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Review Article

TIGECYCLINES: A BRIEF REVIEW

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ABSTRACT

Tigecycline is a tetracycline derivative of glycylcycline group of antibiotics. It is broad spectrum bacteriostatic antibiotics discovered with aim of fighting havoc of bacterial resistance. Its antibiotic spectrum covers almost all the bacteria including *Clostridium diffcile* and can be prescribed to immunocompromised patients suffering from cancer. The N,N-dimethyglycylamido (DMG) moiety attached to the 9-position of tetracycline ring D increases its spectrum activity. It falls under the group of protein synthesis inhibitors.

Key words: Tigecycline, glycylcycline, broad spectrum

INTRODUCTION

Tigecycline is a broad spectrum antibiotic[1,2] along with activity against drug resistant gram positive organism which is known as the first drug of glycylcycline class of antibiotics. Tigecycline is given intravenously in every 12 hours. It is a tetracycline derivative whose discovery was to combat the rising antimicrobial resistance as well as multidrug resistance.

MEDICINAL USES

Tigecycline can be used to treat complicated skin infections caused by; *E. coli*, vancomycin-susceptible *Enterococcus faecalis,* methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus agalactiae, S. anginosus* group, *S. pyogenes, Enterobacter cloacae, Klebsiella pneumoniae* and *Bacteroides fragilis*.[3]

Tigecycline is prescribed for treatment of severe intra-abdominal infections that are caused by *Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, vancomycin-susceptible Enterococcus faecalis,* methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus anginosus* grp., *Bacteroides fragilis, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens*, and *Peptostreptococcus* micros.[3] Tigecycline can be used for treatment of community-acquired bacterial pneumonia which is is caused by penicillin susceptible *Streptococcus pneumoniae, Haemophilus influenzae* and *Legionella pneumophila*.[3] Tigecycline is also recommended by European society of clinical Microbiology for *Clostridium difficile* infection.[4] Tigecycline can be used for vulnerable immunocompromised cancer patient.[4] It can be used for acute myeloid leukemia.[5]

STRUCTURE ACTIVITY RELATIONSHIP

Tigecycline is a third generation tetracycline derivative of a glycylcyclines which carry a N,N-dimethyglycylamido (DMG) moiety attached to the 9-position of tetracycline ring D.[6] Structural modifications as a 9-DMG derivative of minocycline, tigecycline improved its minimal inhibitory concentrations against Gram-negative and Gram-positive organisms, when compared to tetracyclines.[6]

MECHANISM OF ACTION

Tigecycline is broad-spectrum, bacteriostatic antibiotic and functions as the bacterial protein synthesis inhibitor. It binds to the 30S ribosomal subunit during translation process of bacteria and blocks the interaction of aminoacyl-tRNA with the A site.[7] Tigecycline is mostly bacteriostatic, but it acts as bactericidal against *S. pneumoniae* and *L. pneumophila*.[8]

PHARMACOKINETICS

Tigecyclines need dose adjustment[8] as it undergoes glucuronidation conjugation.[9]. It is primarily excreted un-metabolised in the feces and secondarily excreted through kidneys for which renal dose adjustments are not necessary.[9]

DRUG INTERACTIONS

Tigecycline with concurrent use with oral contraceptives reduces the efficacy of oral contraceptives by reducing the concentration. Tigecyclines also show interaction with warfarin when administered with it. As both Tigecycline and warfarin bind to serum plasma protein, they have the protein binding interactions.[10]

SIDE EFFECTS

Gastrointestinal symptoms are reported.[11] They also have side effects like nausea and vomiting.[12] Rare side effects such as swelling, pain and irritation in injection site is being seen. Anorexia, jaundice, hepatic dysfunction pruritus, acute pancreatitis and increased prothrombin time is also found.[8]

RESISTANCE MECHANISMS

Enterobactericeae become resistant to the Tigecyclines occur by genetic mutations resulting in the upregulation of bacterial efflux pump receptor i.e. AcrAB.[10,13]

CONCLUSION

Natural resistance to Pseudomonas bacteria occurs because of constant over expression of the efflux pump. Few *Enterobacteriaceae* species have been found to be resistant to Tigecycline due to mutations in ribosomal genes such as *rpsJ.*

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