Ventilator Inspiratory Trigger Sensitivity Adjustment Versus Threshold Device Training On Difficult To Wean Guillain Barre Patients

Marian A. Aziz, M.Sc.¹, Nesreen G. Mohamed, Ph.D.¹, Mohamed A. Elgendy, M.D.², And Donia M. El Masry, Ph.D.¹

ABSTRACT

Background: Neurological dysfunction like guillain barre is a common condition necessitating prolonged mechanical ventilation (PMV). Inspiratory muscle weakness is common in these patients which may cause failure of weaning. Purpose of this study: To compare the effect of both ventilator inspiratory trigger sensitivity adjustment and threshold device training on difficult to wean guillain barre patients.

Material and methods: There were 30 male and female (23 women &7 men) patients on mechanical ventilation who had guillain-barré syndrome with an age range of 25 to 55 years old took-part in the study. Twenty-six of these patients fully completed the study while three of them died and one was re-intubated. They were recruited from neurological intensive care unit (ICUs) in Al- kaser Al- ainy medical school, Cairo university. The practical work of the study was carried out in the period starting from January 2022 to December 2022. All patients were randomized into two study groups; group (A) threshold inspiratory muscle trainer was used and group (B) changes in ventilator pressure setting. Primary outcome was time to complete weaning (in days), secondary out comes were changing in mechanical ventilation sittings including: Negative inspiratory force (NIF), Inspiratory positive air-way pressure (IPAP), Positive end-expiratory pressure (PEEP), Minute ventilation (VE), Respiratory endurance (Index of Tobin), and the PaO2/FIO2 ratio.

Results: After management in both groups the results of primary outcome indicate a statistically significant change in the MV group that patients spent substantially fewer days on a ventilator on average (9.27±4.74) compared to the IMT group (16.67±6.86) with a t test = -3.436 (p=0.002). Also there were no significant differences in NIF, IPAP, PEEP, Index of Tobin, and PaO2/FIO2 levels between the MV group and the IMT group. There was a borderline significant difference in minute ventilation (MV) between the MV group the IMT group.

Conclusion: It could be concluded that inspiratory muscles training by ventilator inspiratory trigger sensitivity adjustment helped to reduce days on mechanical ventilator more than threshold device training, with no significant differences between two techniques regarding to ventilator variables in difficult to wean guillain barre patients.

Introduction

Rapidly rising, bilateral weakness and sensory abnormalities characterize Guillain-Barré syndrome (GBS), the most prevalent cause of acute neuropathy. Approximately 30 % of patients experience respiratory muscle weakness, and 10% have autonomic impairment; both conditions may necessitate intensive treatment as well as close monitoring [1].

Problems of GBS include cranial nerve impairments, sensory problems, weakness, ataxia, pain, as well as autonomic dysfunction. Approximately 50% of patients suffer cranial nerve abnormalities [2]. These deficits most commonly manifest as bilateral facial paralysis, difficulty swallowing, and occasionally extraocular motor dysfunction. The absence of airway protection, insufficient cough, and various pulmonary problems in patients with Guillain-Barré syndrome (GBS) are all caused by respiratory muscle weakness [3]

Patients with GBS who need prolonged ventilation have a bad prognosis than those who don't. Nevertheless, GBS is thought to be a self-limiting disease with a monophasic medical course, and most patients are expected to recover to some degree. Clinical improvement and regaining mobility have been reported in previously studied GBS patients with severe impairments who required MV [4,5,6]

Significant delays in weaning off of mechanical ventilation and an increased risk of major consequences like re-intubation, tracheostomy, as well as prolonged ventilation have been linked to the development of diaphragm atrophy throughout mechanical ventilation [7] Successful weaning is facilitated by respiratory muscle training, which may also shorten the patient's hospital stay [8]

Keywords:

Guillain barre -Mechanical ventilator -Weaning -Inspiratory muscles training.

