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Review Article

Comparative Study between Penicillin and Ampicillin

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Abstract: Antibiosis history began with the observations made by Sanderson and Roberts on the inhibition of bacterial growth by other organisms, at the end of the XIX Century. Biomedical research in this field advanced importantly during World War II, after the discovery of penicillin by Fleming. Now-a-days the number of antibiotics plays an important role in the society particularly animal and human life. In this case Ampicillin is a beta-lactam Antibiotic that has been extensively to treat different bacterial diseases and controlled since 1961. Antibiotic action is against different types of bacteria like Gram positive or Gram negative bacteria. This is a good anti-biotic to the animals and human to prevent the different microbial diseases. The ability of some bacteria to now produce penicillinase to break down and render penicillin completely useless has come about due to the wide scale use of the drug and has therefore limited the effectiveness of penicillin as a clinical treatment. In order to combat this, scientists have turned to semi-synthetic derivatives of penicillin in the hope that these will have the properties necessary to beat the resistance problem.
Keywords: Penicillin, Ampicillin, Resistance, Beta-lactam antibiotic.

INTRODUCTION

Antibiotics are specific chemical substances derived from or produced by living organisms that are capable of inhibiting the life processes of other organisms. The first antibiotics were isolated from micro-organisms but some are now obtained from higher plants and animals. Over 3,000 antibiotics have been identified but only a few dozen are used in medicine. Antibiotics are the most widely prescribed class of drugs comprising 12% of the prescriptions in the United States.The Penicillin were the first antibiotics discovered as natural products from the mold Penicillium. Ampicillin is a beta-lactamantibiotic that is part of the aminopenicillin family and is roughly equivalent to its successor, amoxicillin in terms of spectrum and level of activity [1].

COMPARATIVE STUDY

Penicillins are the antibiotics that have been used in the treatment towards bacteria invasion. Penicillin was discovered by Alexander Fleming in September 1928 while he was working at St. Mary's Hospital London. He left for holidays and left the culture of the microbe at the window of his lab. After he came back from the holidays, he found an unusual phenomenon of the culture of microbe that he had left. It was found that the absence of fully developed colonies of a common microbe, Staphylococcus aureus and a round a large colony of a common mould, Penicillium notatum. The discovery of his findings led to the use of penicillin as an antibiotic in the present days [2]. Penicillin is produced by Penicillium chrysogenum. Alteration of the culture medium by feedingprecursors, phenylacetic acid for Penicillin G or phenoxyacetic acid for Penicillin V is used forlarge scale production. Other penicillins are produced semi-synthetically.

Penicillin are classified as Natural penicillin (Penicillin G, Penicillin V), Penicillinase resistant Penicillin (Methicillin, Cloxacillin), Extended Spectrum Penicillin (Ampicillin, Amoxicillin), Broad Spectrum Penicillin (Carboxypenicillin), β-Lactamase combinations (Augmentin) [3].

Spectrum of Penicillin

1. *Strep. Pneumonia. Strep. pyogenes*, Group B Strep. viridans group, however penicillin-resistant strains of *Strep. pneumoniae* are emerging (as high as 60% in endemic areas). If MIC <0.1µg/ml - Pen G or V is DOC.
2. *Staphylococcus aureus* (non penicillinase producing strains)
3. *Enterococcus faecalis, E. faecium* (incombination with aminoglycosides)
4. *Neisseria meningitides*
5. *Treponema pallidum* (syphilis)
6. *Listeria monocytogenes*
7. *Corynebacterium diphtheria*
8. Anaerobes -*Clostridum perfringens & C. tetani* (not *C. difficile), Bacteroidesfragilis* (non-penicillinase producing strains), *Fusobacterium, Peptostreptococcus.*

Spectrum of Ampicillin

1. Have similar Gram + spectrum to Penicillin V & K (slightly less active)
2. *E.coli, Proteus mirabilis* - especially for UTIs (however 25-50% make ß-lactamase)

3. *Haemophilus influenzae* - resistance is common (30-40%) &*Neisseria sp., Listeria.*
4. *Shigella* &*Salmonella* - usually treat with ampicillin for GI infections (resistance is over 50% for Shigella in U.S.).

Uses of Penicillin

Used in Streptococcal infection, Meningococcal infections, Syphilis, Prophylaxix for scarlet fever.

Uses of Ampicilin

Used in Enterococcal endocarditis, in Meningitis – Ampicillin - alternative choice to 2nd gen. cephalosporins (+chloramphenicol). Also in urinary tract infection, Prophylaxis for bacterial endocarditis [4].

