

Review

The clinical use of mechanical insufflation-exsufflation in children with neuromuscular disorders in Europe

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Educational aims

The reader will be able:

- To report the mechanical insufflation-exsufflation settings actually being used in European children with NMD, highlighting a considerable variation.
- To provide an overview of variable use of modes across all ages, and how the settings for in- and exsufflation time and pressure alter with age but not between diagnoses in the same age group.
- To discuss the use of symmetric and asymmetric time and pressure settings as this may provide enhanced possibilities to individualize the treatment.
- To consider the reported settings in clinical use which may assist when titrating the MI-E settings in children with NMD.

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ABSTRACT

Mechanical insufflation-exsufflation (MI-E) is a strategy to treat pulmonary exacerbations in neuromuscular disorders (NMDs). Pediatric guidelines for optimal setting titration of MI-E are lacking and the settings used in studies vary. Our objective was to assess the actual MI-E settings being used in current clinical treatment of children with NMDs and a survey was sent in July 2016 to European expertise centers. Ten centers from seven countries gave information on MI-E settings for 240 children aged 4 months to 17.8 years (mean 10.5). Settings varied greatly between the centers. Auto mode was used in 71%, triggering of insufflation in 21% and manual mode in 8% of the cases. Mean (SD) time for insufflation (Ti) and exsufflation (Te) were 1.9 (0.5) and 1.8 (0.6) s respectively, both ranging from 1 to 4 s. Asymmetric time settings were common (65%). Mean (SD) insufflation (Pi) and exsufflation (Pe) pressures were 32.4 (7.8) and -36.9 (7.4), ranging 10 to 50 and -10 to -60 cmH₂O, respectively. Asymmetric pressures were as common as symmetric. Both Ti, Te, Pi and Pe increased with age ($p < 0.001$). In conclusion, pediatric MI-E settings in clinical use varied greatly and altered with age, highlighting the need of more studies to improve our knowledge of optimal settings in MI-E in children with NMDs.

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Abbreviations: NMD, neuromuscular diseases; MI-E, mechanical insufflation-exsufflation; PCF, peak cough flow; Ti, insufflation time; Te, exsufflation time; Tp, pause time; Pi, insufflation pressure; Pe, exsufflation pressure.

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Introduction

Children with neuromuscular disorders (NMDs) often have impaired ability to cough, causing respiratory complications. The use of mechanical insufflation-exsufflation (MI-E) is a strategy to treat respiratory tract infections, as it increases peak cough flow (PCF) [1,2], thus removes bronchial secretion. MI-E settings such

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as in- and exsufflation times and pressures and inspiration flow can be titrated.

The respiratory physiology of children is characterized by small breathing volumes and narrow and soft airways. In addition there is a reported high thoracic compliance in small children with NMDs [3], which alters with age and becomes decreased as the children become adults [4]. In pediatric mechanical ventilation, these factors are considered when titrating settings, as it also should impact our clinical choice of MI-E settings.

A wide range of settings have been used in pediatric MI-E studies [1,5–18], possibly adapted from adult studies. To our knowledge, neither guidelines nor evidence of optimal MI-E settings for infants and children are available. On this background, we aimed to assess the currently clinically used MI-E settings in the treatment of children with NMDs. Secondly, we aimed to investigate if the used settings altered with age and diagnosis of the child.

Materials and methods

A survey requesting representative anonymous MI-E settings for children with NMDs (<18 years), was sent in July 2016 to 15 European centers with expertise in long term mechanical ventilation. Data requested were diagnosis, age, PCF, and primary settings of insufflation and exsufflation times (Ti and Te), pressures (Pi and Pe), the mode (Manual/Auto), use of triggering function or Pause time (Tp), and the inspiratory flow.