¹ The Department of Physical Therapy for Cardiovascular/ Respiratory Disorder and Geriatrics ,Faculty of Physical Therapy, Cairo University

² The Department of Anesthesia and Critical Care Medicine Faculty of Medicine ,Ain-shams University

It is possible to train the inspiratory muscles in patients on ventilation in several methods, including isocapnic/normocapnic hyperpnoea training, resistive flow training, threshold pressure training, as well as adjusting the ventilator to create a training load. It is possible to gradually raise the inspiratory load by altering the pressure trigger sensitivities. This is often calculated as a MIP fraction of the (the maximum inspiratory pressure).[9]

PATIENTS AND METHODS

There were 30 male and female (23 women &7 men) patients on mechanical ventilation who had guillain-barré syndrome with an age range of 25 to 55 years old took-part in the study. Twenty-six of these patients fully completed the study while three of them died and one was re-intubated. They were recruited from neurological intensive care unit (ICUs) in Al- kaser Al- ainy medical school, Cairo university. The ethical committee of faculty of physical therapy no. P.T.REC/012/003421. The study's practical part was conducted from January to December of 2022. All patients were randomly assigned into 2 groups: Group A (IMT group): This group was including 15 MV guillain barre patients. These patients received inspiratory muscle training using threshold inspiratory muscle trainer for 3-5days a week till extubation (from first failed spontaneous breathing trial (SBT). Group B (MV group): This group was including 15 MV guillain barre patients, who received inspiratory muscle training via changes in ventilator pressure setting. Inclusion criteria: individuals who have been receiving MV for a minimum of 48 hours, Age: >18 years, Both sexes, BMI≥18.5-30, Ventilator mode: Pressure support mode with FiO2≤ 0.5, positive end expiratory pressure (PEEP) was <8-10cm/H2Oand respiratory rate < 25, Conscious oriented patient with Glasgow coma score ≥13, Alertness was titrated to a Riker Sedation Agitation Score of 4, PH>7.25, arterial oxygen saturation >90%, Cardiovascular stable, MIP from 15 to 30 cm H2O and able to trigger spontaneous breaths on Exclusion Criteria: hemodynamic instability as life threatening arrhythmias, acute heart failure, angina, Severe breathlessness when spontaneously breathing, Nonstationary course of any neuromuscular illness that prevents improvement with inspiratory muscle training. Injury to the spinal cord, Chest wall as well as rib mobility severely compromised by a skeletal disease (such as scoliosis, flail chest, or spinal instrumentation), Patients with profound sedation as well as paralysis of the respiratory muscles, High peak airway pressure (barotraumas), BMI \geq 35.

Procedures of the study:

-Evaluation procedures:

1.Primary out comes: time for complete weaning(in days) 2.Secondary out comes: Mechanical ventilator (CARESCAPE -R860/USA) Variables and lung mechanics measured [10]:

1)Data directly measured (absolute values):

1-Negative inspiratory force (NIF): to calculate the pressure for training procedures .2-Inspiratory positive air-way pressure (IPAP) 3-Positive end-expiratory pressure (PEEP) 4-Minute ventilation (VE) 5-Respiratory endurance: (Index of Tobin) The rapid shallow breathing index (RSBI) was utilized in clinical practice to estimate the likelihood of a

patient's complete recovery after MV. Rapid shallow breathing index (RSBI: the ratio of respiratory frequency to tidal volume). Extubation failure has been seen in patients with a normal RSBI. (<105 breaths/min/L).[11]

6-The Horowitz index (also known as the Carrico index): The ratio of partial pressure of arterial oxygen (PaO2) to the fraction of inspired oxygen (FIO2), the PaO2/FIO2 ratio, It's essential to the agreed-upon definition of ARDS and is often used to quantify the extent to which individuals with respiratory failure are hypoxemic. It ranged >300 not ARDS, >200-300 mild, >100-200 moderate, ≤100 sever.[12]

Therapeutic procedures:

- Threshold Inspiratory Muscle Training: (group A) Patients started breathing in a supine 45 deg. Up position at a resistance equivalent to 20% of their Negative inspiratory force (NIF) evaluated at baseline.[13] Patient performed 10 breaths for 3 sets, one time per day for 5 d/w 2min rest between sets, and if adverse signs were occurring treatment was stopped. [8] According to the patient's RPE as measured by a modified Borg Scale, training was progressed gradually. If the rate of perceived exertion was lower than 5, the inspiratory threshold trainer's resistance was raised by 2cmH2O. When the rate of perceived exertion was between 6 and 8, no change was seen in the resistance, but when it was between 9 and 10, a drop of 1 to 2 cmH2O was seen [14]

