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TIGECYCLINE

Goal

To review the pharmacology, microbiology, resistance, pharmacokinetics, pharmacodynamics, clinical efficacy, adverse effects, drug interactions, precautions, and administration of tigecycline.

Objectives

After reviewing this article, the reader should be able to:

1. identify the pharmacologic class and spectrum of activity of tigecycline;
2. determine when dosage adjustments are required for tigecycline, based on the patient's renal and hepatic function;
3. given a case study, identify any drug interactions that may occur and how to manage them;
4. given a case study, be able to manage any adverse reactions that may occur due to tigecycline.

Test Questions

1. Tigecycline is a member of which of the following classes of semisynthetic antibiotics?
 - (a) macrolides
 - (b) penicillins
 - (c) glycolcyclines
 - (d) carbapenems
2. Which of the following statements regarding tigecycline is true?
 - (a) Tigecycline's activity against *P. aeruginosa* is superior to that of the cephalosporins.
 - (b) Tigecycline was developed to overcome tetracycline mechanisms of resistance, such as efflux pumps and ribosomal protection.
 - (c) Due to its structural similarities to tetracycline, cross resistance to tigecycline is a concern.
 - (d) Tigecycline should be used first line in the treatment of infections caused by *Proteus* spp.
3. Tigecycline has in vitro activity against all of the following microorganisms except:
 - (a) *Proteus* spp.
 - (b) *A. baumannii*.
 - (c) *S. pneumoniae*.
 - (d) *C. difficile*.
4. Overexpression of which of the following multidrug efflux pumps decreases tigecycline susceptibility?
 - (a) QacA
 - (b) NorA
 - (c) Smr
 - (d) AcrAB
5. Which of the following is the most commonly reported adverse event associated with intravenous tigecycline therapy?
 - (a) nausea
 - (b) tremors
 - (c) dizziness
 - (d) abdominal cramping
6. Which of the following statements regarding the pharmacokinetics and pharmacodynamics of tigecycline is false?
 - (a) Tigecycline may not be an appropriate choice for bacteremia due to low serum concentrations (<1 µg/mL).
 - (b) Results of human studies suggest that the best link to efficacy is the AUC/MIC ratio.
 - (c) Tigecycline is unable to concentrate in the cerebrospinal fluid, after concentrations observed with a single intravenous dose of 100 mg were less than 0.1% of concurrent serum concentrations.
 - (d) Tigecycline has a prolonged postantibiotic effect in vitro.
7. A 65-year-old patient with a severe penicillin allergy and renal dysfunction is diagnosed with an *S. aureus* skin infection on the right lower extremity and the pharmacist is asked to recommend a dose of tigecycline. The patient's glomerular filtration rate (GFR) is 26 mL/min. Which of the following is a correct intravenous dose?
 - (a) 100 mg as a loading dose, followed by 25 mg every 12 hours
 - (b) 100 mg as a loading dose, followed by 50 mg every 12 hours
 - (c) 100 mg as a loading dose, followed by 50 mg every 24 hours
 - (d) 50 mg every 12 hours; no loading dose required
8. The pharmacist is asked to recommend a dose of intravenous tigecycline in a 45-year-old patient with severe hepatic impairment (Child-Pugh Class C). Which of the following is an appropriate dose?
 - (a) 100 mg as a loading dose, followed by 25 mg every 12 hours
 - (b) 100 mg as a loading dose, followed by 50 mg every 12 hours
 - (c) 100 mg as a loading dose, followed by 50 mg every 24 hours
 - (d) 50 mg every 12 hours; no loading dose required
9. A 55-year-old patient with a history of atrial fibrillation is admitted to the hospital with an intraabdominal infection secondary to recent surgery. The patient is currently on warfarin, with an international normalized ratio (INR) of 2.6 (goal 2.0–3.0). The physician wants to start tigecycline empirically and consults the pharmacist for recommendations regarding a possible interaction between warfarin and the antibiotic. What should the pharmacist's recommendation be?
 - (a) Tigecycline and warfarin should never be administered together; another antibiotic should be recommended.
 - (b) The warfarin dose should be decreased by half and the patient's INR should be monitored.
 - (c) The warfarin dose should be doubled and the patient's INR should be monitored.
 - (d) The patient's INR should be monitored once tigecycline treatment begins and the warfarin dose should be adjusted as necessary to achieve the INR goal.
10. A 25-year-old patient who was started on tigecycline 2 days ago for a complicated skin and soft tissue infection is experiencing nausea and has vomited once. Microbiologic data are pending. What should the pharmacist's recommendation be?
 - (a) Discontinue tigecycline and start vancomycin.
 - (b) Discontinue tigecycline and start piperacillin/tazobactam.
 - (c) Continue tigecycline, as nausea is usually transient. If vomiting continues, any antiemetic could be started, as no interactions between tigecycline and antiemetics have been reported.

