Inspiratory Muscle Training in Children: Moderate Loads (60%) Are Safe and Promote an Increase in PIMAX

Milena Siciliano Nascimento (milenasn@einstein.br)
Hospital Israelita Albert Einstein https://orcid.org/0000-0002-0515-3933

Cristiane do Prado
Hospital Israelita Albert Einstein

Fernanda Ejzenberg
Hospital M'Boi Mirim

Simone Sayuri Kushida
Hospital M' Boi Mirim

Amanda Fontes
Hospital M'Boi Mirim

João Fernando Almeida
Hospital Israelita Albert Einstein

Daniela Nasu Medeiros
Hospital Israelita Albert Einstein

Research article

Keywords: Inspiratory muscle training, maximal respiratory pressure, muscle strength, pediatrics

Posted Date: September 15th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-71590/v1

Abstract

Background: Weaning failure are complex outcomes as it involves some aspects including weakness of the respiratory muscles. Ventilator-induced diaphragmatic dysfunction has been described as one of the main complications of IMV. Inspiratory muscle training with moderate loads was described in adults as having excellent results in terms of disconnection from the IMV literature. On pediatric population there is still a scarcity of and most of it consists of descriptions of isolated case reports**.**

Methods: This study aims at evaluating whether muscle training using moderate loads will cause an increase in maximal inspiratory pressure (PIMAX) in patients dependent on mechanical ventilation. This is a retrospective study conducted in 2 Pediatric Intensive Care Units from January 2016 to December 2017. All patients who underwent muscle training during the period of the study were included. PIMAX was measured using a manovacuometer. Three measurements were made with an occlusion time of 15 seconds and a recovery interval of 2 minutes between them. Muscle training was performed following the institutional protocol (4 sets of 6 repetitions with a load equivalent to 60% of PIMAX) 1x/day, 6 days a week, excluding the day of the measurement of PIMAX.

Results: Six patients undergoing prolonged mechanical ventilation (average time of mechanical ventilation of 9647 hours) who underwent muscle training to disconnect mechanical ventilation were included. The measurements of PIMAX pre-training were compared to weeks 1 to 4. A significant difference on PIMAX was observed after the second week of training ($p < 0.001$). Five patients progressed to IMV disconnection.

Conclusion: Our study supports the performance of IMT using moderate loads (60%), with no risk of muscle fatigue as it resulted in a significant increase in PIMAX after 2 weeks of training, with positive outcomes regarding weaning from mechanical ventilation.

Background

For most patients under invasive mechanical ventilation (IMV), the weaning process takes place naturally. However, about 30% of patients evolve to prolonged weaning, and 5% present chronic dependence on IMV. Weaning failure is a complex outcome as it involves aspects such as inadequate respiratory drive, increased respiratory effort, and weakness of the respiratory muscles.[1] For decades, ventilator-induced diaphragmatic dysfunction has been described as one of the main complications of IMV, and it involves structural myofibrillar lesions leading to atrophy and functional abnormality. [2–4] The mechanism that reduces the strength capacity of the diaphragm is multifactorial, and it includes changes in excitation-contraction coupling, decreased myofibrillar protein synthesis, and increased muscle proteolysis.[5] Immobility, systemic infection and inflammation are associated with skeletal muscle dysfunction in critically ill patients.[6, 7]

Inspiratory muscle training (IMT) with a linear load device has been performed in adult patients with chronic diseases. The outcomes observed are increased inspiratory muscle strength, increased inspiratory muscle resistance, dyspnea reduction, increased exercise tolerance and improved quality of life. [8]

Initially, the loads used were extremely low (20–30% of PIMAX) as it was feared high loads would cause muscle fatigue. However, this training profile had no impact on PIMAX or on outcomes of disconnection from IMV.[9, 10] The training of adults with moderate to high loads was described by Martin et al as having excellent results in terms of disconnection from the IMV, with no report of muscle fatigue and significant increase in PIMAX.[11, 12]

There is still a scarcity of literature on pediatric population, and most of it consists of descriptions of isolated case reports evaluating low-load muscle training in patients with difficult ventilator weaning. [13–14]

Methods

This study aims at assessing whether moderate-load muscular training increases the inspiratory muscle strength, which was evaluated by measurements of maximal inspiratory pressure (PIMAX) in patients dependent on mechanical ventilation.

This is a retrospective study conducted using analysis of medical records data from patients who met the inclusion criteria determining for the design of the sample. The research was submitted to the ethics committee, number: 62561516.9.2001.0071 and the informed consent term were waived by the ethics and research committee. This study received no funding.