Adjustment of ventilator trigger sensitivity: (group B)

In a supine 45-degree-up posture, we reduced the ventilator's trigger sensitivities to 20% of the patient's baseline NIF. Session length was 5 minutes twice every day for 5 days, with a maximum of 30 minutes each session. Each session, the NIF was raised by 10%, and if any adverse effects appeared, treatment was discontinued [9] according to the patient's RPE as measured by the modified Borg Scale, the resistance was progressively raised. If the rate of perceived exertion was under 5, then the time and pressure were raised gradually. When the rate of perceived exertion was between 6 and 8, the resistance changed accordingly.

-After weaning we recorded number of days on mechanical ventilator and ventilation parameters at last SBT.

-Statistical producers: SPSS Inc., Chicago, Illinois, USA) version 23.0 statistical tool for the social sciences was used to analyze the collected data. When the quantitative data followed a parametric (normal) distribution, we reported the mean, standard deviation, as well as ranges; if the data did not follow a normal distribution, we reported the median as well as interquartile ranges. Quantitative and percentage representations of qualitative factors were also provided. The Kolmogorov-Smirnov Test as well as the Shapiro-Wilk Test were utilized to investigate the data for normality.

Results

I- Demographic data:

Thirty patients (23 women and 7 men) on mechanical ventilator with guillain barre syndrome were assigned in two groups that received inspiratory muscle training. They aged from 20 to 55 years. The demographic data comparison

between the MV group (n=15) and IMT group (n=15). First, regarding age, there is no statistically significant difference among the two groups (p=0.270). On average, the MV group is slightly younger with a mean age (±Standard Deviation) of 37.93(±9.79) years, while the IMT group has a mean age of 41.87(±9.33) years.

Secondly, when considering gender distribution, there is also no statistically significant difference (p=0.666). Both groups have a predominantly female composition, with 12 (80.0%) in the MV group as well as 11 (73.3%) in the IMT group as shown in table (1).

Primary outcome (days on vent):

Descriptive analysis of the primary outcome:

As shown in table (2); presents a comparison of the primary outcome, "days on ventilator," between the MV group and IMT group. On average, patients in the MV group spent significantly fewer days on a ventilator, ranging from (4 to 21 days) with a mean of 9.27 (± 4.74) days, compared to the IMT group, where the range was (5 to 30 days) with a mean value $16.67(\pm 6.86)$ days.

Comparative analysis of the primary outcome:

The un-paired t-test was employed to test the significance of differences between the groups.

The findings indicate a statistically significant distinction, patients in the MV group spent substantially fewer days on a ventilator on average (9.27 ± 4.74) compared to the IMT group (16.67 ± 6.86) with a t test = -3.436 (p=0.002*) as shown in table (2).

Case sequence:

Descriptive analysis of Case sequence:

As found in Table (3) compares case sequences and outcomes between the MV group and IMT group. In the "Continue" category, 93.3% of the MV group and 80.0% of the IMT group continued treatment. There were no reported deaths in the MV group, while 20.0% of patients in the IMT group unfortunately died. Re-intubation was required for 6.7% of MV group patients, but none in the IMT group.

Comparative analysis of Case sequence:

Chi-square as well as Fisher's exact tests were utilized to test differences among the MV group and IMT group concerning case sequence and outcomes.

In the "Continue" category, 93.3% of the MV group and 80.0% of the IMT Group continued treatment, resulting in a Fisher's Exact test p-value of 0.125, indicating some difference but not highly significant. Notably, no deaths occurred in the MV group, whereas 20.0% of IMT group patients unfortunately died. Additionally, re-intubation was needed for 6.7% of MV group patients but none in the IMT Group with X2=4.154 (0.125) as shown in table (3).

pre-management

As shown in table (4) presents a comprehensive comparison of pre-management data of mechanical

ventilator variables and lung mechanics between MV group and IMT group, using an un-paired t-test sample t-test to test statistical significance.

