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Long term conditions

Investigating the use of Mechanical Insufflation – Exsufflation in young people with Cystic Fibrosis during inpatient admission

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Abstract

Background

People with Cystic Fibrosis (CF) are productive of sticky sputum which becomes a site for bronchial wall damage. During pulmonary exacerbations, People with CF often require increased airway clearance support. Mechanical Insufflation- Exsufflation (MI-E) has been suggested as a method of airway clearance in this group.

Aim

To describe the routine use and impact of MI-E devices in an inpatient acute population of children and young people with CF and to compare it to a historical cohort prior to the introduction of MI-E use.

Method

A retrospective medical notes review was conducted for all children with CF admitted during a pulmonary exacerbation over two, one-year periods: Feb 2019–Feb 2020 (18 admissions) and Feb 2020–Feb 2021 (26 admissions), at a single CF centre in the East of England. Outcomes including pulmonary function, length of stay, and the choice to include MI-E in airway clearance were all taken from electronic records.

Results

Between Feb 2019-Feb 2020 none of the 18 admissions utilised MI-E. In Feb 2020-Feb 2021 10 of 26 admissions incorporated MI-E. Settings varied based on patient tolerance and no adverse events were noted.

MI-E was employed in patients with a more significant drop in FEV1 Z score at admission, although no differences were observed in FEF2575. Length of stay trended longer for MI-E users (15.2 days) compared to non-users (13.3 days), likely reflecting greater initial illness severity.

Conclusion

MI-E shows promise in supporting airway clearance during pulmonary exacerbations in children with CF. Further research is needed before this becomes common practice.

INTRODUCTION

Cystic Fibrosis (CF) is a genetic condition affecting around 10,000 people in the UK and is the most common lethal genetic disease in the Caucasian population.[1] Patients with CF can have symptoms related to the digestive system, fertility, liver, pancreas, bones and importantly the lungs.[2] The damage to the lungs occurs from a build-up of sticky sputum, this sputum provides an environment for further bacteria colonisation and damage to surrounding tissues causing a bronchiectatic picture. This area of bronchiectasis can result in impaired mucociliary clearance of sputum and result in further microbial growth .[3] The trend is for this to begin in the small airways and gradually to effect larger airways.[4,5] To reduce this effect, a mixture of airway clearance techniques to facilitate sputum clearance, and nebulised antibiotics to eradicate or control bacterial sputum growths is seen as standard treatment.[6]

Airway clearance techniques can come in many forms with treatment regimes decided between patients, their families and clinicians.[7] Traditional options for airway clearance include exercise, oscillatory positive expiratory pressure (OPEP), positive expiratory pressure, autogenic drainage, manual techniques and/or postural drainage.[8]

Infective pulmonary exacerbations (IE) are when symptoms of infection become more severe.[9] Usually this entails one or more of the following symptoms: change in cough frequency and sound, chest pain, increased sputum production, change in sputum consistency/colour, dyspnoea, decreased energy level and appetite, weight loss, and decreases in pulmonary function results.[10] These IEs are a well-recognised as a part of the disease in people with CF and the associated with a need for increased treatment.[11] IEs can decrease the effectiveness of usual airway clearance techniques due to patient fatigue, dyspnoea or pain limiting treatment completion, or an increased sputum load reducing effective clearance through a reduction of lung function.[12] Approximately one in three people with CF will not recover their baseline Forced Expiratory Volume in 1 second (FEV1), following IE, with an ~3% sustained decrease.[13] There is no standardised measure for pulmonary exacerbations in CF, however, a decrease in pulmonary function (which includes FEV1 and FEF2575) are commonly cited as indicators.[14] CF transmembrane conductance regulator modulators, such as Kaftrio, Symkevi and Orambi have changed the landscape of CF care and physiotherapy involvement in IEs.[9]

Currently, there is no universal standardised airway clearance for people with CF. Instead, clinicians often recommend or implement personalised techniques that adapt to the individual's clinical presentation.[15,16] An adjunct, not routinely used, which may be useful in facilitating clearance is the Mechanical Insufflator-Exsufflator (MI-E). MI-E produces changes in the airflow inside the bronchial tree, through the provision of alternating positive and negative pressures.[17] To date, it has been mainly used in patients with an ineffective cough clearance, such as individuals with neuromuscular pathologies or respiratory muscle deficiency.[17,18] MI-E is recommended in use for children with neuromuscular weakness[19] but it's use outside of this population is poorly evidenced in paediatrics.