Continuous normal distributed variables are presented as mean and standard deviation (SD) or 95% confidence intervals [95% CI], and categorical variables as counts and percentages (*n*;%). To assess the relationship between age and settings, the subjects were divided into four age spans (0–2, 3–6, 7–12 and 13–17 years). Statistical comparisons between groups were made using analysis of variance (ANOVA) and analysis of correlation was made using the Pearson two tailed test. The significance level was set at 0.05. Statistical analyses were conducted using SPSS v 23.0 (IBM, Armonk, USA). As the requested data were anonymous the institutional data protection authority denied need for informed consent and approval from an ethical board.

Theory

The MI-E can be used in different modes and wide range of settings has been used in the sparse published studies concerning MI-E. It has been shown benefits even with the use of low pressures (± 15 cmH₂O) (1), but also improvement of PCF with increasing symmetric in- and exsufflation pressure (± 40 cmH₂O) [7]. Some studies advocate the use of high pressures (± 40 up to 60 cmH₂O) [10], also in infants [5]. Reported time settings vary from the use of slow rate with an automatic mode (2–4 s inspiration and 4–5 s expiration) [6], to the use of manual mode at rapid rate in infants [12,19]. Further, in an infant lung model study, sufficient insufflation time and exsufflation pressure were most important for an effective PCF [20]. Despite increasing use in the clinics and recommendation to use MI-E for airway clearance in NMD in guidelines [21–26], it remains unclear how to titrate the treatment parameters and to give recommendations for use in stable state and during airway infections.

Results

Subject characteristics

Ten centres from the following countries (number of cases) answered the survey: Belgium (34), England (40), Italy (99), Netherlands (16), Norway (29), Spain (14) and Sweden (8), resulting in 240 cases.

The most common diagnoses were Spinal muscular atrophy (SMA) type 1–3, including SMA with respiratory distress (SMARD) (49%), congenital myotonies and dystrophies (24%) and Duchenne Muscular Dystrophy (DMD) (22%) [Fig. 1].

Age ranged from 4 months to 17.8 years, the mean value was 10.5 years (5.1). PCF (*n* = 134) ranged from 0 to 300 l/min with a mean value of 132 l/min (62.9). Interfaces (*n* = 150) were mask (87%) and trach (13%).

MI-E settings

The modes (*n* = 233) used were: 'Auto' with preset pause (71%), triggering of the insufflation (21%) and 'Manual' mode with assistant controlled timing (8%). All modes were used across all ages. Two centers used preset settings (Ti/Te–2/2 s or 2/3 s and Pi/Pe of 35–45/–35–45) for all children regardless of age and diagnosis. In spite of this the mean in- and exsufflation times and pressures all increased with age ($p < 0.001$) [Fig. 2]. The values are presented in Table 1. The mean Tp was 1.3 s (0.5), ranging from 0 to 3.0 s.

The time settings (*n* = 228) were asymmetric in 148(65%) cases; 81 individuals having longer Ti than Te. The pressure settings (*n* = 240) were asymmetric in 121(50%) cases with higher Pe than Pi in 116 cases. A positive relationship was found between Ti and Te ($r = 0.483$; $p < 0.01$) and Pi and Pe ($r = 0.568$, $p < 0.01$) [Fig. 3]. In total, higher insufflation time- and pressure settings were used in subjects with DMD but we found no differences in MI-E settings between diagnoses when adjusted for age (data not shown). Reported insufflation flow (*n* = 135) was high (73%), medium (21%) or low (6%).

Discussion

The present survey showed a wide variation of MI-E settings used in children with NMDs and that settings altered with age. To our knowledge, this is the first study reporting such a wide variation in pediatric MI-E use in NMDs. Although using longer times and higher pressures with age suggests a practice of adjusting MI-E settings with growth, the great variability of settings from this study is in line with great variation used in previous MI-E studies [1,6–13], highlighting the lack of evidence and guidelines in pediatric MI-E titration.

