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Effect of mechanical insufflation-exsufflation in children with neuromuscular weakness

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Abstract

Introduction: Children with neuromuscular diseases develop cough impairment. Airway clearance techniques (ACTs) may help to prevent recurrent respiratory tract infections (RTIs). A commonly used ACT is mechanical insufflation-exsufflation (MI-E), but evidence for efficacy is limited. We hypothesize that MI-E has beneficial effect on RTI related hospital admission rate.

Methods: In this single-center retrospective study, we reviewed all children who used daily MI-E between 2005 till June 2019. Primary outcome studied was the number of RTIs requiring hospital admission. Patient satisfaction and burden experienced by MI-E use were explored by questionnaires using a Likert scale. The relative number of RTIs requiring admission and the number of admission days per eligible period before and after the introduction of MI-E were compared using the Friedman test and the Wilcoxon signed-rank test.

Results: Thirty-seven children were included.

The median number of RTI related hospital admissions per 1000 eligible days after the introduction of MI-E was 0.9 (interquartile range [IQR] 0.0-3.1) compared to the 3 preceding years (median 3.7; IQR 1.4-5.9; $P = .006$). The median number of RTI related admission days per 1000 eligible days after the introduction of MI-E was significantly lower with a median of 2.7 (IQR 0.0-17.4) compared to the 3 preceding years (median 33.6; IQR 15.0-51.1; $P = .001$). Patient satisfaction was high with low burden, even in patients who discontinued treatment.

Conclusion: A significantly lower number of RTIs requiring hospital admission and shorter admission duration after the introduction of MI-E was found, with high patient satisfaction and low burden.

Esther S. Veldhoen and Laura P. Verweij-van den Oudenrijn contributed equally.

KEYWORDS
cough, neuromuscular disease, pediatrics

1 | INTRODUCTION

Neuromuscular disorders (NMDs) with onset in infancy and childhood such as spinal muscular atrophy (SMA), Duchenne muscular dystrophy (DMD) and congenital myopathies or muscular dystrophies may be complicated by weak cough and increased susceptibility to recurrent respiratory tract infections (RTIs). This is a major cause of morbidity and mortality[1-3] and various care guidelines, therefore, advise early start of airway clearance techniques (ACTs) to prevent RTIs.[4-6]

Airstacking (AS) is probably the most accepted form of ACT in the Netherlands, but mechanical insufflation-exsufflation (MI-E) is used increasingly despite the fact that evidence for efficacy, especially in children, is scarce.[5,7] We identified only one randomized controlled trial that compared the effect of MI-E and AS on frequency of RTIs among patients with amyotrophic lateral sclerosis, showing a trend towards better outcome for MI-E.[8] Experts prefer to use MI-E in very weak patients, those who cannot cooperate with AS and MAC, or in whom these techniques are not effective.[4] Recently, a consensus meeting of the European Neuromuscular Center concluded that the clinician can decide on what ACT to use, depending on forced vital capacity (FVC) and peak cough flow (PCF), but also on local availability, efficacy, tolerance, and preference.[5] MI-E was introduced in The Netherlands in 2005, but the lack of evidence for its efficacy has hampered reimbursement arrangements with health insurance companies. The aim of this study was to retrospectively analyze the number of hospital admissions and admission days due to RTIs before and after initiation of MI-E in a large single-center cohort of children. Our second aim was to prospectively evaluate patient and caregiver experience and burden of MI-E use by using a questionnaire. We hypothesized that the number of RTIs requiring hospital admission would decrease after the introduction of MI-E and that patient satisfaction would be high.