To the authors knowledge, only one abstract has been published on the use of MI-E in Children and Young People (CYP) with CF. Helper et al.,[20] found a 36% improvement in clearance of sputum in CYP using MI-E when compared to autogenic drainage ($P<0.0001$). However, the sample was small (n=22) and the project did not consider other treatments or outcomes, such as pulmonary function. Two small studies – one case study and one abstract - in adults with CF (combined n=7) concluded that when routine airway clearance is compromised due to fatigue or chest wall discomfort that MI-E could be considered and subjectively measured.[12,21]

Since the work by Helper et al,[20] the clinical team at a large tertiary teaching hospital has been using MI-E with CYP with CF.

AIMS

This paper aims to describe the routine use and impact of MI-E devices in an inpatient acute population of CYP with CF and to compare it to a historical cohort prior to the practice change.

METHOD

A retrospective review of routinely collected patient records was undertaken. All children with CF admitted to a tertiary hospital in the UK during two 12-month time windows with a pulmonary exacerbation who were able to do pulmonary function tests (PFT) were included. The first period was from Feb 2020-Feb 2021 (Period 1) and the second from Feb 2021-2022 (Period 2). A historical time window prior to the introduction of MI-E within this patient cohort (Period 1) was used to provide comparison to the main time window of (Period 2) illustrating current practice which included children who did and did not use MI-E. This project was approved by the hospital governance department as a service evaluation investigating routinely collected data and therefore ethical approval was not needed.

The following routinely documented variables were collected from the electronic records:

- Age at admission.
- Sex.
- Best FEV1 and FEF25/75 Z scores in the year- to describe the population.
- FEV1 and FEF2575 Z scores at the start and end of each admission- to describe the clinical picture.
- Length of admission.
- Use of MI-E or not.
- Other physiotherapy treatments used for sputum clearance.

Primary outcome:

- Change in FEV1 Z score throughout admission.

Secondary outcomes:

- Change in FEF 2575 Z score throughout admission,
- Change in length of admission.

Data was analysed using IBM SPSS Statistics version 28. Where data was parametric an two tailed independent T test was used to compare two groups and One-way ANOVA was used to compare the three groups (Period 1: Non MI-E historic cohort, Period 2: MI-E recent cohort, Period 2: non MI-E recent cohort). For non-parametric data Mann-Whitney U was used to compare two groups and Kruskal-Wallis ANOVA was used to compare the three groups.

RESULTS

PATIENT DEMOGRAPHICS

On review of medical records during Period 1, there had been 18 admissions of 10 CYP who had completed pulmonary function tests, six of which had multiple admissions, none had used MI-E. In Period 2 there had been 26 admissions of children with CF who had completed pulmonary function tests, from 11 patients, 6 of which had multiple admissions. MI-E was used in 10 admissions. Each admission was taken as a new data point. No participant was on Kaftrio during this data collection, though all were on either Orkambi or Symkevi. Comparisons were made be-

Table 1. Descriptive Statistics of Each Group.

	Period 1 (n=17)	Period 2 Using MI:E (n=10)	Period 2 Not Using MI:E (n=16)
Age	Mean=10.12 S.D=3.00	Mean= 9.58 S.D=0.98	Mean=9.74 S.D=1.92
Number Female	1	3	5
Best FEV1 Z Score in the year	Median= -0.417 IRQ= 3.47	Median=-0.57 IRQ =2.65	Median=-0.42 IRQ=4.22
Best FEF25/75 Z Score in the year	Median= -0.486 IRQ= 3.6565	Median=-1.00 IRQ=5.43	Median=-1.00 IRQ=5.34
FEV1 Z score on admission	Median= -2.59 IQR= 2.76	Median= -3.375 IQR= 4.02	Median= -2.23 IQR= 2.66
FEF25/75 Z Score on admission	Median= -2.97 IQR= 3.72	Median= -4.81 IQR= 4.07	Median= -2.92 IQR= 3.49
FEV1 Z score on discharge	Median= -1.13 IQR= 3.06	Median= -2.105 IQR= 4.5	Median= -1.97 IQR= 2.27
FEF25/75 Z Score on discharge	Median= -1.45 IQR= 3.77	Median= -3.44 IQR= 5.02	Median= - 2.45 IQR= 4.91
Length of Stay	Median=14 IQR=4	Median= 15 IQR=3	Median= 13.5 IQR=2
Number of treatments including OPEP	Median= 17 IRQ= 7 (14-21)	Median=20 IRQ= 17.5 (18.5-36)	Median=18 IRQ= 9 (12.5-21.5)
Number of treatments including Exercise	Median= 22 IRQ= 13 (12-25)	Median=20 IRQ= 4 (19-23)	Median=18 IRQ=11.25 (12-23.25)
Number of treatments including MI-E	0	Median=19 IRQ= 15.5 (15.5-31)	0