A borderline significant difference in NIF among the MV group (-8.80 \pm 2.83, SE = 0.73) and the IMT group (-6.47 \pm 2.10, SE = 0.54), with a t-value of -1.812 and a p-value of 0.081.

Significant difference in IPAP levels among the MV group (17.80 \pm 2.81, SE = 0.73) and the IMT group (22.33 \pm 4.20, SE = 1.08), with a t-value of -3.473 and a p-value of 0.002.

No significant difference in PEEP levels among the MV group (5.27 \pm 1.03, SE = 0.27) and the IMT group (5.20 \pm 1.32, SE = 0.34), with a t-value of 0.154 and a p-value of 0.879.

No significant difference in MV among the MV group (6.44 \pm 1.33, SE = 0.34) and the IMT group (5.45 \pm 1.29, SE = 0.33), with a t-value of 1.437 and a p-value of 0.162.

No significant difference in the Index of Tobin among the MV group (55.27 ± 15.40 , SE = 3.98) and the IMT group (58.60 ± 15.98 , SE = 4.12), with a t-value of -0.355 and a p-value of 0.725.

No significant difference in the Horowitz Index among the MV group (207.27 \pm 58.90, SE = 15.27) and the IMT group (216.87 \pm 67.48, SE = 17.42), with a t-value of -0.415 and a p-value of 0.681.

post-management:

As found in table (5) presents a comprehensive comparison of post-management data of mechanical ventilator variables and lung mechanics between the MV group and IMT group, using an unpaired sample t-test to test statistical significance. No significant difference has been detected in NIF among the MV group (-14.64 \pm 4.25, SE = 1.10) and the IMT group (-12.58 \pm 4.12, SE = 1.19), with a t-value of -1.248 as well as a p-value of 0.224.

No significant difference has been detected in IPAP levels among the MV group (12.07 \pm 3.08, SE = 0.79) and the IMT group (13.25 \pm 2.56, SE = 0.74), with a t-value of -1.051 as well as a p-value of 0.304.

No significant difference has been detected in PEEP levels among the MV group (4.00 ± 1.04 , SE = 0.27) and the IMT group (4.33 ± 0.98 , SE = 0.28), with a t-value of -0.836 as well as a p-value of 0.412.

There was a borderline significant difference in MV between the MV group $(9.59 \pm 1.96, SE = 0.51)$ and the IMT group $(8.12 \pm 1.66, SE = 0.43)$, with a t-value of 2.052 and a p-value of 0.051.

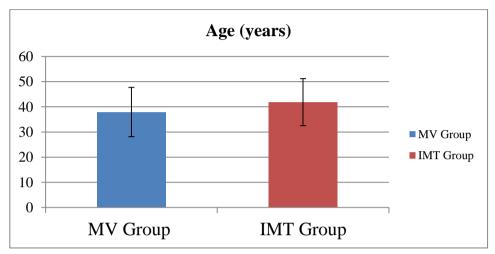
No significant difference has been detected in the Index of Tobin among the MV group $(36.93 \pm 21.38, SE = 5.51)$ and the IMT group $(29.75 \pm 9.91, SE = 2.56)$, with a t-value of 1.067 and a p-value of 0.297.

There was no significant difference in the Horowitz Index among the MV group (434.93 \pm 99.83, SE = 25.83) and the IMT group (367.25 \pm 61.49, SE = 15.87), with a t-value of 1.126 and a p-value of 0.271.

Results

Table (1): Comparison among groups based on demographic data.

