Hypertonic saline nebulisation for pulmonary disease in people with cystic fibrosis

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In people with cystic fibrosis (CF), a defective protein (CFTR) in the airway epithelial cells disrupts the homeostasis of sodium and chloride ions on the airway surface. The resulting dehydration of the airway surface disrupts the normal mucociliary clearance of mucus from the airways. The retained mucus traps inhaled infectious organisms, which causes chronic lung infection and inflammation, which eventually prgresses to respiratory failure.

Nebulized hypertonic saline improves sputum transportability, airway hydration, mucociliary clearance, and ease of expectoration. It may also affect *P. aeruginosa* motility and the viability of the mucoid sub-population in biofilms.

Short-term use of hypertonic saline improves lung function and a benefit in lung function is maintained with long-term twice-daily nebulizations. Other benefits of long-term use include fewer respiratory exacerbations, less absenteeism, and improved quality of life. Although chronic twice-daily nebulizations is laborious, fast nebulizers can now deliver the saline in about 5 minutes and the faster delivery does not appear to reduce the tolerability of the treatment.

When people with CF are admitted to hospital for management of an exacerbation of their respiratory disease, this typically consists of intravenous antibiotics, intensive physiotherapy for airway clearance, and nutritional support. If hypertonic saline is nebulized three-times daily in addition to this standard care, patients will show significantly faster resolution of their symptoms and significantly greater restoration of their lung fuction. This may lead to a reduced length of stay in hospital, although once a course of antibiotics is commenced, a minimum duration is recommended so the potential to shorten length of stay is limited by this.

A recent multi-centre randomized trial of hypertonic saline *versus* placebo in children with CF between the age of 4 and 60 months showed a non-significant trend of benefit in the primary endpoint, which was pulmonary exacerbations. A subgroup of patients underwent infant pulmonary function testing and this showed a significant benefit from hypertonic saline. Some other secondary outcomes also showed some benefit. Safety outcomes included the rate of intolerance to the test dose of HS at enrolment, adverse events and withdrawal rates, and treatment emergent respiratory cultures positive for CF pathogens. Tolerability of the first dose was good and withdrawals through the course of the trial were low in both groups (9% in the HS group and 7% in the IS group). Other stafety outcomes were reassuring.