Tigecycline: - "A novel antibiotic"

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Introduction

In the present era bugs are developing resistance against multiple drugs and research in this field to develop new antibiotics is relatively lagging behind. Medical fraternity is facing acute shortage of antibiotics acting against multi drug resistant organisms. Pathogens like methicillin resistant stroplococcus aureus (MRSA) Vancomycin resistant entcrococci (VRE) & extended spectrum Beta lactamase. (ESBL) producing gram negative baclli harbour genetic determinants, which render them resistant to most of the available anhmicrobials. Metello.B lactemase (MBL) producing pseudsmonas aeruginosa & Acinetobacter spp. have also developed resistance against carbepenam. In this scenario the development of a new class of antimicrobial agents, glycylcyclines is a significant development.

Tigecycline is the first drug in glycylcycline, a new class of semisynthetic antibiotics. It is a tetracycline analogue. Tigecycline has primary backbone of minocycline with an N-alkyl – glycyclamido group substituted at the 9 position , which gives the drug its broad spectrum activity & protection from resistance mechanisms.

Mechanism & action

Tigecycline binds to the bacterial 305 ribosome, blocking the entry of transfer RNA. This ultimately prevents protein synthesis by haulting the incorporation of amino acids in a pcptide chain & thus limit bacterial growth. The addition & N,N dimethylglycyclamido group at 9 position of minocycline molecule increases the affinity of the tigecycline for the ribosomal target upto 5 times when compared with minocycline or tetracycline. This allows expanded spectrum of activity & decreased susceptibility to the development of resistance.

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Pharmacokinetics & pharmacodynamics

- Tigecycline is administered by intravenous infusion hence has 100% bioavailability when given intravenously. It is highly protein bound & has large volume of distribution. Tigecycline is not extensively metabolised. It has eljmination half life approximately 36 hours. It is mainly eliminated unchanged in biles & faces & partly in urine.
- No dosage adjustment is required in mild and molderate hepatic impairment but patients with severe hepatic impairment should be given 100 mg loading dose followed by 25 mg 12 hourly.
- No dose adjustment is required in patient with impaired renal function or patients with ESRD on hemodialysis.

Spectrum of activity

Tigecycline has a broad spectrum of activity against many gram positive, gram negative & anaerobic organisms . Coverage includes many mulitidrug resistant strains of gram positive organisms.

In vitro activity of tigecycline against common pathogens

Gram Positive bacteria	Gram Negative bacteria
Staphylococcus Aureus **(MRSA)**	Escherichia coli
Enterococcus faecium	Klebsiella pneumoniae
Enterococcus faecalis	**Acinetobacter baumannii**
Streptococcus agaloctiae	Enterobacter cloacae
Steptococcus pneumonia	Enterobacter aerogenes
Streptococcus pyogcns	Streptrophomonas maltophilia
Anaerobic organisms	
Bacteroides fragilis	
Prevotella spp.	
Pcptostreptococcus spp.	
Clostridium perfringens	

Generally tigecycline is bacteriostatic but has shown bacteriocidal activity against S. pneumonias & H.influenza.

Indications

In order to prevent the development of resistance tigecycline should not be used rampently& used only in selected cases

- Skin & skin structure infections (cSSI)
- Complicated intraabdominal infection (cIAI)
- Study in community acquired & nosocomial preumonias

Adverse effects

- Nausea & vomiting
- Diarhoea, anorexia, dyspcpsia
- Increased rate of infections
- Hepatic toxicity (Rarely)
- Photosecnsitivity (Rarely)

Dosage & preparation

- 100mg loading dose & then 50mg every 12 hourly.

  53mg/vial + 5.3 ml NS

  5ml of above solution + 100ml 1v fluid infusion real 30 to 60 min

Contraindications

- Children below 8 year of age
- Pregnant ladies
- ? lactating mother

Drug interactions

Tigecycline does not inhibit or induce hepatic cytochrome P 450 enzyme system & hence it does not alter metabolism of drugs metebolised by this system. So there are no significant drug interaction.

Summary

Tigecycline is a novel antibiotic of present era. It has broad spectrum activity & is effective against various multidrug resistant pathogens. Presently it is indicated in cSSI & cIAI & possibly will be of great help in community acquired & nosocomial pneumonias in recent future. At present only few MDR pathogens have started showing little resistance to this drug. It is need of the day that antibiotics should be used smartly & only when indicated.

Bibliography

1. A review of tigecycline - the first

glycylcycline int. J. antimicrob Agents, 2008 Dec; 32 suppl 4:5215-22

2. Tigecycline: a critical update J.Chemother,2008 Aug;20(4):411-9

3. Livermore DM. Tigecycline: what is it, and where should it be used? J Antimicrob Chemother 2005;56:611-4.

4. Christine M Slover, PharmD Tigecycline: A Novel Broad-Spectrum AntimicrobialPublished Online, 22 May 2007,DOI 10.1345/aph.1H543. The Annals of Pharmacotherapy: Vol. 41, No. 6, pp. 965-972. DOI 10.1345/aph.1H543