. The available β -lactamase inhibitors in combination with β -lactam agents include the oral agents amoxicillin/clavulanate, ticarcillin/clavulanate, ampicillin/ sulbactam, and piperacillin/tazobactam (42-47). The addition of the β -lactamase inhibitor to the β -lactam agent enhances the spectrum of the parent β -lactam drug toward β -lactamase-producing organisms (e.g., oxacillin-susceptible *S. aureus* [MRSA], *H. influenzae*, and anaerobes). The indications for prescribing this class of antibiotics in the elderly are similar to those given for third-generation cephalosporins, but they may exert less selective pressure for strains with extended spectrum beta-lactamases.

Fluoroquinolones. The fluoroquinolones (also referred to as quinolones) are class of antibiotics with a wide spectrum of antimicrobial activity (48-52). Similar to β -lactam antibiotics, the quinolones have favorable characteristics for the treatment of infections in the older person. They are particularly useful clinically because of their excellent activity against gram-negative bacilli, oral

and parenteral preparations, and relative safety. Quinolones are analogues of nalidixic acid and are bactericidal by inhibiting the bacteria's DNA topoisomerases. The older quinolones (e.g., ciprofloxacin) are active against most *enterobacteriaceae* and *P. aeruginosa*; are moderately active against *S. aureus*, *M. catarrhalis*, *H. influenzae*, and *C. trachomatis*; and have variable activity against streptococci and little activity against *S. pneumoniae*. Quinolones are relatively inactive against anaerobes with possible exception of in-vitro activity of moxifloxacin and a lesser extends gatifloxacin. More recently, emerging resistance in some organisms has been reported, in particular MRSA, *E. faecalis*, *S. pneumoniae*, and *P. aeruginosa* (49,53-55). The newer generation fluoroquinolones (e.g., levofloxacin, gatifloxacin, moxifloxacin) have improved gram-positive (including *S. pneumoniae*) activity over that of the older agents in this class and are now considered agents of choice for the treatment of community-acquired pneumonia in adults, including the older person (56-57,63). Quinolones are well absorbed orally, have long serum half-lives that allow once-daily or twice-daily dosing, penetrate into most tissues and body fluids, and are eliminated by renal and nonrenal routes. Because of their excellent bioavailability when administered by the oral route, the quinolones may be useful in early transition from the parenteral to oral preparations, potentially reducing hospitalization and the overall cost of health care. In general, there appears to be no significant age-specific alterations in absorption, metabolism, and excretion of quinolones. Dose adjustment in older patients should be based on renal function. Ciprofloxacin doses should be reduced by 50% for creatinine clearance of less than 30 mL/min; for levofloxacin and gatifloxacin, the dose is reduced by 50% for creatinine clearance values of less than 50 mL/min, for moxifloxacin.

Quinolones have been associated with drug interactions with several other medications or compounds. Decreased theophylline clearance associated with increased serum levels of this drug occurs with ciprofloxacin but not with norfloxacin or levofloxacin; magnesium-containing, calcium-containing, and aluminum-containing antacids significantly reduce absorption of quinolones from the upper gastrointestinal tract.

In the older person, quinolones are useful in the treatment of complicated urinary tract infections, bacterial prostatitis, skin and soft tissue infections, pneumonia, malignant external otitis, and bacterial diarrhea caused by susceptible pathogens (50). Because adverse effects of quinolones in the elderly occur in 5% to 15% of cases, including gastrointestinal (nausea, vomiting, diarrhea) and central nervous system (dizziness, headache, insomnia) effects, these drugs are used for more serious gram-

negative bacillary infections, particularly those resulting from *P. aeruginosa* and antibiotic-resistant organisms (58).

Trimethoprim-sulfamethoxazole. Trimethoprim-sulfamethoxazole is an antibiotic commonly prescribed in the older person, in the setting of urinary tract infections, chronic bacterial prostatitis, lower respiratory tract infections, and bacterial diarrhea caused by susceptible pathogens (59). There are only limited data on the pharmacokinetics of this drug in older persons (60-62). Oral drug absorption does not appear to be affected by age. Renal clearance of trimethoprim is decreased in older persons. The recommended doses for use in the older are comparable to those prescribed in younger persons; with renal impairment and a creatinine clearance of less than 30 mL/min but greater than 15 mL/min, the dosage is reduced by half. The drug should be avoided if the creatinine clearance is less than 15 mL/min.