Demographic data	MV Group (n=15)	IMT Group (n=15)	Test value	P-value
Age (years)				
Mean±SD	37.93±9.79	41.87±9.33	t=1.126	0.270
Range	20-52	24-55	ι=1.126	0.270
Sex				
Female	12 (80.0%)	11 (73.3%)	x2:0.186	FE:0.666
Male	3 (20.0%)	4 (26.7%)	XZ.U. 100	FE.U.000



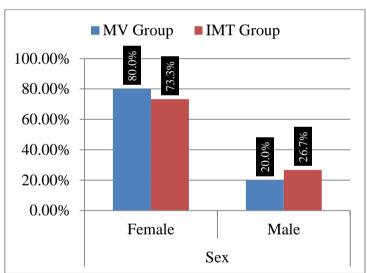


Table (2): Comparison between groups according to primary outcome "days on vent"

Primary outcome (Days on Vent)	MV Group (n=15)	IMT Group (n=15)	t-test	P-value
Mean±SD	9.27±4.74	16.67±6.86	-3.436	0.002*
Range	4-21	5-30	-3.430	

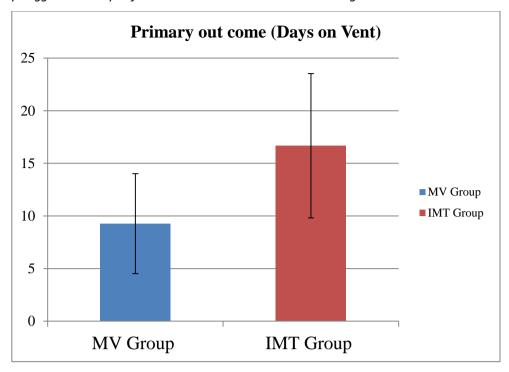


Table (3): Comparison between groups according to case sequence.

Case sequence	MV Group (n=15)	IMT Group (n=15)	x2	P-value
Continue	14 (93.3%)	12 (80.0%)		
Died	0 (0.0%)	3 (20.0%)	4.154	FE0.125
Re-intubation	1 (6.7%)	0 (0.0%)	4.154	FEU. 125
Total	15 (100%)	15 (100%)		

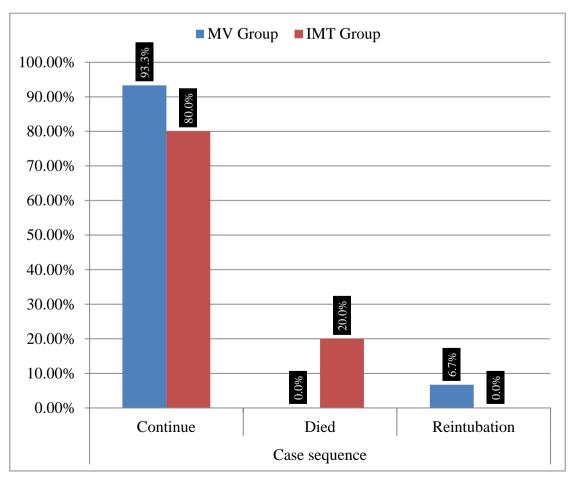


Table (4): Comparison between groups according to pre-management mechanical ventilator variables and lung mechanics data.

Pre-management data	MV Group (n=15)	IMT Group (n=15)	t-test	P-value
NIF				
Mean±SD	-8.80±2.83	-6.47±2.10	-1.812	0.081
Range	-155	-204	-1.612	0.061
IPAP				
Mean±SD	17.80±2.81	22.33±4.20	-3.473	0.002*
Range	14-25	16-28	-3.4/3	0.002
PEEP				
Mean±SD	5.27±1.03	5.20±1.32	0.154	0.879
Range	5-9	3-8	0.134	0.679
MV				
Mean±SD	6.44±1.33	5.45±1.29	1.437	0.162
Range	3.09-11.66	3.3-7.95	1.437	0.162
Index of tobin				
Mean±SD	55.27±15.40	58.60±15.98	-0.355	0.725
Range	12-106	22-119	-0.355	0.725
Horowitz Index				
Mean±SD	207.27±58.90	216.87±67.48	-0.415	0.681
Range	130-358	131-379	-0.415	0.001

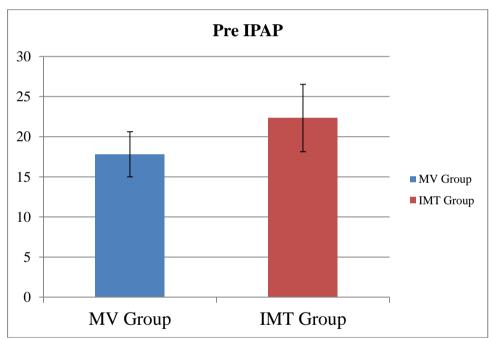


Table (5): Comparison between groups according to post-management mechanical ventilator variables and lung mechanics.