Lacking guidelines is confirmed by the wide variation in the use of symmetric or asymmetric settings across all age spans. Asymmetric time settings with longer Ti than Te were used by one third in the youngest age span. This can be rationalized by allowing longer insufflation to achieve sufficient filling of the lung with a naturally rapid respiratory rate and through narrow airways. The opposite may be justified by the assumption that filling of small volumes happens fast. Anyhow, the wide variation may indicate little evidence and few available recommendations.

In our study, the insufflation and exsufflation pressures ranged 10 to 50 and minus 10 to minus 60 cmH₂O, respectively. This represents almost the whole range of available pressures, illustrating lacking evidence to titrate the pressure. Half of the children used asymmetric pressure settings, but larger Pe than Pi were then mainly used. In fact, symmetric pressure settings are commonly reported [5,7,8,10,14,16] but their possible advantages have not been studied systematically. There may be an assumption that symmetric pressures ensure a balance between the insufflation and exsufflation volumes, which makes little sense as the given volumes are not controlled during MI-E use. In the pediatric clinical setting, the use of asymmetric pressures may be preferred in situations with abdominal distention related to insufflation or problems with reflux or emesis that might be related to the exsufflation.

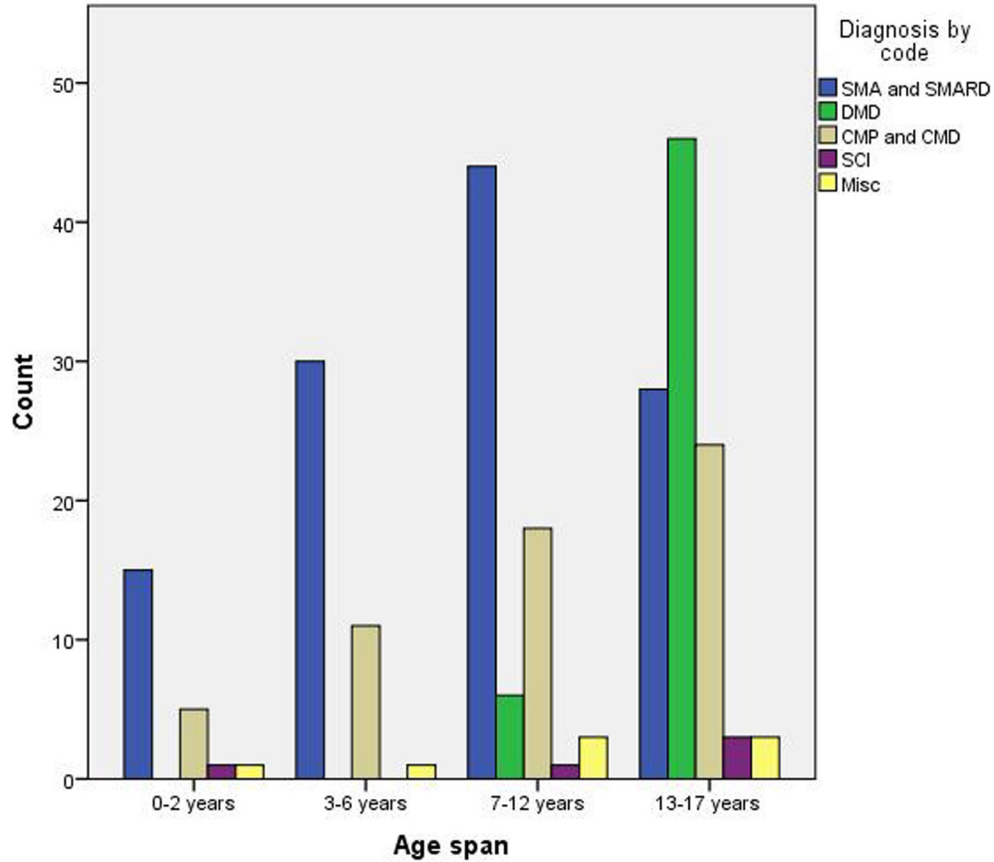


Fig. 1. Distribution of the diagnoses Spinal muscular atrophy (SMA) type 1–3, including SMA with respiratory distress (SMARD), congenital myopathies and dystrophies CMP and CMD, Duchenne Muscular Dystrophy (DMD), Spinal cord injury (SCI) and miscellaneous in the four different age spans.

