

E-TEST METHOD FOR DETECTING ANTIBIOTIC SYNERGY AGAINST *PSEUDOMONAS AERUGINOSA* FROM NEUTROPENIC PATIENTS: A COST-EFFECTIVE APPROACH

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SUMMARY

The aim of this study was to evaluate the accuracy of E-test for the detection of synergy or antagonism of antibiotic combinations against *Pseudomonas aeruginosa* isolates from neutropenic patients. The activity of levofloxacin or grepafloxacin combined with ceftriaxone or cefotaxime against 20 *P. aeruginosa* clinical strains was assessed by checkerboard technique in comparison with results performed by E-test. The combination grepafloxacin + ceftriaxone appeared to be most effective (synergy, 55%) by checkerboard technique. The agreement between checkerboard and E-test results was 71.2%.

Synergy was detected by checkerboard and E-test methods in 35 (43.8%) and 23 (31.3%) of 80 possible combinations, respectively. Antagonism was detected once (1.2%) by checkerboard method only. No major errors were recorded. E-test was preferable to checkerboard method for the total cost (reagent cost + cost of technologist time) (8,60 vs 21,80 euros/test, respectively). E-test appeared a promising alternative for testing antibiotic combinations although further testing should be performed to better refine this methodology.

KEY WORDS: *Pseudomonas aeruginosa*, E-test, synergy, checkerboard, neutropenic, cost-analysis

Received March 22, 2004

Accepted June 3, 2004

INTRODUCTION

Pseudomonas aeruginosa is recognized as one of the leading causes of severe hospital-acquired infections, determining significant morbidity and mortality, especially in cancer patients (Chatzinikolaou *et al.*, 2000; Spencer, 1996). However, the use of empirical therapy with broad-spectrum combinations of antibiotics has led to a dramatic decrease of mortality over the last three decades. Currently, in the treatment of *P. aeruginosa* infections combination antibiotic therapy including beta-lactam agents and aminoglycosides is widely used (Rolston, *et al.*, Solberg and Sjrursen, 1995). Although these antibiotic

combinations are clinically well proven to provide effective treatment, the increasing resistance of *P. aeruginosa* to beta-lactam and aminoglycoside antibiotics and the toxicity associated with aminoglycoside therapy necessitate a continuous search for new antibiotic combinations (Gould and Milne, 1997; Kolar *et al.*, 1999).

Combination of fluoroquinolones with other antimicrobial agents has been investigated extensively. However, few studies have to date evaluated the efficacy of combinations including levofloxacin against *P. aeruginosa* (Isemberg *et al.*, 1999; Visalli *et al.*, 1997; Visalli *et al.*, 1998). No data exist concerning grepafloxacin. Numerous methods have been proposed to detect