tween the 3 groups (Period 1 Cohort, Period 2 MI-E Cohort, Period 2 non MI-E Cohort). Descriptive statistics of patients can be seen in Table 1.

The baseline status of each group as measured by the highest achievedFEF25/75 and FEV1 Z score in the year (usually at routine annual review as an outpatient) were similar in all groups (Table 1).

At admission Z scores for both FEV1 and FEF25/75 were worse than "best in year" for all groups. This was pronounced in the Period 2 MI-E group who had worse median (IQR) scores -4.81(4.07) then either those in period 1 -2.97(3.72) or those in period 2 who did not use MI-E -2.23(2.66) indicating that this group was in general more unwell.

By discharge all groups had improved in both scores but remained worse than best scores of the year. The group in period 2 using MI-E remained the most impaired with median (IQR) FEV1 z scores -3.375(4.02) when compared to period 1 -1.13(3.77) and period 2s non MI-E comparison group -1.97(2.27)The Period 2 MI-E group had however had the biggest improvement.

Three patients who used MI-E had presented with atelectasis on admission X-ray as recorded in radiology report, two of these had resolved by the end of admission. No one outside of this group showed any acute radiological changes on chest X-ray. One patient continued to have atelectasis and had a one-month home trial of MI-E and on clinic review following this, atelectasis had resolved, and MI-E treatment was terminated. Across all groups two patients were on oxygen on admission, for both the physiotherapist used MI-E. This is in keeping with the MI-E group having the most impaired lung health at point of admission.

STANDARD TREATMENT

Amount and composition of physiotherapy sessions can be seen in table 1. OPEP devices varied but included Aerobika, Acapella and Bubble PEP. Exercise included active travel (including: walking/running/stair climbing) games (including: hide and seek, football, bulldog) and gym work (treadmill, exercise bike, body weight exercises).

USE OF MI-E

There was no formalised protocol for patients who started on the MI-E device. In all cases where MI-E was undertaken a NIPPY Clearway (Breas Medical LTD, Stratford-Upon-Avon, Warwickshire, UK) was used. In 9 patients, manual mode setting was used and in 1 triggered auto. All ratios of insufflation to exsufflation were 5:1 or less, notes indicate that this was dependent on how well this was tolerated and the child's clinical presentation. Both NIPPY Clearway 1 and 2 were used; where NIPPY clearway 2 was used the ramp was set to 10 during insufflation. Mouthpieces and face masks were used dependent on patient preference. In all cases, asymmetrical pressure settings were used. The largest pressure swing was 45cmH2O, with settings of +15cmH2O to -30cmH2O and this was also the most common pressure used in this group. Pressures were regularly changed and titrated for patient comfort and ef-

Table 2. Pulmonary Function Tests by Group.

Variable	Period 1: (n=17)	Period 2: MI:E (n=10)	Period 2 No MI:E (n=16)	Period 2: MI-E vs Non-MI-E	Period 2 MI-E vs Period 1	Period 2 Non MI-E vs Period 1	Comparison of all groups One Way Anova/ Kruskal-Wallis ANOVA
Change in FEV1 Z-score on admission in comparison to best score in year	Mean= -2.02 SD (1.23)	Mean= -2.56 SD (0.98)	Mean= -1.38 SD (1.19)	**T= 2.597 P=0.016***	T=-1.175 P=0.252	T=1.472 P=0.152	F(2,38)=3.210 P=0.052
Change in FEF25/75 Z-score on admission in comparison to best score in year	Median = -1.848 Q1=-5.11 Q3=-0.90 IQR (4.21)	Median = -1.96 Q1=-3.03 Q3=-1.24 IQR (1.79)	Median = -1.39 Q1=-2.1 Q3=-0.52 IQR (1.58)	U=41.00 P= 0.262	U=32.00 P=0.184	U=68.00 P=0.839	H=2.046 P=0.359
Change in FEV1 Z-score from admission to discharge	Median = 1.25 Q1=0.71 Q3=1.49 IQR (0.78)	Median = 1.55 Q1=0.88 Q3=2.74 IQR (3.62)	Median = 0.34 Q1=1.28 Q3=-0.90 IQR (2.18)	**U=39.00 P = 0.031***	U=57.00 P=0.466	U=67.00 P=0.064	**H=6.052 P=0.049***
Change in FEF25/75 Z-score from admission to discharge	Median = 1.29 Q1=0.54 Q3=1.95 IQR (1.41)	Median = 1.33 Q1=0.82 Q3=1.96 IQR (1.14)	Median = -0.04 Q1=-0.16 Q3=0.94 IQR (1.1)	**U= 23.00 P = 0.011***	U=57.50 P=0.729	**U=50.00 P=0.027***	**H=7.787 P=0.020***
Length of admission (days)	Mean= 14.7 SD (3.69)	Mean= 15.2 SD (2.82)	Mean= 13.3 SD (2.70)	T=-1.681 P=0.107	T=0.368 P=0.716	T=-1.151 P=0.260	F(2,37)=1.205 P=0.311