Post-management data	MV Group (n=14)	IMT Group (n=12)	t-test	P-value
NIF				
Mean±SD	-14.64±4.25	-12.58±4.12	-1.248	0.224
Range	-258	-259	-1.246	0.224
IPAP				
Mean±SD	12.07±3.08	13.25±2.56	-1.051	0.304
Range	10-19	10-17	-1.051	0.304
PEEP				
Mean±SD	4.00±1.04	4.33±0.98	-0.836	0.412
Range	3-5	3-5	-0.636	0.412
MV				
Mean±SD	9.59±1.96	8.12±1.66	2.052	0.051
Range	6.6-14.05	5.2-11.1	2.052	0.051
Index of tobin				
Mean±SD	36.93±21.38	29.75±9.91	1.067	0.297
Range	17-105	13-49	1.007	0.297
Horowitz Index				
Mean±SD	434.93±99.83	367.25±61.49	1.126	0.271
Range	227-1070	279-480	1.126	0.271

DISCUSSION

The findings of the study were consistent with the study conducted by Chang, Hsiao [15] Check the trigger sensitivity of the ventilator Following six weeks of training, patients on extended MV for greater than 21 days improved their maximum inspiratory pressure from 10% at the beginning to 40%. This study revealed that improving the MIP, RSBI, TV, as well as P/F ratio in patients with PMV by adjusting the ventilator trigger sensitivity increased the likelihood that these patients may wean off from MV.

Patients weaning from MV in the ICU can benefit greatly from threshold pressure training or adjusting the sensitivity of their ventilators, as was found in a systematic review by Elkins & Dentice[8]. These benefits involve a more efficient breathing pattern, more effective weaning, a possible decrease in duration of stay, and briefer usage of non-invasive ventilatory assistance after extubation. These gains can be achieved without risk if the training is used on suitable patients while they are under close observation and other precautions are taken.

The study done by Ibrahiem, Mohamed [16] on 30 mechanically ventilated patients with respiratory failure. The individuals in study group A were given both conventional chest physiotherapy as well as training for their respiratory muscles with a threshold device. The individuals in control group B, on the contrary, only were given conventional chest physiotherapy. Results showed that training the respiratory muscles as well as conventional physiotherapy might help oxygenation and the strength of the respiratory muscles for individuals who are mechanically ventilated. The study group as well as the control group had significantly different mean values after treatment for PaO2, SaO2%, as well as PaO2/FiO2. Group A showed greater increases in all of the evaluated respiratory variables compared to Group B. There was no significant difference between the two groups in terms of breathing muscles strength (NIP) before treatment; the P-value was 0.89.

Also the results coincides with single-blind, randomized controled trial of Martin [17], examined if inspiratory muscle strength training (IMST) could help FTW patients wean more easily. 69 of the 129 patients who were considered for engagement were actually enrolled and studied. 35 people were randomized into the IMST condition as well as 34 individuals were assigned into the SHAM condition. A threshold inspiratory device was used for IMST. It was adjusted to the highest pressure that could be managed and progressed every day. A constant low inspiratory pressure load was administered during SHAM training. The peak inspiratory pressure (MIP) did not change significantly between the groups (-43.5 \pm 17.8 vs. - 45.1 ± 19.5 cm H2O, P = 0.39), but it improved in the IMST group (-44.4 \pm 18.4 vs. -54.1 \pm 17.8 cm H2O, P < 0.0001). Concerning the IMST or SHAM treatments, there were no negative impacts seen. Out of 35 IMST subjects, 25 weaned (71%; 95% CI = 55% to 84%), while only 16 of 34 SHAM subjects weaned (47%; 95% CI = 31% to 63%), P = .039. For the treatment to be effective, it had to be given to four individuals (95% CI = 2 to 80). IMST can lead

to higher MIP and better preventing outcomes for FTW patients when compared with SHAM treatment.