Mechanism of Action (Penicillin and Ampicillin)

Penicillin and other cell wall inhibitors are primarily specific against Gram –positive bacteria because of higher percentage of peptidoglycan in the cell walls of these organisms. Cell walls in growing bacteria are always being synthesized, so inhibition of synthesis is effective at controlling growth. Since humans lack cells walls antibiotics of this class have low toxicity. Allergy to penicillin occurs in a low percentage of the population and should be looked for in patients. Transpeptidation is an unusual type of peptide bond formation that is responsible for the formation of the peptide cross-links between adjacent glycan chains in cell-wall synthesis. Inhibition of transpeptidation by penicillin leads the formation of a weakened peptidoglycan. As autolysins continue to act, further damage is done to the cell which will result in lysis and eventually death. Also, the cell wall becomes weaker & osmotic lysis occurs as new peptidoglycan cross-links cannot occur. But lysis by penicillin can be prevented by adding an osmotic stabilizing agent like sucrose. Under such conditions, protoplasts will be formed if there is continued growth in the presence of penicillin. Penicillin-induced lysis only occurs with growing cells. Action of autolysins does not occur in non growing cells. Therefore the breakdown of the cell wall peptidoglycan is prevented [5].

Ampicillin belonging to the penicillin group of beta-lactam antibiotics, ampicillin is able to penetrate Gram-positive and some Gram-negative bacteria. It differs from penicillin only by the presence of an amino group. That amino group helps the drug penetrate the outer membrane of gram-negative bacteria.

Ampicillin acts as a competitive inhibitor of the enzyme transpeptidase, which is needed by bacteria to make their cell walls. It inhibits the third and final stage of bacterial cell wall synthesis in binary fission, which ultimately leads to cell lysis [6].

Table 1: Absorption, Disposition and Metabolism [7-12]

Characterstics	Penicillin	Ampicillin
Route of administration	IV, IM, PO	IV, IM, PO
Resistant Strains	M.pyogenes, Streptococcus pyogenes, or Diplococcuspneumonia, Staphylococcus aureus , *N. gonorrhoeae*	*Haemophilus influenza, Pseudomonas,Klebsiella*
Pharmacokinetic Property		
• **Oral Absorption**	PenicillinG:30% PenicillinV:60%	40%
• **Food ↓Absorption**	PenicillinG:Yes PenicillinV:No	Yes
• **%Protein Bound**	PenicillinG:55 PenicillinV:80	17
• **%Metabolism**	PenicillinG:20 PenicillinV:55	10
• **Total Concentration (µg/Ml)**	PenicillinG:2 PenicillinV:4	3.5
• **Free Concentration (µg/Ml)**	PenicillinG:0.9 PenicillinV:0.8	2.9
• **T1/2(Hrs)Normal**	PenicillinG:0.5 PenicillinV:1.0	0.5
• **T1/2(Hrs)Renal Impairments**	PenicillinG:10 PenicillinV:4	1.5

Adverse Reactions	Anaphylaxis(IgEmediated) Early urticaria (<72 h), Hemolytic anemia due to cytotoxic antibodies, Serum sickness (Ag-Ab complex disease), Neutropenia, Sodium overload, Seizures(Rare).	Delayed hypersensitivity, Contact dermatitis, Maculopapular skin rash, Fever, Late onset urticaria, Diarrhea, Enterocolitis.
Dosage	Penicillin G Potassium (250 mg = 400,000 units) Penicillin V Potassium Tablets:125,250,500 mg	Adult: 250-500mg po q6h 1-2g IV q4h Pediatric: < 1 week: 25 mg/kg IV/IM q 8-12h

Table 2: Comparison of MIC Values between Penicillin G and Penicillin V (for non-penicillinase producing strains) [13]

Organism	MIC for Pen G (µg/ml)	MIC for Pen V (µg/ml)
Staph. aureus	0.03	0.03
Strep. pyogenes	0.007	0.015
Strep. pneumoniae	0.015	0.03
Enterococcus faecalis	2.0	4.0
E. coli	64.0	128.0
Salmonella typhi	4.0	64.0
Neisseria gonorrheae	0.007	0.03
N. meningitidis	0.03	0.25
Haemophilus influenzae	1.0	4.0

Table 3: MIC Values (µg/ml) of Ampicillin vs. Gm – Bacteria [14]

Organisms	Ampicillin
Escherichia coli	3
Proteus mirabilis	3
Klebsiella sp.	200
Enterobacter spp.	>500
Citrobacter diversus	>100
Citrobacter freundii	50
Serratia	>500
Salmonella	1.5
Shigella	1.5
Proteus vulgaris	>500
Providencia	>500
Morganella	200
Pseudomonas Aeruginosa	>500
Acinetobacter	250
Pseudomonas, other	>500

CONCLUSION

Ampicillin is semi-synthetic penicillin with an additional amino chain synthesized onto the penicilin molecule. This allows the ampicillin to be effective against gram negative organisms as well as the gram positive organisms covered by penicillin. From the study, we can conclude that ampicillin better as a 'broad spectrum antibiotic'.

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