ficacy throughout stays in keeping with Morrison et al., (2015).

On review of the medical notes, there were no adverse events noted when using MI-E, though one patient did not tolerate this well only managing a ratio of 5 insufflations to 1 exsufflation for 2 sets, which was documented as being suboptimal. This poor tolerance was partially related to increased coughing and clearance of sputum and partially related to the behaviour of the patient.

CLINICAL OUTCOMES

In all groups FEV1 Z scores were worse on admission than their best in year scores. With Period 1 having a mean(S.D) drop from best in year scores of −2.02(1.23),Period 2 MI-E=-2.56(0.98) and Period 2 non MI-E −1.38(1.19). All groups also improved by the end of admission. With Period 1 having a median (IRQ) improvement in FEV1 Z scores between admission and discharge of +1.25(0.78), Period 2 MI-E = +1.33 (3.62), and Period 2 non-MI-E =+0.34(2.18). This was reflected in FEF25/75 Z scores as well apart from in the Period 2 non-MI-E group which showed a slight median(IRQ) drop in scores between admission and discharge of −0.04 (1.1).

DIFFERENCES IN OUTCOMES BY GROUPS

LUNG FUNCTION AT ADMISSION COMPARED TO BEST LUNG FUNCTION IN YEAR

A one-way ANOVA found no difference between groups in change in FEV1 Z Scores from best in year to admission F(2,38)=3.210,p=0.052. However, mean (S.D) scores for those in Period 2 who had MI-E had dropped more -2.56(0.98) z scores than those who clinicians didn't use MI-E -1.38(1.19). Indicating that clinicians selected to use MI-E with on average more unwell patients. This was significant using t(25)=2.597,p0.016. There was no significant difference in drop of FEF25/75 Z score on admission when compared to best of year scores between any of the groups.

IMPROVEMENT IN LUNG FUNCTION DURING ADMISSION

There was a difference found between the groups when a Kruskal- Wallis ANOVA was calculated for change in FEF25/75 Z score from admission to discharge (H=7.787,P=0.020). Post hoc analysis using a Mann-Whitney found those in period 2 who had had MI-E median(IRQ)= 1.33(1.14) had improved significantly more than those who hadn't -0.04(1.1) U=23.00, p=0.011. A difference was again found between the groups in FEV1 Z score from admission to discharge(H=6.052,P=0.049). Post hoc analysis again found that this was between those in period 2 who had used MI-E median (IQR)=1.55(3.62) had a significantly bigger

improvement then those who hadn't 0.34(2.18) U=39.00,P=0.031.

LENGTH OF STAY

A one-way ANOVA found no difference in length of stay between the three groups. However, the group using MI-E in period 2 had a higher mean(S.D) length of stay 15.2(2.70) then those who did not use it 13.3(2.70). While not statistically significant, 1.9 days difference may be considered clinically significant.

DISCUSSION

This paper has illustrated the use of MI-E in children with CF in an inpatient setting at one regional CF centre. Some interesting points can be found in the data.

