ANTIMICROBIALS - I

PHARMACODYNAMICS AND PHARMACOKINETICS OF ANTIMICROBIAL THERAPY - CLINICAL APPLICATION

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Abstract: *Emergence of antimicrobial resistance and poor clinical outcome consequently, are mostly because of inappropriate drug choice and suboptimal dosing. Strategies for better clinical outcomes include selection of an appropriate antibiotic and optimization of antimicrobial dosing regimen. Hence, one must primarily understand the antimicrobial pharmacodynamics and pharmacokinetics of a particular drug to decide on the dosing regimen. Pharmacodynamics denotes the mechanism of action of the drug such as a drug's molecular, biochemical and physiologic effects. Pharmacokinetics deals with absorption, distribution, metabolism and excretion of the drug simplified and abbreviated as ADME.*

Keywords: *Pharmacodynamics, Pharmacokinetics, Minimal inhibitory concentration, Antimicrobial resistance.*

Points to Remember

- ***Antimicrobial therapy for the treatment of infection not only require appropriate choice of antimicrobial agent but also appropriate dosing regimen, route and duration. To decide this, site of infection, type of bacteria and age of patients are other important variables.***
- ***Dose optimization of antimicrobial agent requires understanding of pharmacokinetic and pharmacodynamic properties.***
- ***Antimicrobial efficacy of concentration dependent antimicrobial agents (e.g. aminoglycoside, quinolones) depends on the peak concentration (C max) to MIC ratio.***
- ***Antimicrobial efficacy of time dependent antimicrobial agents (e.g. β-lactam, vancomycin) depends on the percentage of time that free plasma concentration of antimicrobial agent is maintained above MIC.***
- ***Dose adjustment is required in certain situations, renal impairment being the most important of them.***

References

1. Manjunath P Pai, Mackenzie L Cottrell, Angela DM Kashuba, et al. Pharmacokinetics and Pharmacodynamics of Anti-infective Agents. Bennett JE, Dolin R, Blaser MJ, Eds. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 8th edn. Saunders; Philadelphia. 2015; pp252-262.
2. Barbour A, Scaglione F, Derendorf H. Class-dependent relevance of tissue distribution in the interpretation of anti-infective pharmacokinetic/pharmacodynamics indices. Int J Antimicrob Agents 2010; 35:431-438.
3. Zanger UM, Schwab M. Cytochrome P450 enzymes in drug metabolism: regulation of gene expression, enzyme activities, and impact of genetic variation. Pharmacol Ther 2013; 138:103-141.
4. Bebitoðlu BT, Oðuz E, Nuhoðlu Ç, Dalkýlýç AEK, Çirtlik P, Temel F, et al. Evaluation of potential drug-drug

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interactions in a pediatric population. Turk Pediatr Ars 2020; 55:30-38.

5. Levison ME. Pharmacodynamics of antimicrobial agents. Bactericidal and postantibiotic effects. Infect Dis Clin North Am 1995; 9:483-495.
6. Mouton JW, Dudley MN, Cars O, Derendorf H, Drusano GL. Standardization of pharmacokinetic/pharmacodynamic (PK/PD) terminology for anti-infective drugs: an update. J Antimicrob Chemother 2005; 55:601-607.
7. Lacy MK, Nicolau DP, Nightingale CH, Quintiliani R. The pharmacodynamics of aminoglycosides. Clin Infect Dis 1998; 27:23-27.
8. Lode H, Borner K, Koeppe P. Pharmacodynamics of fluoroquinolones. Clin Infect Dis 1998; 27:33-39.
9. Kasiakou SK, Lawrence KR, Choulis N, Falagas ME. Continuous versus intermittent intravenous administration of antibacterials with time-dependent action: a systematic review of pharmacokinetic and pharmacodynamic parameters. Drugs 2005; 65:2499-2511.
10. Zhanel GG, Hoban DJ, Harding GKM. The Postantibiotic Effect: A Review of in Vitro and in Vivo Data. DICP 1991; 25:153-163. doi:10.1177/106002809102500210.
11. Bush K. Synergistic Antibiotic Combinations. In: Fisher JF, Mobashery S, Miller MJ. (eds) Antibacterials. Topics in Medicinal Chemistry, 2017 vol 25. Springer, Cham. https://doi.org/10.1007/7355_2017_23.
12. Blot SI, Pea F, Lipman J. The effect of pathophysiology on pharmacokinetics in the critically ill patient-concepts appraised by the example of antimicrobial agents. Adv Drug Deliv Rev 2014; 77:3-11.
13. Felton T, Troke PF, Hope WW. Tissue penetration of antifungal agents. Clin Microbiol Rev 2014; 27:68-88.
14. Gilbert B, Robbins P, Livornese LL Jr. Use of antibacterial agents in renal failure. Infect Dis Clin North Am 2009; 23:899-924.
15. Aloy B, Launay-Vacher V, Bleibtreu A, Bortolotti P, Faure E, Filali A, et al. Antibiotics and chronic kidney disease: Dose adjustment update for infectious disease clinical practice. Med Mal Infect 2020; 50:323-331.
16. Rahul Chanchlani, Aditi Sinha. Drug dosing in renal failure. RN Srivastava and Arvind Bagga, editor. Pediatric nephrology, Ed 5. India: Jaypee Brothers. 2016; pp535-540.
17. Bûdingen FV, Gonzalez D, Tucker AN, Derendorf H. Relevance of Liver Failure for Anti-Infective Agents: From Pharmacokinetic Alterations to Dosage Adjustments. Ther Adv Infect Dis 2014; 2:17-42. doi: 10.1177/2049936113519089.
18. Halilovic J, Heintz BH. Antibiotic dosing in cirrhosis. Am J Health Syst Pharm 2014; 71:1621-1634.