- (d) Continue tigecycline, as nausea is usually transient. If vomiting continues, only prochlorperazine can be used as an antiemetic because numerous interactions between tigecycline and antiemetics have been reported.
11. A 65-year-old patient on digoxin for heart failure is started on tigecycline for an intraabdominal infection. Gram stain shows many gram-negative rods. The house staff consults the pharmacist about how to manage the digoxin–tigecycline interaction. What should the pharmacist's response be?
- Tigecycline increases the AUC of digoxin by 13%. The dose of digoxin should be decreased by half and digoxin concentrations should be monitored.
 - Digoxin increases the AUC of tigecycline by 13%. The maintenance dose of tigecycline should be decreased by half.
 - Tigecycline decreases maximum plasma concentration of digoxin by 13%; however, clearance and AUC of digoxin are not affected. No dosage adjustments or extra monitoring are required.
 - Tigecycline decreases maximum plasma concentration of digoxin by 13% and AUC is increased. Digoxin concentrations should be monitored during therapy with tigecycline.
12. What percentage of patients in Phase III clinical trials developed *C. difficile*-associated diarrhea due to tigecycline therapy?
- 0%
 - 10%
 - 20%
 - 50%
13. A 35-year-old man with HIV is admitted to the hospital for treatment of MRSA deep tissue infection secondary to trauma. The patient was treated with home infusion of vancomycin for one week, after which his renal function began to deteriorate (current GFR 45 mL/min). He is receiving ritonavir, atazanavir, tenofovir, and emtricitabine. The patient's physician wants to start tigecycline therapy. Which of the following statements is *most correct*?
- Tigecycline is metabolized through the cytochrome P450 enzyme system; therefore, it will interact with ritonavir and atazanavir, which are metabolized by CYP3A4.
 - Tigecycline is metabolized through the cytochrome P450 enzyme system; therefore, it will interact with tenofovir, which is metabolized by CYP3A4.
 - Tigecycline is primarily glucuronidated and therefore will not interact with the patient's HIV regimen.
 - Tigecycline is primarily eliminated by biliary excretion and therefore will not interact with the patient's HIV regimen.
14. A 67-year-old man with an intraabdominal abscess secondary to ruptured appendix has positive body fluid cultures from surgery. The microbiology report shows pan-susceptible *E. faecium*, *B. fragilis*, and *P. aeruginosa*. The patient has a past history of diabetes mellitus, hypertension, and prostate cancer. He is currently receiving glyburide, lisinopril, and aspirin. His GFR is 78 mL/min. Which of the following statements is *most correct*?
- Tigecycline would be appropriate because it covers both gram-positive and -negative organisms.
 - Tigecycline would not be appropriate because it has no activity against anaerobes such as *B. fragilis*.
 - Tigecycline would not be appropriate because it has no activity against *Pseudomonas* spp.
 - Tigecycline would be appropriate because it has excellent activity against *Pseudomonas* spp.
15. Due to tigecycline's bacteriostatic nature, it is *not recommended* in the treatment of which of the following types of infections?
- primary bacteremias
 - any infection caused by MRSA
 - pneumonia
 - diabetic foot infections