CHOICE OF PATIENT

Clinicians were more likely to treat more unwell patients with MI-E. Previous work has highlighted the possible benefit of MI-E in patients suffering from Fatigue[21] which is often part of a person with CFs clinical presentation when presenting with an infective exacerbation. It may have been that clinicians see the use of MI-E as a treatment of choice when the patient is less able to participate in other techniques due to the severity of illness or that some aspect of their presentation indicated the use of MI-E such as a higher sputum load which is backed by a recent review.[22]

IMPACTS OF USING MI-E

While the aim of this project was not to explore the effects of MI-E some interesting results were seen. The use of MI-E was associated with improved FEV1 and FEF25 Z scores compared to those patients who were not selected to use MI-E which may warrant further investigation. It must be noted however that those children who were selected by clinicians to start MI-E had a significantly larger drop in FEV1 Z score on admission compared to their score at annual review than those receiving standard treatment. This may have meant that there was greater scope for improvement in this group. The lack of difference between groups in drop in FEF2575 may indicate that obstructions in the airway due to sputum were more related to central airways than peripheral. Previous work has highlighted that clinicians aim to return to baseline with treatment for IE,[23] the current project supports this and provides evidence that those who were the most unwell made the biggest recovery in FEV1. However, in keeping with Waters et al.,[13] patients are still off of their baseline lung function when discharged home.

Improvement in FEF25/75 has been found after effective airway clearance[24] and may indicate a higher level of clearance of the small airways in this population due to the use of MI-E.[25] This may partly explain the larger improvement in these scores seen in the MI-E group. While the volume of sputum is difficult to measure in children who often don't expectorate to command we can hypothesise that a larger volume of sputum may have been cleared by those using MI-E which may have impacted on this change in this measure. Small airways are the first affected in people with CF, therefore ensuring these remain as clear as possible is paramount in treating children with CF.[5]

LENGTH OF STAY

The increased length of admission (1.9 days), though not statistically significant, could arguably be described as clinically significant. This could be due to the use of MI-E and either a true negative effect or more likely that those that were selected for MI-E were a more unwell cohort and therefore less likely to be discharged quickly. FEV1 Z scores is an objective measure to help determine a patient's readiness for discharge.[26] The larger reduction of this on admission in the MI-E group, and the subsequent longer time to reach close to complete FEV1 recovery, may have been the cause for the increased length of stay. This project did not record the reason for the difference in admission length so it may be other factors such as other procedures or lack of weight gain. There is an expectation of weight gain so where this does not occur, length of admission can be lengthened.[27] However, this difference is likely to have a financial burden on the NHS,[28] as well as impacts on patients and families, and warrants further investigation in the future.

ADVERSE EVENTS

There were no adverse events reported throughout the medical notes and on the whole this was a well-tolerated adjunct in this population. This is in keeping with previous safety and efficacy reports in children with other respiratory conditions[29] and with adults.[30] It is important to note that this was not tolerated well by every patient though and this was managed by the treating therapist by reducing the number of sets and increasing the ratio of insufflation to exsufflation.

LIMITATIONS AND STRENGTHS

The retrospective nature of this project limits the conclusions we can draw. There was no attempt to standardise a protocol or power the project to enable us to understand if MI-E was the driver of the changes seen. The small sample and limitation to one team also restricts the generalisability of the results. The project was also limited by the level of documentation found. While MI-E use was found to be well documented other treatments such as "Exercise" were often less fully documented, with usually a time period or list of activities used documented without a fine detail which would allow for a more detailed description.

The reflection of real practice during a period of an introduction of a new treatment modality does illustrate current practice, however, and illustrates the need for more formal research in this area.

CONCLUSION

Clinicians routinely used MI-E in children with CF during inpatient admissions for infective exacerbations. It was generally well tolerated, and clinicians were more likely to use MI-E in patients who were more unwell. Among the children who used MI-E, a greater improvement in FEV1 and FEF25/75 Z-scores was observed. However, FEV1 had dropped significantly further from baseline in the MI-E group, providing a greater scope for improvement.

This is in area which would benefit from further research with prospective studies and a more robust review of adverse events to improve the generalisability of results, though does show promise in this population.

Key points

1. Physiotherapists working with children and young people with CF use a variety of treatment modalities during infective exacerbations. In the studied centre, manual Insufflation-Exsufflation tended to be used in more unwell patients.
2. Manual Insufflation-Exsufflation caused no adverse events in children and young people with CF.
3. Manual Insufflation-Exsufflation was well tolerated in children and young people with CF.
4. Further, more robust, research may provide greater detail into the mechanisms and effect of Manual Insufflation-Exsufflation in children and young people with CF.

DECLARATION OF INTEREST

The authors report no conflicts of interest.

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