

Timing of hypertonic saline inhalation for cystic fibrosis

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

Randomized and quasi-randomized trials. Any trial of hypertonic saline in people with cystic fibrosis where timing of inhalation was the randomised element in the study protocol with either: inhalation up to six hours before airway clearance techniques compared to inhalation during airway clearance techniques compared to inhalation up to six hours after airway clearance techniques; or morning compared to evening inhalation with any definition provided by the author.

List of included studies (3)

Dentice 2012; O'Neill 2016; Van Ginderdeuren 2011

Participants

People of all ages and of both sexes with CF diagnosed by genetic testing or evidence on sweat chloride or nasal potential difference, including all degrees of disease severity.

Interventions

Nebulised hypertonic saline, where timing of inhalation was the randomised element in the study protocol: 1. hypertonic saline inhalation up to six hours before airway clearance techniques, compared to inhalation during airway clearance techniques; 2. hypertonic saline inhalation up to six hours before airway clearance techniques, compared to up to six hours after airway clearance techniques; 3. hypertonic saline inhalation during airway clearance techniques, compared to up to six hours after airway clearance techniques; 4. morning compared to evening inhalation with any definition provided by the author.

Outcome measures

Primary outcomes: 1. Lung function (absolute change and change in per cent predicted if possible, otherwise final values) i) forced expiratory volume at one second (FEV1) ii) forced vital capacity (FVC) 2. Patient-reported outcomes i) measures of quality of life (QoL) ii) symptom scores (including cough, tolerability, subjective ease of clearance, or treatment satisfaction)

Main results

The searches identified 104 trial reports which represented 51 trials, of which three cross-over trials (providing data on 77 participants) met our inclusion criteria. We present three comparisons: inhalation before versus during airway clearance techniques; inhalation before versus after airway clearance techniques; and inhalation during versus after airway clearance techniques. One trial (50 participants), given its three-arm design, was eligible for all three comparisons. No trials compared morning versus evening inhalation of hypertonic saline. The evidence from the three trials was judged to be of low quality downgraded for limitations (high risk of bias due to blinding) and indirectness (all participants are adults, and therefore not applicable to children). Intervention periods ranged from one treatment to three treatments in one day. There were no clinically important differences between the timing regimens of inhaling hypertonic saline before, during or after airway clearance techniques in the mean amount of improvement in lung function or symptom scores (77 participants), with the between-group comparisons being non-significant (low-certainty evidence). While there may be little or no difference in the rating of satisfaction when hypertonic saline was inhaled before versus during the airway clearance techniques (64 participants) (with the 95% confidence interval including the possibility of both a higher and lower rating of satisfaction), satisfaction may be lower on a 100-mm scale when inhaled after the airway clearance techniques compared to before: mean difference (MD) 20.38 mm (95% confidence interval (CI) 12.10 to 28.66) and when compared to during the techniques, MD 14.80 mm (95% CI 5.70 to 23.90). Perceived effectiveness showed similar results: little or no difference for inhalation before versus during airway clearance techniques (64 participants); may be lower when inhaled after the airway clearance techniques compared to before, MD 10.62 (95% CI 2.54 to 18.70); and also when compared to during the techniques, MD 15.60 (95% CI 7.55 to 23.65). There were no quality of life or adverse events reported in any of the trials.

Authors' conclusions

Timing of hypertonic saline inhalation makes little or no difference to lung function (low-certainty evidence). However, inhaling hypertonic saline before or during airway clearance techniques may maximise perceived efficacy and satisfaction. The long-term efficacy of hypertonic saline has only been established for twice-daily inhalations; however, if only one dose per day is tolerated, the

time of day at which it is inhaled could be based on convenience or tolerability until evidence comparing these regimens is available. The identified trials were all of very short intervention periods, so longer-term research could be conducted to establish the effects arising from regular use, which would incorporate the influence of changes in adherence with long-term use, as well as generating data on any adverse effects that occur with long-term use.

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See also

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Keywords

Drug Administration Schedule; hydration; Hypertonic Solutions; Inhalation OR nebulised; pharmacological_intervention; Respiratory System Agents;