primary studies - published RCT

No detectable improvements in cystic fibrosis transmembrane conductance regulator by nasal aminoglycosides in patients with cystic fibrosis with stop mutations.

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

multicenter randomized, double-blinded, crossover and parallel study; two cohorts of patients with CF.

Participants

11 CF patients with stop mutations were enrolled in a crossover fashion to receive each drug; 18 CF patients without stop mutations were randomized 1:1 in a parallel fashion to receive one drug.

Interventions

gentamicin and tobramycin administered over a 28-d period

Outcome measures

Primary aim was to test whether nasally administered gentamicin or tobramycin could suppress premature stop mutations in CFTR, resulting in full-length, functional protein. A secondary objective was to obtain data to aid in the design of multicenter trials using the nasal potential difference as a study endpoint.

Main results

After demonstration of drug delivery, neither aminoglycoside produced detectable changes in nasal ion transport or CFTR localization in brushed cells from either study group. These results with first-generation suppressive agents suggest the need for improved drug delivery methods and/or more potent suppressors of nonsense mutations to confer CFTR correction in subjects with CF heterozygous for nonsense mutations.

Authors' conclusions

The study provides valuable information on parameters of the nasal potential difference measurements for use in future multicenter clinical trials.

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See also

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Keywords

Adolescent; Adult; Aminoglycosides; Anti-Bacterial Agents; Child; CFTR Modulators; Genetic Predisposition to Disease; Gentamicin; Heterozygote; Intranasal; pharmacological_intervention; Tobramycin; transmembrane; Bacterial Infections; Respiratory Tract Infections; Respiratory Tract Diseases; Infection;