Alternatively, Caruso [18] demonstrated As soon as patients with severe critical illnesses started training their inspiratory muscles, the rate of reintubation did not go lower or the time it took to stop artificial ventilation was shortened. The strength of the muscles used for breathing in and out kept mostly the same during MC, with or without this special training for those muscles. Prospective, randomized clinical study in an adult surgical ICU. 12 patients practiced their inspiratory muscles two times a day, while thirteen patients didn't (control). The ventilator's sensitivity was changed based on the maximum inspiratory pressure during training. The maximum inspiratory pressure was checked on the patients every day. Weaning took 31 \pm 22 hours for the control group and 23 \pm 11 hours for the training group (P = .24), and 5 time for the control group and 3 times for the training group (P = .39), so there was no statistical difference between them. Individuals in the control group had a slight tendency for their maximum inspiratory pressure to increase. The training group, on the other hand, showed a slight reduction (P = .34).

On the other hand, Condessa[19] found that training the respiratory muscles didnt significantly lessen the weaning period, but it did improve the strength as well as tidal volume of the respiratory muscles. 92 patients who were getting pressure support breathing were part of the study. They were tracked until they were taken off the ventilator, had a tracheostomy, or died. The experimental group got regular care as well as inspiratory muscle training with a threshold device. They did 5 sets of 10 breaths, two times a day, seven days a week, with an effort of 40% of their maximum inspiratory pressure. The individuals in the control group only were given normal care. The length of the weaning time was the main outcome. Changes in tidal volume, the rapid shallow breathing index, as well as the power of the respiratory muscles were the secondary dependent variables. Weaning took a mean of 8 hours less time in the experimental group, but this difference wasn't statistically significant (95% CI: -16 to 32). The experimental group had higher maximum inspiratory as well as expiratory pressures than the control group. The experimental group had mean values of 10 cmH2O (95% CI 5 to 15) for inspiratory pressures and 8 cmH2O (95% CI 2 to 13) for expiratory pressures. The experimental group's tidal volume additionally increased up while the control group's dropped down (mean difference 72 ml, 95% CI 17 to 128). There wasn't significant difference among the groups in the rapidly shallow breathing score.

Conclusion:

Based on the findings, it could be concluded that there is a significant difference between inspiratory muscle training by ventilatory trigger sensitivity adjustment and threshold device in days on vent.

References

Carpentier VT, Le Guennec L, Fall SAA, Viala K, Demeret S, Weiss N. (2022). Syndrome de Guillain-Barré: physiopathologie et aspects diagnostiques [Pathophysiological and diagnostic aspects of Guillain-Barré syndrome]. Rev Med Interne. 2022 Jul;43(7):419-428. French. doi: 10.1016/j.revmed.2021.12.005. Epub 2022 Jan 6. PMID: 34998626.

Asbury, A. K. & Cornblath, D. R. (1990). Assessment of current diagnostic criteria for Guillain-Barré syndrome. Ann. Neurol. 27 (Suppl.), S21-S24 (1990)

Hahn, A. F. (2001). The challenge of respiratory dysfunction in Guillain-Barre syndrome. Arch. Neurol. 58, 871-872. doi:10.1001/archneur.58.6.871.

Dhar R, stitt L, hahn aF.(2008). The morbidity and outcome of patients with Guillain-Barré syndrome admitted to the intensive care unit. J Neurol Sci 2008;264:121-8

Fletcher DD, Lawn ND, Wolter TD, et al.(2000). Long-term outcome in patients with Guillain- Barré syndrome requiring mechanical ventilation. Neurology 2000;54:2311-5.

de Boisanger L. (2016). Outcomes for patients with Guillain-Barré syndrome requiring mechanical ventilation: a literature review. Ir J Med Sci 2016;185:11-15

Goligher, E. C., Dres, M., Fan, E., Rubenfeld, G. D., Scales, D. C., Herridge, M. S., Vorona, S., Sklar, M. C., Rittayamai, N., Lanys, A., Murray, A., Brace, D., Urrea, C., Reid, W. D., Tomlinson, G., & Slutsky, A. S. (2018). Mechanical Ventilation induced Diaphragm Atrophy Strongly Impacts Clinical Outcomes. 197(2), 204-213. https://doi.org/10.1164/rccm.201703-0536OC