The study included patients who underwent muscle training and were admitted to the Pediatric Intensive Care Units of two hospitals – one private and the other public – in the city of São Paulo, from January 2016 to December 2017.

Measurement of maximal inspiratory pressure

For the PIMAX measurements we used a Murenas manovacuometer (Juiz de Fora, MG, Brazil) with a scale from 0 to 150 cmH2O and variations of 5 cmH2O. Three measurements were made, with an occlusion time of 15 seconds and a 2-minute interval between them. During the interval, the patient was reconnected to the mechanical ventilator for recovery. Ventilation was measured using the pre-established protocol by trained physiotherapists.

Muscle training

Low intensity muscle training is defined when loads below 50% are used, moderate intensity muscle training when the loads used range from 60 to 80%, and high intensity muscle training when loads are

greater than 90%. The higher the load, the lower the number of repetitions must be used. The training followed an institutional protocol of 1x/day, 6 days a week, excluding the day of the measurement of PIMAX. The training consisted of 4 sets of 6 repetitions for each section with a load calculated at 60% of PIMAX. The device used for muscle training was Threshold IMT (Respironics Inc; Murrysville, PA, USA).

Statistical Analysis

Regarding quantitative variables, the sample was characterized by mean, standard deviation, minimum and maximum, median and percentages; regarding qualitative variables, the sample was characterized by relative and absolute frequencies. To assess patients' strength gain, we used the Generalized Estimation Equation Model – GEE. The dependent variable was PIMAX, and the independent variables were time (in weeks) and age (in months). Residual analysis was performed graphically. The analyses were performed using SPSS software (IBM Corp, 2016), v23.0, and a significance level of 5% was considered.

Results

Six patients in prolonged mechanical ventilation and undergoing muscle training in to be disconnected from mechanical ventilation were included. Table 1 presents the main demographic characteristics and post-training outcomes.

Table 1
Demographic characteristics and main clinical interventions

Characteristics		
Patient diagnosis		
Bronchiolitis obliterans	1	16.70%
Carcinoma of bulb	1	16.70%
Prematurity + Single ventricle	1	16.70%
Prematurity + Short bowel syndrome	1	16.70%
Rickets + Genetic Syndrome	1	16.70%
Down syndrome + Hypogammaglobulinemia	1	16.70%
Gender		
Masculine	5	83.30%
Feminine	1	16.70%
PIM 2	4,0	(3.0; 13.0)
Age (months)	23	(17.0; 99.0)
Patient weight (Kg)	8,9	(8.0; 13.0)
Duration of MV (hours)	7704	(2952; 10704)
Length of hospital stay (days)	464	(303; 818)
Interface		
Orotracheal cannula	1	16.70%
Tracheostomy	5	83.30%
Post-training outcome		
Disconnection and decannulation	1	16.70%
Disconnection	3	50.00%
Extubation + NIVI	1	16.70%
Disconnection 2 hours/day	1	16.70%
PIM 2: Pediatric Index of Mortality; MV: mechanical ventilation		

Values are presented as the median and interquartile range

Table 2 shows the estimated averages in a model that considered age as a control covariate given the variability of patients age. It also includes comparisons between the different stages with Bonferroni correction of the p-value.

Table 2
Estimated mean of PIMAX values pre-training and at weeks 1, 2, 3 and 4.

Stage	Mean	Error	IC 95% (Estimated mean)	*p*-value
Pre-training	27.22	4.182	(20.14; 36.78)	
Week 1	40.68	6.048	(30.39; 54.44)	n.d
Week 2	49.31	5.377	(39.83; 61.06)	< 0.001
Week 3	72.20	5.699	(61.85; 84.28)	< 0.001
Week 4	93.12	4.795	(84.18; 103.01)	< 0.001
Generalized Estimation Equation Model				

95% confidence intervals

Pre-training PIMAX was compared to the PIMAX on weeks 1 to 4; only two patients showed results at week 4. We observed a significant difference in PIMAX after the second week of training.

Figure 1 shows the patients' average PIMAX profiles over time. We can observe a significant increase in PIMAX from the second week on.

Discussion

Our study was the first to conduct moderate load (60% of PIMAX) inspiratory muscle training in pediatric population. In addition to the excellent tolerance observed in patients, a significant increase over time in the PIMAX was demonstrated.

In the last decade, several studies have observed that atrophy of the diaphragm and other skeletal muscles in patients dependent on mechanical ventilation is quite common and occurs fast, starting within the first 24 hours of hospital admission. [3,17–19] Glau CL et al assessed 56 IMV dependent children using ultrasound and found that the diaphragm loses 3.4% of its thickness per IMV day, and that diaphragmatic atrophy is associated with increased IMV time and increased hospital stay.[18] Despite the impact of diaphragmatic atrophy on late outcomes, studies discussing the functional rehabilitation of those patients are extremely rare.

