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Clinical Pharmacology of Ampicillin

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ABSTRACT

Ampicillin is a semi-synthetic derivative of penicillin that functions as an orally active broad-spectrum antibiotic. Ampicillin prevents bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs), which are the enzymes accountable for the formation of the cell wall structure. Ampicillin is a penicillin derivative used for treatment of a variety of infections caused by gram-positive and gram-negative bacteria as well as certain anaerobes. The half-life of ampicillin is nearly three hrs during continuous venovenous hemofiltration. Most ubiquitous adverse effects of ampicillin are rash and diarrhea. Coincident administration of ampicillin and oral contraceptives increased the risk of breakthrough bleeding and decreased the efficacy of the contraceptive by interruption of the enterohepatic cycling of ethinylestradiol by means of decreasing the bacterial population of the small intestine, which is responsible for the hydrolysis of the conjugated hormone.

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Introduction

Ampicillin is in a group of medications known as penicillins. Ampicillin is classified under aminopenicillins (broad spectrum penicillins). Ampicillin is a semi-synthetic derivative of penicillin that functions as an orally active broad-spectrum antibiotic [1-4].

Mechanism of Actions

Ampicillin prevents the final transpeptidation step of peptidoglycan synthesis in bacterial cell wall by binding to one or more of the penicillin-binding proteins, thus preventing cell wall biosynthesis resulting in bacterial lysis; Ampicillin exerts bactericidal action on both gram positive and gram-negative organisms. Its spectrum involves gram positive organisms such as, example streptococcus pneumoniae and other streptococci, Listeria monocytogenes, and gram negative, example Moraxella catarrhalis, Neisseria meningitidis, Escheria coli, Salmonella.

Ampicillin exerts its action by preventing the synthesis of bacterial cell wall or ampicillin prevents bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs), which are the enzymes accountable for the formation of the cell wall structure. Ampicillin, like all penicillins, acts as a structural analogue of acyl-D-alanyl-D alanine and acylates the transpeptidase enzyme responsible for the final stage of the formation of the peptidoglycan, which is the chief component of the cell wall [4-6].

Spectrum of Activity

Semisynthetic penicillins with increased activity against g (-) bacteria analogized to natural and penicillinase-resistant penicillins besides to streptococcal (enclosing pneumococcal) strains, ampicillin and amoxicillin are also effective against multiple strains of haemophilus influenzae, E. coli, streptococcus faecalis and salmonella. Streptococcus pneumoniae, H. influenzae and Moraxella catarrhalis are pathogens that exhibit high susceptibility rates to ampicillin. Among Enterobacteriaceae, the genera Morganella, Enterobacter and Serratia have the highest resistance rates to ampicillin [7].

Spectrum of Resistance

The principal mechanism of resistance against ampicillin includes inactivation by β-lactamases, which are the hydrolytic enzymes responsible for the formation of an acidic derivative of β-lactams deprived of antibacterial activity. Resistance to βlactams can also arise from a decreased number of porin channels, which are the proteins that regulate the permeability of the outer membrane of Gram-negative bacteria for antibacterials and the interaction with their environment. Mutations to genes that encode PBPs are another mechanism of resistance, as alterations in the structure of PBPs perhaps importantly decrease their affinity with β-lactams. There perhaps more than one resistance mechanism present in a bacterium, i.e., methicillin-resistant Staphylococcus aureus (MRSA) exhibits resistance by mecA gene expression, which encodes for the altered PBP2, and by accelerated production of β-lactamases

Clinical Use

Ampicillin is a penicillin derivative used for treatment of a variety of infections caused by gram-positive and gram-negative bacteria as well as certain anaerobes. They are used for a diverseness of chest infections (e.g., bronchitis, pneumonia), sepsis in the paediatric population, otitis media, aspiration pneumonia, intra-abdominal infections, urinary tract infections, skin and soft tissue infections, lower respiratory tract infections, typhoid fever, uncomplicated gonorrhea, biliary infections and the precluding

of bacterial endocarditis. Ampicillin is effective treatment for meningitis caused by Listeria monocytogenes [8-10].

Pharmacodynamics

Ampicillin is a penicillin beta-lactam antibiotic used in the treatment of bacterial infections caused by vulnerable, often gram-positive, organisms. Ampicillin has group of antibiotics derived from the penicillins. Ampicillin has invitro activity against gram-positive and gram-negative aerobic and anaerobic bacteria. The bactericidal activity of ampicillin results from the suppression of cell wall synthesis and is mediated through ampicillin binding to penicillins binding proteins. Ampicillin is stable against hydrolysis by a variety of beta-lactamases, involving penicillinases, and cephalosporinases and extended spectrum beta-lactamases [11-14].