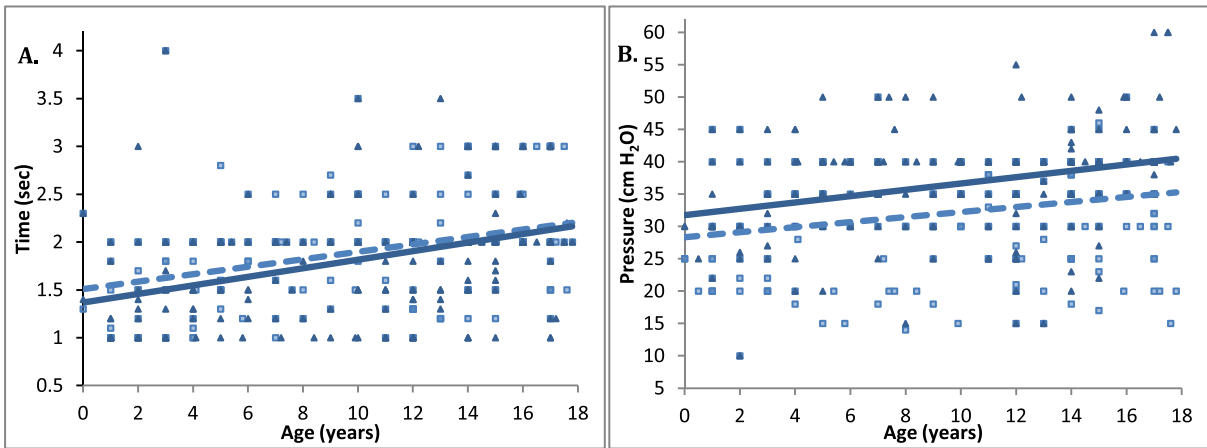


Fig. 2. Scatterplots with age (x-axis) and time and pressure settings in figure A and B, respectively (y-axis). Positive relationships were found for insufflation time ($r = 0.385$), exsufflation time ($r = 0.414$), insufflation pressure ($r = 0.254$) and exsufflation pressure ($r = 0.334$) (all $p < 0.001$). Regression lines are presented with dashed lines for insufflation and solid lines for exsufflation. \square = insufflation Δ = exsufflation.

No clear evidence nor consensus are available regarding optimal pressure settings for children with NMDs. MI-E has been shown beneficial with the use of pressures down to 15 cmH₂O [1,8,11], despite others advocating higher pressures [7,10]. However, to achieve maximal PCF, the use of submaximal lung volumes are found optimal [27]. Given the high thoracic compliance in infants [3], further evidence is needed to evaluate if the use of

low insufflation pressures are sufficient or if high pressures are necessary due to pediatric narrow airways and rapid respiratory rate limiting the time available to achieve adequate filling of the lung.

The impact of insufflation flow adjustments is unknown. High flow was most frequently used in the present study, although we do not know if this is necessary to achieve a sufficient insufflation

Table 1
Insufflation and exsufflation settings.