The patients included in our study presented complex diagnoses with multiple organ dysfunctions, with 9,000 hours of IMV time. Several authors have identified that specific risk factors such as prolonged

mechanical ventilation [20, 21], use of neuromuscular blockers [18], sepsis and multiple organ dysfunction syndrome [22, 23] aggravated muscle mass loss. Most of these risk factors were identified in our population.

In our study, muscle atrophy was characterized by loss of muscle strength, which was assessed through PIMAX. Measurement of PIMAX is an effective method for assessing inspiratory muscles strength. [24, 25] The maximum negative pressure generated during temporary airway occlusion is commonly used to measure inspiratory muscle strength in children under mechanical ventilation as it is easy to execute and is not invasive. A normal or almost normal rate of PIMAX is useful to rule out weakness of the respiratory muscles and obviates the need for complex and/or invasive testing. [25–28]

So far, few pediatric studies have evaluated the effect of inspiratory muscle training on muscle strength and on clinical outcomes, such as the duration of ventilatory assistance [12–14], limiting themselves to the description of clinical cases. When considering a protocol for inspiratory muscle training, it was unclear whether moderate load training could cause muscle fatigue since the diaphragm contracts 24 hours/day without a break.

Our protocol was designed based on the recommended load for a peripheral muscle strength training program, in which it is established by physiology that 6 maximal or submaximal contractions produce an almost optimal increase in strength and no muscle fatigue.

Our study has limitations. The first is the small number of patients in the sample. However, although our sample is small, we share how challenging it is to gather this number of patients and this study is the largest so far conducted with the pediatric population. The second is that the presence of complex diagnoses caused the stabilization of patients and the indication for IMT to occur after a long period of mechanical ventilation. The third is that there was no control group to compare strength gains in patients not submitted to the training protocol. Our study presented a safe and effective protocol for gaining Pimax that favored the weaning of patients on prolonged mechanical ventilation, however, a randomized study and the presence of a control group is necessary for the validation of these findings.

Conclusion

Our study supports performance of IMT using moderate loads (60%) with no risk of muscle fatigue, as it resulted in a significant increase in PIMAX after 2 weeks of training and in positive outcomes in weaning from mechanical ventilation. Finally, we suggest increase in PIMAX measurements for all children with prolonged use of IMT due to its low cost, applicability and to help clinicians to find the right time in the difficult decision of disconnecting these patients off the ventilator.

List Of Abbreviations

PIMAX: maximal inspiratory pressure

IMV: invasive mechanical ventilation

IMT: Inspiratory muscle training

GEE: Generalized Estimation Equation Model

Declarations

Ethics approval and consent to participate: The research was approval by the Albert Einstein Hospital's research ethics committee and is registered under CAAE number (Certificate of Presentation of Ethical Appreciation, acronym in Portuguese) 77279317.4.0000.0071 and the informed consent requirement was waived by Albert Einstein Hospital's ethics committee

Consent for publication: not applicable

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: This study received no funding

Authors' contributions

MSN made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, been involved in drafting the manuscript and revising it critically for important intellectual content; FE, SSK and AF made substantial contributions to conception and design and acquisition of data, analysis and interpretation of data; CP and JFA been involved in drafting the manuscript given final approval of the version to be published and revising it critically for important intellectual content; DNM made substantial contributions to conception and design, analysis and interpretation of data and been involved in drafting the manuscript given final approval of the version to be published.

Acknowledgements: We are grateful to the statistical team that carried out the analysis of this study

References

1. Powers SK, Kavazis AN and Levine S. Prolonged mechanical ventilation alters diaphragmatic structure and function. Crit Care Med 2009; 37(10 Suppl): S347–S353.

2. Vassilakopoulos T, Petrof BJ (2004) Ventilator-induced diaphragmatic dysfunction. American Journal of Respiratory and Critical Care Medicine 169: 336–341.

3. Levine S, Nguyen T, Taylor N, Friscia ME, Budak MT,Rothenberg P, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. New England Journal of Medicine 2008; 358:

1327–1335.

4. Tobin MJ, Laghi F and Jubran A. Ventilator-induced respiratory muscle weakness. Ann Intern Med. 2010; 153(4): 240–245.

