MEDIBEATS
The Medical Bulletin

Drug Corner

Typhoid fever is caused by Gram negative flagellated rod shaped bacteria known as salmonella typhi, which has a polysaccaharide capsule that deceives the host immune system by preventing phagocytosis. The mortality rate with Salmonellosis was around 15% until the introduction of Chloramphenicol in 1948 that reduced the mortality rate to <1%.There is increasing evidence of the incidence of XDR salmonella typhi. The plasmid mediated resistance to chloramphenicol was documented in 1970 and since there was also an increased chronic carrier state and bone marrow toxicity with chloramphenicol,Ampicillin and Trimethoprim-Sulphamethoxazole were the preferred choice.

In 1989,the organism became Multi drug resistant with resistance conferring to chloramphenicol, ampicillin, trimethoprim-sulphamethoxazole (TMP-SMZ), streptomycin, sulfonamides and tetracycline. This resistance is also plasmid encoded.The MDR was athreat in high prevalence areas including Indian subcontinent, Southeast Asia and Africa.Quinolones (ciprofloxacin & ofloxacin)have become the popular choice as it effectively penetrates the macrophages and achieve high concentration in the bowel and bile lumen also targeting the carrier state.Due to extensive inappropriate usage of Quinolones for Typhoid fever,the organism became partially resistant and there was introduction of 3rd generation Cephalosporins that include Cefotaxime, Ceftrioxone and Cefaperazone as short course therapy of 3 days

MDR resistance pattern is often associated with the dominant H58 haplotype.The transfer of Antimicrobial Resistance(AMR) genes between bacteria is commonly facilitated by either plasmid or transposon.In H58,the AMR genes are associated with IncHI1 plasmid that harbour a composite transposon which include multiple resistance genes namely bla-TEM-1 (Ampicillin resistance), dfrA7, sul1, sul2(TMX-SMZ) and catA1(chloramphenicol).Ceftrioxone resistance was predominantly due to acquisition of ESBL gene probably from E.coli due to inappropriate Antibiotic use.Multiple QRDR single nucleotide polymorphism and plasmid mediated quinolone resistance resulted in Fluoroquinolone resistance.The preferred combination for treating XDR salmonellosis would be either azithromycin or meropenem alone or in combination.

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