	0–2 years	3–6 years	7–12 years	13–17 years	All
Time settings					
Insufflation time(Ti) * Min–Max (sec)	n = 22 1.4 (0.5) 1.23–1.65	n = 40 1.7 (0.4) 1.60–1.87	n = 66 1.9 (0.5) 1.80–2.05	n = 100 2.1 (0.5) 2.0–2.19	n = 228 1.9 (0.5) 1–4
Exsufflation Time (Te) * Min–Max (sec)	1–2.5 1.4 (0.6) 1.13–1.64	1–3 1.5 (0.4) 1.4–1.68	1–4 1.8 (0.6) 1.65–1.96	1–3.5 2.1 (0.6) 1.96–2.19	1–4 1.8 (0.6) 1–4
Pressure settings					
Insufflation pressure (Pi) * Min–Max (cmH ₂ O)	n = 22 27.2 (8.8) 23.3–31.1	n = 42 31.2 (7.8) 29.0–34.0	n = 72 31.7 (7.4) 29.7–33.4	n = 104 34.4 (7.3) 33.0–35.9	n = 240 32.4 (7.8) 10–50
Exsufflation pressure (Pe) * Min–Max (cmH ₂ O)	10–45 30.6 (7.6) 27.2–33.9	15–40 35.3 (6.6) 33.3–37.4	14–50 36.4 (7.4) 34.6–38.2	15–50 39.1 (6.8) 37.8–40.4	10–60 36.9 (7.4) 10–60

Data are presented as mean (SD) with [95% confidence interval] and min and max values in the different age spans and in total. * $p < 0.001$ (ANOVA) for the group means in the different age bands. Times are given in seconds, pressures in cmH₂O.

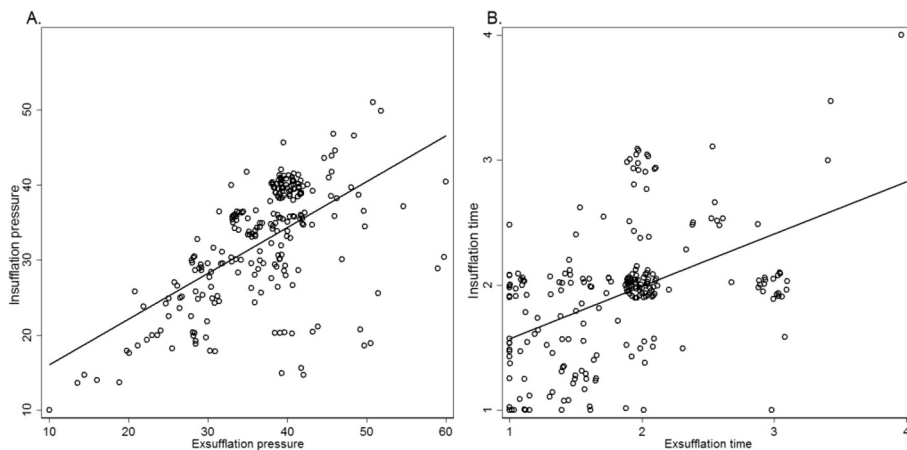


Fig. 3. Scatterplot graphs with the combination of insufflation (y-axis) and exsufflation (x-axis) pressure settings in cmH₂O (panel A) and time settings in seconds (panel B).

volume in the short time given a rapid respiratory rate, or if it could be counterproductive given their soft airways are vulnerable to collapse.

An important limitation of this study is that it is a pure descriptive study with no outcome data describing efficacy. We simply asked the primary settings being used. Information on the frequency and extent of use and the perceived need to adjust the settings in the presence of pulmonary exacerbation would have been helpful to facilitate clinical decision making. These aspects need to be added in future research.

The reported wide variation of MI-E settings highlights the need to understand which settings should be used in children in general and in infants in particular for optimal efficacy, comfort and safety.

Conclusions

Pediatric MI-E settings used by European centers alter with age but vary greatly, indicating the need to improve our knowledge on the optimal use of MI-E. Evidence and guidelines on both optimal settings and MI-E titration in children with NMDs are needed.

Future research directions

- To determine the optimal use of MI-E in children with NMD.
- To determine the optimal time and pressure settings in terms of efficacy, comfort and safety which take the children's age and physiological status into account, including possible effects of pulmonary exacerbation.

- To understand the impact of the use of asymmetric and symmetric settings.
- To provide specific guidelines for infants and small children.

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