Drug Review

Terizidone

Agam Vora

Terizidone is WHO categorized group IV anti TB drug.[1] It is an antibiotic effective against Mycobacterium tuberculosis and also M. avium for the treatment of tuberculosis, both pulmonary and extra pulmonary. It is classified as a second-line drug, i.e. its use is only considered if one or more first line drugs cannot be used.

Terizidone is obtained by combining two molecules of Cycloserine and one molecule of terephtalaldehyde and is a broad spectrum antibiotic which greatly improved the disadvantages associated with Cycloserine.

Terizidone has potent and extended antimycobacterial activities, and exerts remarkable effects against not only strains causing pulmonary tuberculosis or urinary tract infections but also strains which have become resistant to existing antimycobacterial drugs.

Mechanism of Action

Its mode of action is similar to Cycloserine i.e. It acts by inhibiting cell wall synthesis by competitively inhibiting two enzymes, L-alanine racemase and D-alanine ligase, thereby impairing peptidoglycan formation necessary for bacterial cell wall synthesis.

Although, being broad spectectrum, the molecule in principle active against other bacteria as well, terizidone is not recomanded for use in the treatment of infections other than tuberculosis.

Pharmacokinetics

MICs of Terizidone for susceptible strains are 4-130 mg/ml.

Terizidone is completely and rapidly absorbed after oral administration. Maximum concentration in blood are achieved in 2 to 4 hrs. It was noted that the blood concentration of Terizidone was higher at all time intervals than the concentration attained in the blood after the same doses of Cycloserine.

Excretion in urine is quicker in the young ones. Its concentration in the urine after 30 hr administration sufficiently exceeded its minimum inhibitory concentration. This justifies its use in the treatment of urogenital TB. It was found that the increase in the dose does not cause a proportional increase in the concentration of the drug in the blood. It is well distributed in all body fluids and tissues.

The half-life of Terizidone was significantly greater than that of Cycloserine with doses of 250 mg and 500 mg. Also, it was significantly higher in the elderly than the young patients. The molecule does not have cumulative toxicity and hence better tolerability.

Indication

Terizidone capsules of 250 mg each is recommended for tuberculosis both pulmonary or extra pulmonary by resistant strains of Mycobacterium tuberculoisis or avium. It is not recomanded for use as monotherapy for infections with tuberculosis. As it has higher concentrations in urine it makes it a better choice of drug for urogenital tuberculosis, specially bladder and epididymoorchitis. It may also be a drug of choice for patients with psychiatric comorbidity. Also it may be of use in cases where drug-induced psychiatric disturbances limits the use of cycloserine. Also it may be advantageous in cases of chronic alcoholism and schizophrenia.

No toxic reactions were observed with Terizidone which are quite common with cycloserine even on prolonged therapy with the drug. Also unlike cycloserine it does not have hypotensive effect. Terizidone was found to be better tolerated in drug-resistant cases of tuberculosis requiring dialysis.[2]

Precausions and contraindications

It is to be used with caustion in pateins with psychitric comorbidities and epilepsy. Also patients who are intolerant to cycloserine.

Adverse effets

Terizidone intensifies the activating effect on ascending section of the reticular formation of brainstem and increase in overall reaction of brain but lower than cycloserine. Dizziness, slurred speech, headache and convulsions are amongst the few reported side effects. Others include tremors, insomnia, confusion, depression. The most dangerous side effects is suicidal tendency.

Nausea, vomiting, skin allergies and rashes are also reporeted. When used in higher doses that is more than 1 gm per day liver function disorders, congestive cardiac failure, convulsions and coma are reported.

Dosage and administartion :

It is available as hard gelatine capsule of 250 mg each. The usual adult dose ia 15 – 20 mg/kg per day in three to four divided doses. Maximum recomanded dose is 4 capsules a day ie 1 gm daily.

Advantages over cycloserine

1. the reported adverse events are far lesser than cycloserine (1% v/s 11 %).[3]
2. it is better tolerated in patients of drug resistant TB requiring dialysis.
3. Because of its better tolerability it leads to better compliance and better treatment outcomes.
4. In children it is found to be more effective than cycloserine.[4]
5. Better tolerated in patients with psychitric co morbidity or drug-induced psychiatric manifestation.
6. It does not produce hypotension.
7. Terizidone maintains higher concentration in blood and

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urine and also these levels are maintained for a longer duration.

8. It has lower MIC than cycloserine for M. tuberculosis and is better tolarated in elderly.

Place in Treatment

It can be considered in the treatment of drug resistant TB both in intensive and continuation phase. It has efficacy similar to that of Cycloserine but has much lesser side effects and also it has advantage of usefulness in schizophrenics and alcoholics and with its higher concentration in urine it may be a better option for urogenital TB.

References

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4. T. Chrapowicki. Uroxalidin administered in children. Praxis, 1974;63(23), 713