Hypertonic Saline

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Introduction

The airway surface liquid (ASL) is normally kept at the height of the cilia (the hair-like projections) that line the airways. These beat in a synchronised fashion to clear the lungs of debris and keep them free of infection. This mechanism is referred to as mucociliary clearance and the process as the mucociliary escalator. Dysfunction of the cystic fibrosis transmembrane conductance regulator (CFTR) protein results in failure of chloride movement across the airways’ apical cell surfaces and excess movement of sodium into the cells. Water passively follows the movement of sodium, reducing the volume of the ASL. This is one reason for the excess viscosity (stickiness) of the airway mucus and the failure of the lungs’ self cleansing mechanism, the mucociliary clearance, to work effectively. The retained, viscous mucus is a focus for infection (Elkins & Bye, 2006; Enderby & Doull, 2007).

Mechanism of action

Hypertonic saline inhalation increases the ion concentration in the ASL and osmotically draws fluid into the airway lumen, thereby replenishing the fluid layer and accelerating mucus clearance (Robinson et al, 1997).

The lungs in CF are full of neutrophil white blood cells that migrate into the lungs in response to infection. When these cells die they release their own DNA that binds with mucoprotein in the airways. This increases sputum viscosity by protecting the mucoprotein from being broken down and expelled from the lung. Hypertonic saline separates the DNA/mucoprotein complex allowing normal degradation of the latter.

Inhalation of hypertonic saline usually causes coughing. This aids mucus clearance by stimulating large shear stresses and promoting the separation of mucus plaques from the airway walls.

Effectiveness of treatment

Long term and regular use results in a sustained increase in mucociliary clearance, a slight increase in respiratory function, less frequent respiratory exacerbations and better quality of life (Elkins & Bye, 2006; Donaldson et al, 2006). These are important outcome parameters in CF but should be assessed in the following context: although in these studies more than 75% of patients had *P. aeruginosa* infection, less than 15% were taking inhaled antibiotics, few patients were receiving oral antibiotics, confidence intervals for improvements in FEV1 in the active and placebo arms overlapped at all times, there was no fall in lung function in the control group suggesting that the combination of isotonic saline and salbutamol was not a placebo, and most of the trial patients were adults (Ratjen, 2006; Enderby & Doull, 2007). The Cochrane Systematic Review had previously concluded that there was not sufficient evidence to recommend hypertonic saline for routine treatment in CF (Wark et al, 2005).

Hypertonic saline was compared to alternate day and daily rhDNase in a prospective, open labelled, crossover trial in children (Suri et al, 2002). Patients were allocated treatment, in random order over consecutive 12 week periods. Hypertonic saline was significantly less effective than rhDNase.

Patient tolerance

For some patients the coughing bouts precipitated by inhalation of hypertonic saline preclude its use. Patients may also suffer bronchoconstriction, especially if they have a history of asthma. Cough, chest tightness and pharyngitis may resolve after a few doses or after a temporary break in treatment. Some patients cannot tolerate the salty taste. Overall about 8% of patients are not able to tolerate treatment (Elkins & Bye, 2006).

Practicalities of treatment
Bronchodilator inhalation is recommended for all patients before administration of hypertonic saline. Patients should have an initial supervised test dose with pre and post dose monitoring of lung function.

Patients do not like inhalation of large volumes (=10 mls) or frequent (>4) inhalations (Donaldson et al, 2006). The relative importance of variations in saline volume and inhalation frequency are not fully understood and have not been subject to direct comparison in clinical trials. With greater concentrations mucus clearance is increased but at the expense of an increase in adverse events.

Administration of 10 mls of 7% hypertonic saline twice daily increased FEV1 by 12% with a delivery time up to 84 minutes daily (Ballmann & von der Hardt, 2002; Wark et al, 2005). Administration of 4-5 mls twice daily increased FEV1 by 3% with a delivery time of about 40 minutes daily (Suri et al, 2002; Elkins et al, 2006). Treatment with hypertonic saline is a significant additional burden for the patient. Faster delivery with the new nebuliser systems is being studied (Elkins & Bye, 2006).

Key points

- The low volume of ASL in the CF airway interferes with mucociliary clearance and predisposes to endobronchial infection
- Hypertonic saline restores the ASL volume, allows normal degradation of mucoprotein, and aids mucus clearance by stimulating coughing
- Data showing that treatment produces a slight increase in respiratory function, a reduction in respiratory exacerbations and a better quality of life may not be applicable to our patient population
- Additional treatment with hypertonic saline is a significant extra burden for the patient
- Patients should be individually assessed for treatment
- All patients should inhale a bronchodilator before hypertonic saline administration

References


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