Pharmacokinetics

Ampicillin is moderately well absorbed after oral administration, but peak levels are delayed and reduced if it is ingested with food. Peak blood levels of 3 microgram per milliliter appear one to two hrs after ingestion of 500mg; levels peak later in diabetic patients with neurologic disease and in patients with renal failure. After intramuscular injection of zero-point five-gram, peak levels of ten microgram are achieved at one hr. The elimination half-life is approximately eighty minutes. Ampicillin is well distributed to body compartments and after parenteral administration achieves therapeutic concentrations in cerebrospinal, pleural, joint, and peritoneal fluids in the presence of inflammation. The drug undergoes enterohepatic circulation, and important levels appear in bile and stool. The half-life of ampicillin is nearly three hrs during continuous venovenous hemofiltration [15-19].

Contraindications

Contraindications of ampicillin include a former history of severe allergic reaction or penicillin and its derivatives. Ampicillin is also contraindicated in patients who have had SJS after administering penicillin or a penicillin derivative, alcoholic patients [20, 21].

Adverse Drug Reaction

Most known adverse effects of ampicillin are rash and diarrhea. Allergic reactions such as urticaria, pruritus, angioedema is the also occur as side effects of aspirin commonly. Ampicillins are the most ubiquitous cause of drug allergy. Anaphylaxis: laryngealedema, bronchoconstriction, severe hypotension in 0.2% of patients. The ampicillins can also cause acute interstitial nephritis, a damage characterized by inflammation of the tubules and interstitium of the kidneys. Acute interstitial nephritis can also present with hematuria, fever, and rash. Other certain adverse drug reactions of ampicillin are blood dyscrasias, shock, pseudomembranous colitis, electrolyte imbalance, neuromuscular hypersensitivity, seizures [22-27].

Drug Interactions

Coincident administration of ampicillin and oral contraceptives increased the risk of breakthrough bleeding and decreased the efficacy of the contraceptive by interruption of the enterohepatic cycling of ethinylestradiol by means of decreasing the bacterial population of the small intestine, which is responsible for the hydrolysis of the conjugated hormone. The suppression of hydrolysis can lead to an accelerated fecal loss of the hormone, resulting in lower circulating levels of ethinylestradiol. Concomitant administration of ampicillin and gentamicin are frequently given for severe infections in hospitalized patients owing to penicillin mediated cell injury, facilitate entry (intracellular uptake) of the aminoglycosides in to the cell, which causes the subsequent bactericidal effect against the enterococci. Probenecid causes increases in the number of penicillins in the body by precluding excretion of penicillin by the kidneys. Combining ampicillin with allopurinol can accelerate the occurrence of medicine-related skin rash. Penicillin antibiotics perhaps decrease the effect of BCG live vaccine and typhoid live vaccine. Acetaminophen perhaps decreases the excretion rate of ampicillin which could result in a higher serum level. If ampicillin taken with0020alcohol, it increases the risk of disulfiram reaction caused by alcohol. Acetazolamide perhaps increase the excretion rate of ampicillin which could result in a lower serum level and potentially a reduction in efficacy. Coincident administration of anticoagulant medications such as warfarin, ampicillin increases the effects of anticoagulants medications [28-33].

Conclusion

Ampicillin is in a group of medications known as penicillins. Ampicillin is classified under aminopenicillins (broad spectrum penicillins). Ampicillin prevents the final transpeptidation step of peptidoglycan synthesis in bacterial cell wall by binding to one or more of the penicillin-binding proteins. Ampicillin is a penicillin beta-lactam antibiotic used in the treatment of bacterial infections caused by susceptible, usually gram-positive, organisms. Most ubiquitous adverse effects of ampicillin are rash and diarrhea. Concomitant administration of ampicillin and gentamicin are frequently given for severe infections in hospitalized patients owing to penicillin mediated cell injury, facilitate entry (intracellular uptake) of the aminoglycosides in to the cell, which causes the subsequent bactericidal effect against the enterococci.

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References

1. Lima LM, Da Silva BN, Barbosa G, Barreiro EJ (2020) β-lactam antibiotics: An overview from a medicinal chemistry perspective. European Journal of Medicinal Chemistry 112829.
2. Fernandes R, Amador P, Prudêncio C (2013) β-Lactams: chemical structure, mode of action and mechanisms of resistance. Reviews in Medical Microbiology 24: 7-17.
3. Penwell WF, Shapiro AB, Giacobbe RA, Gu RF, Gao N, et al. (2015) Molecular mechanisms of sulbactam antibacterial activity and resistance determinants in Acinetobacter baumannii. Antimicrobial agents and chemotherapy 59: 1680-1689.
4. Baranowski C, Welsh MA, Sham LT, Eskandarian HA, Lim HC, et al. (2018) Maturing Mycobacterium smegmatis peptidoglycan requires non-canonical crosslinks to maintain shape. Elife 7: e37516.
5. Hauser AR (2020) Antibiotic basics for clinicians. Wolters kluwer india Pvt Ltd.