Elkins, M., & Dentice, R. (2015). Inspiratory muscle training facilitates weaning from mechanical ventilation among patients in the intensive care unit: A systematic review. Journal of Physiotherapy, 61(3), 125-134. https://doi.org/10.1016/j.jphys.2015.05.016

Elbouhy, M. S., AbdelHalim, H. A., & Hashem, A. M. A. (2014). Effect of respiratory muscles training in weaning of mechanically ventilated COPD patients. Egyptian Journal of Chest Diseases and Tuberculosis, 63(3), 679-687.

https://doi.org/10.1016/j.ejcdt.2014.03.008 Ghiani, A., Paderewska, J., Sainis, A. et al.(2020). Variables predicting weaning outcome in prolonged mechanically ventilated tracheotomized patients: a retrospective study. j intensive care 8, 19. https://doi.org/10.1186/s40560-020-00437-4

Goharani, R., Vahedian-azimi, A., Galal, I. H., Souza, L. C. De, Farzanegan, B., Bashar, F. R., Miller, A. C. (2019). A rapid shallow breathing index threshold of 85 best predicts extubation success in chronic obstructive pulmonary disease patients with hypercapnic respiratory failure, 11(4), 1223-1232.

https://doi.org/10.21037/jtd.2019.03.103
Brown, S. M., Duggal, A., Hou,et al., (2017).
Nonlinear Imputation of PaO2/FIO2 From
SpO2/FIO2 Among Mechanically Ventilated Patients
in the ICU: A Prospective, Observational Study.
Critical care medicine, 45(8), 1317-1324.
https://doi.org/10.1097/CCM.00000000000002514

Bissett, B., Science, A., & Leditschke, I. A. (2019). Australian Critical Care Inspiratory muscle training for intensive care patients: A multidisciplinary practical guide for clinicians. Australian Critical Care, 32(3), 249-255. https://doi.org/10.1016/j.aucc.2018.06.001 Overend T.J., Anderson C.M., Jackson J., Lucy S.D., Prendergast M. and Sinclair S. (2010): Physical therapy management for adult patients undergoing cardiac surgery: A Canadian practice survey. Physiother Can.; 62: 215-21.

Chang, H. Y., Hsiao, H. C., & Chang, H. L. (2022). Impact of Inspiratory Muscle Training on Weaning Parameters in Prolonged Ventilator-Dependent Patients: A Preliminary Study. SAGE Open Nursing, 8(1492).

https://doi.org/10.1177/23779608221111717 Ibrahiem, A., Mohamed, A., & Egypt, H. (2015). Effect Of Respiratory Muscles Training In Addition To Standard Chest Physiotherapy On Mechanically Ventilated Patients. Journal of Medical Research and Practice, 3(3), 52-58

Martin, A. D., Smith, B. K., Davenport, P. D., Harman, E., Gonzalez-Rothi, R. J., Baz, M., Layon, A. J., Banner, M. J., Caruso, L. J., Deoghare, H., Huang, T. T., & Gabrielli, A. (2011). Inspiratory muscle strength training improves weaning outcome in failure to wean patients: A randomized trial. Critical Care, 15(2), 1-12. https://doi.org/10.1186/cc10081

Caruso, P., Denari, S. D. C., Ruiz, S. A. L., Bernal, K. G., Manfrin, G. M., Friedrich, C., & Deheinzelin, D. (2005). Inspiratory muscle training is ineffective in mechanically ventilated critically ill patients. Clinics (São Paulo, Brazil), 60(6), 479-484. https://doi.org/10.1590/S1807-

59322005000600009

Condessa, R. L., Brauner, J. S., Saul, A. L., Baptista, M., Silva, A. C. T., & Vieira, S. R. R. (2013). Inspiratory muscle training did not accelerate weaning from mechanical ventilation but did improve tidal volume and maximal respiratory pressures: A randomised trial. Journal of Physiotherapy, 59(2), 101-107. https://doi.org/10.1016/S1836-9553(13)70162-0