primary studies - published, non RCT

Aerosol and lobar administration of a recombinant adenovirus to individuals with cystic fibrosis. I. Methods, safety, and clinical implications.

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

The effects of adenovirus-mediated CFTR gene transfer to airway epithelium in 36 subjects with CF (34 individuals, 2 of whom received two separate doses of vector), 20 by lobar instillation and 16 by aerosol administration were evaluated. Doses ranged from 8 x 10(6) to 2.5 x 10(10) infective units (IU), in 0.5-log increments.

Participants

36 subjects with CF (34 individuals, 2 of whom received two separate doses of vector), 20 by lobar instillation and 16 by aerosol administration.

Interventions

adenovirus-mediated CFTR gene transfer to airway epithelium by lobar instillation and by aerosol administration. Doses ranged from 8 x 10(6) to 2.5 x 10(10) infective units (IU), in 0.5-log increments.

Outcome measures

clinical symptoms, sputum production, pulmonary function, serum IgG or neutralizing antibodies. Serum, sputum, and nasal cytokines. Cells infected with the vector

Main results

After lobar administration of low doses there were occasional reports of cough, low-grade temperature, and myalgias. At the highest lobar dose (2.5 x 10(9) IU) two of three patients had transient myalgias, fever, and increased sputum production with obvious infiltrates on CT scan. After aerosol administration there were no significant systemic symptoms until the 2.5 x 10(10) IU dose, when both patients experienced myalgias and fever that resolved within 24 hr. There were no infiltrates seen on chest CT scans in any of the patients in the aerosol administration group. There were no consistent changes in pulmonary function tests or any significant rise in serum IgG or neutralizing antibodies in patients from either group. Serum, sputum, and nasal cytokines, measured before and after vector administration, showed no correlation with adenoviral dose. Gene transfer to lung cells was inefficient and expression was transient. Cells infected with the vector included mononuclear inflammatory cells as well as cuboidal and columnar epithelial cells.

Authors' conclusions

No consistent immune response, no evidence of viral shedding, and no consistent change in pulmonary function in response to adenovirus-mediated CFTR gene transfer were found. At higher doses there was a mild, nonspecific inflammatory response, as evidenced by fevers and myalgias. Overall, vector administration was tolerated but transfer of CFTR cDNA was inefficient and transgene expression was transient for the doses and method of administration used here.

http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/732/CN-00385732/frame.html

See also

Human Gene Therapy YR: 2001 VL: 12 DE: CCT NO: 11

Keywords

Inhalation OR nebulised; pharmacological_intervention; Recombinant Proteins; Gene Transfer Techniques; non pharmacological intervention - genetic& reprod; Instillation- Drug;