primary studies - published RCT

Microbiological and immunologic considerations with aerosolized drug delivery.

Code: PM11555566 **Year:** 2001 **Date:** 2001 **Author:** LiPuma JJ

Study design (if review, criteria of inclusion for studies)

randomized, placebo-controlled, double-blind study

Interventions

standard cystic fibrosis (CF) care to placebo plus standard CF care

Outcome measures

percentage of patients with at least one Pseudomonas aeruginosa (PA) strain with a minimal inhibitory concentration (MIC) > 16 microg/mL (ie, the breakpoint for tobramycin resistance delivered by the parenteral route); changes in the levels of the lowest concentration required to inhibit the growth of 50% of strains tested (MIC(50)) and 90% of strains tested (MIC(90)); the percentage of patients with an increase, decrease, or change in the MIC of the most resistant and most prevalent PA strains; and the percentage of patients in whom the PA strain with the highest MIC also was the most prevalent

Main results

During the first 6 months, which included three on-drug and off-drug cycles of 4 weeks' duration each, the percentage of tobramycin-treated patients with at least one PA isolate and with an MIC > 16 microg/mL was 13% at baseline, 26% at 20 weeks, and 23% at 24 weeks vs 10%, 17%, and 8%, respectively, for placebo-treated patients. No significant change was observed in MIC(50) at 20 and 24 weeks. The increase in MIC(90) was not statistically significant. At 24 weeks, there was no increase in the percentage of patients in either group in whom the PA strain with the highest MIC became most the prevalent strain. After the third on-drug cycle, 33% of the tobramycin group showed an increase in the MIC of the strain with the highest MIC. This decreased to 26% after 1 month off drug therapy. A preliminary analysis of the 12-month and 18-month data showed a decrease in the proportion of resistant PA isolates after each off-drug cycle. This return to susceptibility following an off-drug cycle was not observed at 24 months. The mechanism of resistance in this setting is believed to be increased impermeability to drug. At all time points, pulmonary function improved even in patients with MICs of > or = 128 microg/mL. At 6 months, no increase was seen in the rates of superinfection with tobramycin-resistant, Gram-negative pathogens. Increases in Stenotrophomonas maltophilia were detected in patients after 18 and 24 months of tobramycin therapy and were similar to those rates in patients receiving placebo.

Authors' conclusions

These rates may be independent of inhalation therapy.

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See also

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Keywords

Anti-Bacterial Agents; Bacterial Infections; Child; Drug Administration Schedule; Infection; Inhalation OR nebulised; nebuliser; non pharmacological intervention - devices OR physiotherapy; pharmacological_intervention; Pseudomonas aeruginosa; Pseudomonas; Respiratory Tract Diseases; Respiratory Tract Infections; Stenotrophomonas Maltophilia; Tobramycin; Aminoglycosides;