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Neonatal screening for cystic fibrosis

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

Randomised controlled studies comparing topical CFTR gene delivery to the lung, using either viral or non-viral delivery systems, with placebo or an alternative delivery system.

List of included studies (4)

Alton 1999; Alton 2015; Moss 2004; Moss 2007

Participants

Children and adults with CF confirmed by the presence of two disease-causing mutations, or by a combination of positive sweat test and recognised clinical features of CF.

Interventions

CFTR gene replacement therapy

Outcome measures

Adverse events; Change in FEV1 % predicted from baseline; Change in FEV1 (L) from baseline; Change in FVC; Change in validated computerised tomogram (CT) score; Lower airway potential difference change from baseline; Lower airway potential difference change from baseline (amiloride and low chloride); Measurement of CFTR protein expression (SPQ chloride efflux); Number of inpatient episodes; Respiratory exacerbations (episodes)

Main results

Four randomised controlled studies met the inclusion criteria for this review, involving a total of 302 participants lasting from 29 days to 13 months; 14 studies were excluded. The included studies differed in terms of CFTR gene replacement agent and study design, which limited the meta-analysis. One study only enrolled adult males, the remaining studies included both males and females aged 12 years and over. Risk of bias in the studies was moderate. Random sequence generation and allocation concealment was only described in the more recent study; the remaining three studies were judged to have an unclear risk of bias. All four studies documented double-blinding to the intervention, but there is some uncertainty with regards to participant blinding in one study. Some outcome data were missing from all four studies. There were no differences in either the number of respiratory exacerbations or the number of participants with an exacerbation between replacement therapy or placebo groups at any time point. Meta-analysis of most respiratory function tests showed no difference between treatment and placebo groups, but the smallest study (n = 16) reported forced vital capacity (litres) increased more in the placebo group at up to 24 hours. A further study reported a significant improvement in forced expiratory volume at one second (litres) at 30 days after participants had received their first dose of favouring the gene therapy agent, but this finding was not confirmed when combined with at second study in the meta-analysis. The more recent study (n = 140) demonstrated a small improvement in forced vital capacity (per cent predicted) at two and three months and again at 11 and 12 months for participants receiving CFTR gene replacement therapy compared to those receiving placebo. The same study reported a significant difference in the relative change in forced expiratory volume at one second (per cent predicted) at two months, three months and 12 months. One small study reported significant concerns with "influenza-like" symptoms in participants treated with CFTR gene replacement therapy; this was not reported on repeated use of the same agent in a larger recent study. There was no other evidence of positive impact on outcomes, in particular improved quality of life or reduced treatment burden. Two studies measured ion transport in the lower airways; one (n = 16) demonstrated significant changes toward normal values in the participants who received gene transfer agents (P

Authors' conclusions

One study of liposome-based CFTR gene transfer therapy demonstrated some improvements in respiratory function in people with CF, but this limited evidence of efficacy does not support this treatment as a routine therapy at present. There was no evidence of efficacy for viral-mediated gene delivery. Future studies need to investigate clinically important outcome measures.

http://www.gezondheidsraad.nl/sites/default/files/201001E.pdf

See also

The Hague: Health Council of the Netherlands Gezondheidsraad (GR) YR: 2010

Keywords

Gene Transfer Techniques; non pharmacological intervention - genetic& reprod; pharmacological_intervention; transmembrane;