Newer macrolides. Erythromycin, clarithromycin, and azithromycin are the available macrolides. Some (erythromycin) have a limited role in the management of infections in the elderly in general (64-67). Clarithromycin and azithromycin have more favorable dosing regimens, improved antimicrobial activity, and lower gastrointestinal intolerance compared with erythromycin. These agents are active against most strains of streptococci, *M. catarrhalis*, *H. influenzae*, Legionella, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* as well as atypical mycobacteria such as *Mycobacterium avium* complex (66). Some (up to 50%) of penicillin resistant *S. pneumoniae* and a lower percentage of penicillin susceptible strain are resistant to the macrolides. Limited data are available regarding the pharmacokinetics of these newer macrolides in older persons; drug clearance has been found to be reduced predominantly because of reduced renal clearance. The indications for the newer macrolides in the older persons are no different than for those for the general population. They most often are considered in the initial management of community-acquired pneumonia alone or in combination with a second agent (e.g. β -lactam) based on the severity of illness, presence of underlying comorbid illnesses (e.g., diabetes mellitus, congestive heart failure, alcoholism malignancies), and implicated respiratory pathogens.

Aminoglycosides, Vancomycin and others. Antibiotics prescribed in older patients that should be mentioned include vancomycin, aminoglycosides, clindamycin, and metronidazole.

The role of *aminoglycosides* in treating infections in older person is limited with the increasing availability of safer and equally effective antibiotics (i.e., cephalosporins, monobactams, carbapenems, β -lactam/ β -lactamase inhibitor combination antibiotics, and quinolones (68). Renal

impairment (generally reversible) and ototoxicity (generally irreversible) are the two most common and important potential adverse effects of these antibiotics. Aminoglycoside use in older patients should be reserved for those with serious infections including *P. aeruginosa* infections (generally combined with another drug), infections caused by organisms susceptible only to aminoglycosides, serious enterococcal infection (combined generally with ampicillin or vancomycin), or septic shock of unknown cause (in combination with other antibiotics).

Vancomycin is a glycopeptide antibiotic used primarily for gram-positive bacterial infections (69). It is highly active against staphylococci (including MRSA) and streptococci (including vancomycin-sensitive enterococci). In the older person, studies have indicated that reduced clearance of vancomycin is a consequence of reduced systemic and renal clearance as well as enhanced tissue binding of the drug. Lower parenteral doses are recommended for the frail elderly, and the dose should be adjusted according to the serum peak and trough levels as well as the creatinine clearance. The side-effect profile in the elderly is no different from that in the general population. New agents a FDA-approved streptogramin antibiotic, quinupristin-dalfopristin (Synercid) and linezolid are indicated in adults, including the elderly, for the treatment of serious and life threatening bacteremic infection with vancomycin-resistant *E. faecium* (26) and complicated skin and skin structure infection with MSSA and *Streptococcus pyogenes*. The pharmacokinetics of these agents are similar to that in younger adults.

The indications, doses, and toxicities of *clindamycin* and *metronidazole* are no different in the older compared with younger persons (70-71). These latter agents are prescribed commonly in combination with agents active against aerobic gram-positive and gram-negative bacteria, to treat mixed infections in the elderly for infected pressure ulcers, diabetic foot ulcers, intra-abdominal infections, or pyogenic brain abscesses. Oral metronidazole also is the preferred agent for the treatment of *Clostridium difficile* colitis in the older person.

Therapeutic options: empiric use or otherwise. The empiric selection of antibiotics should take into consideration the most likely sites and causes of infection, clinical status of the patient, comparative efficacy of antibiotics that could be selected under similar circumstances, potential adverse effects of the drugs and overall costs incurred in use of the drug (25). The empiric antibiotic regimen ideally should be subsequently replaced by a more focused regimen based on microbiologic data that indicate a specific cause, when possible.

Resumen

Cuando los antibióticos se recetan en el envejeciente, la dosificación necesita cuidado especial, ya que los parámetros farmacocinéticos cambian según envejecemos y los efectos secundarios pueden ser diferentes en la persona mayor. Los cambios en la depuración de creatinina nos llevan a que debemos modificar la manera que prescribimos al envejeciente, calculando la depuración de creatinina. La gran variedad de antibióticos disponibles actualmente nos lleva a la presentación de este trabajo en donde discutimos los agentes antimicrobianos indicados en el tratamiento de infecciones en el envejeciente. Presentamos las penicilinas, cefaloporinas, monobactams, carbapenems los inhibidores indicados de la betalactamasa o el grupo beta-lactámico. Otros son trimetropin-sulfametoaxole los nuevos macrólidos (azitromicina y claritromicina) y otros como los aminoglucosidos, lavancomicina, clidamicina y el metonidazole. Las indicaciones y contraindicaciones presentan y se revisan.

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