6. Hauser A (2018) Antibiotic Basics for Clinicians. Lippincott Williams & Wilkins.
7. Sitohy MZ, Mahgoub SA, Osman AO (2012) In vitro and in situ antimicrobial action and mechanism of glycinin and its basic subunit. International Journal of Food Microbiology 154: 19-29.
8. Rafailidis PI, Ioannidou EN, Falagas ME (2007) Ampicillin/Sulbactam Current Status in Severe Bacterial Infections. Drugs 67: 1829-1849.
9. Nathwani D, Lawson W, Dryden M, Stephens J, Corman S, et al. (2015) Implementing criteria-based early switch/early discharge programmes: a European perspective. Clin Microbiol Infect 21: S47-55.
10. Cunha CB (2018) Antibiotic stewardship program perspective: Oral antibiotic therapy for common infectious diseases. Med Clin North Am 102: 947-954.
11. McCarthy K, Avent M (2020) Oral or intravenous antibiotics? Aust Prescr 43: 45-48.
12. Van den Bosch CM, Geerlings SE, Natsch S, Prins JM, Hulscher ME (2015) Quality indicators to measure appropriate antibiotic use in hospitalized adults. Clin Infect Dis 60: 281-291.
13. Lee SL, Azmi S, Wong PS (2012) Clinicians' knowledge, beliefs and acceptance of intravenous-to-oral antibiotic switching, Hospital Pulau Pinang. Med J Malaysia 67: 190-198.
14. Cyriac JM, James E (2014) Switch over from intravenous to oral therapy: a concise overview. J Pharmacol Pharmacother 5: 83-87.
15. Lode HM (2008) Rational antibiotic therapy and the position of ampicillin/sulbactam. Int J Antimicrob Agents 32: 10-28.
16. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C (2007) Measurement of adult antibacterial drug use in 130 US hospitals: Comparison of defined daily dose and days of therapy. Clin Infect Dis 44: 664-670.
17. Blum RA, Kohli RK, Harrison NJ, Schentag JJ (1989) Pharmacokinetics of ampicillin (2.0 grams) and sulbactam (1.0 gram) coadministered to subjects with normal and abnormal renal function and with end-stage renal disease on hemodialysis. Antimicrob Agents Chemother 33: 1470-1476.
18. Fliser D, Kielstein JT (2006) Technology insight: Treatment of renal failure in the intensive care unit with extended dialysis. Nat Clin Pract Nephrol 2: 32-39.
19. Kumar VA, Yeun JY, Depner TA, Don BR (2004) Extended daily dialysis vs. continuous hemodialysis for ICU patients with acute renal failure: A two-year single center report. Int J Artif Organs 27: 371-379.
20. Khan DA, Knowles SR, Shear NH (2019) Sulfonamide hypersensitivity: fact and fiction. The Journal of Allergy and Clinical Immunology: In Practice 7: 2116-2123.
21. Vorobeichik L, Weber EA, Tarshis J (2018) Misconceptions surrounding penicillin allergy: implications for anesthesiologists. Anesthesia & Analgesia 127: 642-649.
22. Atanaskovic-Markovic M, Gomes E, Cernadas JR, du Toit G, Kidon M, et al. (2019) Diagnosis and management of drug-induced anaphylaxis in children: an EAACI position paper. Pediatric Allergy and Immunology 30: 269-276.
23. Baldo BA (2021) Pham NH (Classification and descriptions of allergic reactions to drugs. In Drug Allergy Springer 17-57.
24. Bogard KN, Peterson NT, Plumb TJ, Erwin MW, Fuller PD, et al. (2011) Antibiotic dosing during sustained low-efficiency dialysis: Special considerations in adult critically ill patients. Crit Care Med 39: 560-570.
25. Kielstein JT, Lorenzen J, Kaever V, Burhenne H, Broll M, et al. (2009) Risk of underdosing of ampicillin/sulbactam in patients with acute kidney injury undergoing extended daily dialysis—a single case. Nephrol Dial Transplant 24: 2283-2285.
26. Matzke GR, Aronoff GR, Atkinson AJ Jr, Bennett WM, Decker BS, et al. (2011) Drug dosing consideration in patients with acute and chronic kidney disease—a clinical update from kidney disease: Improving Global Outcomes (KDIGO). Kidney Int 80: 1122-1137.
27. Kielstein JT, Kretschmer U, Ernst T, Hafer C, Bahr MJ, et al. (200) Efficacy and cardiovascular tolerability of extended dialysis in critically ill patients: A randomized controlled study. Am J Kidney Dis 43: 342-349.
28. Plumb DC (2018) Plumb's Veterinary Drug Handbook: Desk. John Wiley & Sons.
29. De Paepe P, Belpaire FM, Buylaert WA (2012) Pharmacokinetic and Pharmacodynamic considerations when treating patients with Sepsis and septic shock. Clin Pharmacokinet 41: 1135-1151.
30. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, et al. (2015) Group P-P. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 350: g7647.
31. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, et al. (2016) The third international consensus definitions for Sepsis and septic shock (Sepsis-3). JAMA 315: 801-810.
32. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, et al. (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 343: d5928.
33. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, et al. (2018) The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses Accessed.