5. Gayan-Ramirez G and Decramer M. Effects of mechanical ventilation on diaphragm function and biology. Eur Respir J 2002; 20: 1579–1586

6. Prentice CE, Paratz JD, Bersten AD (2010) Differences in the degree of respiratory and peripheral muscle impairment are evident on clinical, electrophysiological and biopsy testing in critically ill adults: a qualitative systematic review. Critical Care and Resuscitation 2010; 12: 111–120

7. Schild K, Neusch C and Schönhofer B. Ventilator-Induced Diaphragmatic Dysfunction (VIDD). Pneumologie 2008; 62(1): 33-38

8. Shoemaker MJ, Donker S, Lapoe A. Inspiratory muscle training in patients with chronic obstructive pulmonary disease: the state of the evidence. Cardiopulm Phys Ther J. 2009 Sep;20(3):5-15.

9. Caruso P, Denari SDC, Ruiz SAL, Bernal KG, Manfrin GA, Friedrich C, and Deheinzelin D. Inspiratory muscle training is ineffective in mechanically ventilated critically ill patients. CLINICS 2005;60(6):479-84

10. Laghi F, D'Alfonso N and Tobin MJ. Pattern of recovery from diaphragmatic fatigue over 24 hours. J Appl Physiol. 1995;79:539-46.

11. Martin AD, Davenport PD, Franceschi AC, Harman E. Use of inspiratory muscle strength training to facilitate ventilator weaning: a series of 10 consecutive patients. Chest 2002; 122(1):192-6

12. Martin AD, Smith BK, Davenport PD, Harman E, Gonzalez-Rothi RJ, Baz M, Layon AJ, Banner MJ, Caruso LJ, Deoghare H, Huang T and Gabrielli A. Inspiratory muscle strength training improves weaning outcome in failure to wean patients: a randomized trial. Crit Care 2011;15(2):R84

13. Smith BK, Bleiweis MS, Zauhar J, Martin D. Inspiratory muscle training in a child with Nemaline Myopathy and organ transplantation. Pediatr Crit Care Med 2011.12(2): e94-e98.

14. Brunherotti MAA, Bezerra PB, Bachur CK, Jacometti CR. Inspiratory muscle training in a newborn with anoxia who was chronically ventilated. Physical Therapy 2012; 92 (6): 865-871.

15. Smith BK, Bleiweis MS, Neel CR, Martin AD. Inspiratory muscle strength training in infants with congenital heart disease and prolonged mechanical ventilation: a case report. Physical Therapy 2013; 93(2):229 – 236.

16. Harikumar G, Moxham J,and Rafferty GF. Measurement of maximal inspiratory pressure in ventilated children. Pediatric Pulmonol 2008;43(11):1085-1091

17. Johnson RW, Ng KWP, Dietz AR, Hartman ME, Baty JD, Hasan N, et al. Muscle atrophy in mechanically-ventilated critically ill children. PLoS ONE 2018; 13(12): e0207720.

18. Glau CL, Conlon TW, Himebauch AS, Yehya N, Weiss SL, Berg RA, et al. Progressive Diaphragm Atrophy in Pediatric Acute Respiratory Failure. Pediatr Crit Care Med. 2018; 19(5):406–11.

19. Jaber S, Petrof BJ, Jung B, Chanques G, Berthet JP, Rabuel C, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. Am J Respir Crit Care Med. 2011; 183(3):364–71

20. De Jonghe B, Sharshar T, Lefaucheur JP, Authier FJ, Durand-Zaleski I, Boussarsar M, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA. 2002; 288(22):2859–67.

21. de Jonghe B, Lacherade JC, Sharshar T, Outin H. Intensive care unit-acquired weakness: risk factors and prevention. Crit Care Med. 2009; 37(10 Suppl):S309–15.

22. de Letter MA, Schmitz PI, Visser LH, Verheul FA, Schellens RL, Op de Coul DA, et al. Risk factors for the development of polyneuropathy and myopathy in critically ill patients. Crit Care Med. 2001; 29 (12):2281–6.

23. Leijten FS, Harinck-de Weerd JE, Poortvliet DC, de Weerd AW. The role of polyneuropathy in motor convalescence after prolonged mechanical ventilation. JAMA. 1995; 274(15):1221–5.

24. Harikumar G, Moxham J, Greenough A and Rafferty GF. Measurement of maximal inspiratory pressure in ventilated children. Pediatr Pulmonol. 2008 ; 43(11): 1085–1091

25. Freitas DA, Borja RO, Ferreira GMH, Nogueira PA, Morganna K and Mendonça PP. Predictive equations and normal values for maximal respiratory pressures in childhood and adolescence. Rev Paul Pediatr 2011;29(4):656-62.