2 | MATERIALS AND METHODS

Our center for home ventilation at the University Medical Center (UMC) Utrecht welcomes 131 children, approximately half of the pediatric patients in the Netherlands who need ventilation. We included all children (n = 37) who had started daily MI-E at home. According to our protocol patients with reduced PCF for age or recurrent RTIs start regular ACT at home by means of AS twice daily.[4,5,9] When technique (eg, due to young age) or efficacy are insufficient, we switch to MI-E using Philips Respironics CoughAssist or Philips Cough Assist E70. Settings are individualized to optimize airway clearance using maximum tolerable pressures up to 40 cmH_2O. We teach caregivers to perform three cycles, each with 5 in- and exsufflations, at a frequency of at least twice a day and more frequently during RTIs. We evaluated all medical files systematically for admissions before and after initiation of MI-E. We contacted Pediatric Intensive Care Units (PICUs) in the other University Hospitals in The Netherlands to check for additional admissions. We collected patient data from birth until 1st of June 2019. In addition, we approached parents or legal guardians of all included study participants to explore their experiences and burden regarding MI-E use, using a questionnaire with answers on Likert scales.

Statistical analysis was performed using IBM SPSS Statistics (version 25). We compared both the number of RTIs requiring admission as well as the number of admission days in the 3 years before and the 3 years after the start of MI-E. As some patients started MI-E before finishing 3 years follow up or had not yet used MI-E for 3 years at the time of data analysis, we calculated the relative number of admissions per 1000 eligible days. Friedman test was used because of the nonparametric distribution of data. The Wilcoxon signed-rank test was used to follow up the Friedman test in case of statistically significant outcomes. The medical ethical committee of the UMC Utrecht waived the need for informed consent.

3 | RESULTS

Totally, 37 children were included with a median age of 5.2 years. An overview of patient characteristics is shown in table 1.The majority of patients were patients with SMA. Of these 23 patients with SMA, 13 patients (56%) were treated with the SMN-protein augmenting drug Spinraza. Six patients started treatment with Spinraza after introduction of MI-E (median 7.5 months after introduction of MI-E, interquartile range [IQR] 3.3-38.8 months), 6 patients started treatment with Spinraza before introduction of MI-E (median 10 months before introduction of MI-E, IQR 7.0-17.3 months) and 1 patient simultaneously started treatment with MI-E and Spinraza. We included 2 children with spinal cord injury, because they experience similar respiratory problems as children with NMDs. The youngest patients who started MI-E were children with infantile-onset SMA (ie, type 1). Four patients discontinued MI-E; two patients learned to perform AS maneuvers later in childhood and two patients discontinued MI-E following an episode of pneumothorax, a known complication of MI-E. A 3-year-old patient with SMA using MI-E with pressures of +20 and −30 cmH_2O developed pneumothorax during an RTI. The other patient with pneumothorax was a 15-year-old girl with polyneuropathy and severe kyphoscoliosis and past medical history of pneumothorax after scoliosis surgery. She used MI-E with pressures of +30 and −35 cmH_2O.

An increase in the frequency of MI-E use was observed over the years, mainly explained by a gradually more aggressive supportive treatment in younger SMA patients.

The median number of RTI related hospital admissions per 1000 eligible days after the introduction of MI-E was 0.9 (IQR 0.0-3.1) and was lower than in the 3 preceding years (median 3.7; IQR 1.4-5.9; Z = −2.754 and $P = .006$). The median number of RTI related admission days per 1000 eligible days after the

TABLE 1 Patient characteristics

Age at start MI-E (y; median; IQR)	**5.2 (2.7-12.4)**
Male gender, n (%)	22 (59)
Diagnosis, n (%)	
Spinal muscular atrophy	23 (62)
Type 1	11 (48)
Type 2	12 (52)
Duchenne muscular dystrophy	2 (5)
Other neuromuscular disease	10 (27)
Cervical spinal cord injury	2 (5)
Tracheotomy, n (%)	
No tracheotomy	20 (54)
Tracheotomy before start MI-E	12 (32)
Tracheotomy after start MI-E	5 (14)
Chronic mechanical ventilation, n (%)	
No chronic mechanical ventilation	4 (11)
Chronic mechanical ventilation started before MI-E	23 (62)
Chronic mechanical ventilation started simultaneously	9 (24)
Chronic mechanical ventilation started after MI-E	1 (3)
Years of MI-E use, median (IQR)	2.4 (1.7-6.3)
Number of days of follow up 3 y before start MI-E, median (IQR)	1095 (531-1095)
Number of days of follow up 3 y after start MI-E, median (IQR)	1095 (523-1095)
Year of MI-E introduction, n (%)	
2005-2009	4 (11)
2010-2014	12 (32)
2015-2019	21 (57)

