Evaluation of *In Vitro* Synergy Testing of South African Invasive *Salmonella* Typhi Isolates Using the Liofilchem® MTS Application System

Arvinda Sooka, Karen H. Keddy

National Institute for Communicable Diseases

Background: The recommended treatment in South Africa for invasive *Salmonella enterica* subspecies Typhi (*Salmonella* Typhi) infections is ciprofloxacin, or alternatively azithromycin or ceftriaxone. Combination therapy with an aminoglycoside and a cephalosporin was used before the introduction of the fluoroquinolones. The objective of this study was to explore a novel method to evaluate combination therapy *in vitro* to aid therapeutic options for typhoid fever. Synergy testing of current antibiotics for usage against typhoid fever was evaluated by *in vitro* testing of two antibiotics, by determining the cross gradient with minimum inhibitory concentration (MIC) strips.

Methods: Synergy testing of twenty-five clinical invasive *Salmonella* Typhi strains was undertaken using Liofilchem® MIC strips. Antibiotic combinations included ciprofloxacin against ampicillin, amikacin, azithromycin, chloramphenicol, ceftriaxone and streptomycin. Isolates were sub-cultured onto Mueller Hinton agar and the MIC strips placed according to the manufacturer's instructions. MIC values were initially determined against single antimicrobials listed above. Ciprofloxacin strips were aligned at 90 degrees to the antibiotics listed at the point of the respective MIC for each isolate against each antimicrobial. A fractional inhibitory concentration index (FIC) calculation was used to interpret synergistic, additive, indifference and antagonistic interactions.

Results: Of the 25 isolates, six FIC values were obtained for each isolate (150 in total). Synergy was seen in 24% (36/150) of combinations, additive inhibitions in 30.6% (46/150), indifference in 34.7% (52/150) and antagonism 10.6% (16/150). Ciprofloxacin and amikacin and ciprofloxacin and streptomycin were the most active combinations.

Conclusions: The MTS method proved to be useful in obtaining rapid results and was easy to use. Combination therapy may be an alternative for treatment of *Salmonella* Typhi infections resistant to one or more of the recommended antimicrobials in South Africa.