26. . Wilson SH, Cooke NT, Edwards RH, Spiro SG. Predicted normal values for maximal respiratory pressures in Caucasian adults and children. Thorax 1984; 39:535-8.

27. Tomalak W, Pogorzelski A, Prusak J. Normal values for maximal static inspiratory and expiratory pressures in healthy children. Pediatr Pulmonol 2002; 34:42-6.

28. Faroux B. Respiratory muscle testing in children. Paediatric Respiratory Reviews 2003; 4, 243–249.

Figures

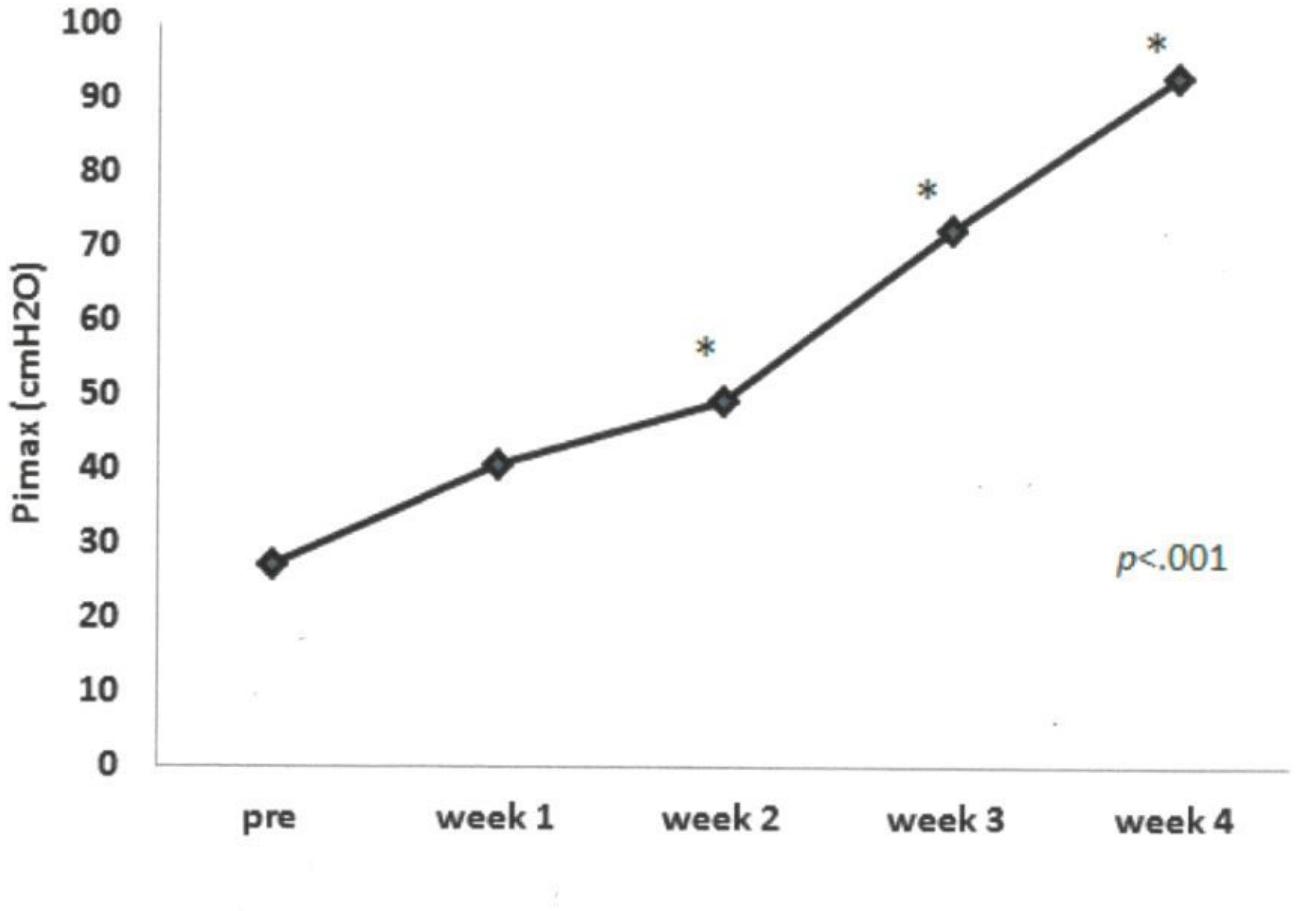

Figure 1

Mean of PIMAX values pre-training and at weeks 1, 2, 3 and 4. *p-value <.001