Abbreviations: IQR, interquartile range; MI-E, mechanical insufflation-exsufflation.

introduction of MI-E was significantly lower with a median of 2.7 (IQR 0.0-17.4) than in the 3 preceding years (median 33.6; IQR 15.0-51.1; $Z = -3.391$ and $P = .001$). When excluding the 9 patients who initiated chronic mechanical ventilation simultaneously we found similar results: with significantly ($P = .003$) fewer RTI related hospital admissions 3 years after introduction of MI-E (median 0.0 per 1000 eligible days; IQR 0.0-2.2) compared to 3 years before introduction of MI-E (median 4.1 per 1000 eligible days; IQR 1.1-6.4). In this subgroup, the number of RTI related admission days per 1000 eligible days was also significantly ($P = .007$) lower 3 years after the introduction of MI-E (median 0.0; IQR 0.0-8.9) compared to 3 years before the introduction of MI-E (median 34.2; IQR 10.3-57.5).

Thirty-one (84%) parents and caregivers returned the questionnaires. The median satisfaction score for secretion removal was 9.0 out of 10 (IQR 8.0-10.0) and 9.0 out of 10 (IQR 7.8-10.0) for RTI prevention. Comfort of the child during MI-E treatment had a median score of 8.5 out of 10 (IQR 6.8-10.0). Three patients reported occasional discomfort after MI-E treatment (sore throat, muscle pain, nausea). All parents, including parents of patients who discontinued MI-E treatment, would recommend MI-E to other patients.

4 | DISCUSSION

This retrospective study suggests that the treatment of children with severe NMDs with MI-E may lead to a decrease in the number of RTIs requiring admission and shorter hospital stays. Patients or their caregivers experienced important benefits with low burden. This is, to the best of our knowledge the first study exploring the possible effects of the introduction of MI-E on the incidence of RTIs requiring admission in children with NMDs. A limited number of previous studies studied the effect of MI-E during RTI. These studies show the reduced need for tracheotomy or intubation, shortening of airway-clearance sessions, shortened duration of symptoms of RTI and reduced odds of hospitalization.[8,10,11] One study in adult patients with spinal cord injury compared hospitalizations in general (and not only due to RTI), which showed a nonsignificant reduction of respiratory hospitalization rate of 34% after introduction of MI-E.[12] It is our impression that physicians often believe that burden of MI-E is high and that these believes, combined with lack of evidence for efficacy, may delay the introduction of MI-E. However, our data suggest that caregivers and patients experience important benefits and low burden.

The major limitation is obviously the retrospective nature of this study. We cannot exclude the possibility that other factors, such as differences in the adherence to standards of supportive care, the introduction of Spinraza (SMA-specific treatment introduced in the course of May 2017 [for infants] to January 2018 [young children with SMA]), influence of aging on the incidence of RTIs or use of maintenance antibiotic therapy, may have confounded our results. Moreover, retrospective data collection could have led to an under- or overestimation of the number of RTIs. Since the standardization of electronic patient files has led to the systematic questioning of RTIs occurrence during every visit, we expect less underreporting of RTIs in recent years compared to earlier years and potentially an underestimation of the beneficial effect of MI-E. We do not have information on the satisfaction of ACT before MI-E. Therefore we can only conclude that patients using MI-E are satisfied, and we cannot draw conclusions on patient satisfaction with MI-E compared to other ACTs.

Despite these limitations, this study suggests a decline in hospital admission rate and admission days after the introduction of MI-E, without an increased burden for patients. The results of this study call for a prospective evaluation comparing AS to MI-E in patients with decreased cough strength.

5 | CONCLUSION

This retrospective cohort study is the first pediatric study which suggests decreased RTI related hospital admission rate and shorter admission duration after the introduction of MI-E. Patient satisfaction was high, with low burden.

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