A Randomized Clinical Trial to Compare the Criteria of Readiness for Extubation and Daily Spontaneous Breathing Test (SBT) on the Duration of Mechanical Ventilation

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Abstract

Background: Successful weaning of the ventilator is a major challenge, especially in children. This study was conducted to compare the criteria of readiness for extubation and daily spontaneous breathing test (SBT) on the duration of mechanical ventilation and extubation failure rates.

Materials and Methods
This randomized clinical trial was conducted in the pediatric intensive care unit (PICU) of a teaching hospital (Imam Hossein Hospital) in Isfahan, Iran. Overall, 68 patients were assigned into two groups of equal number. In the intervention group, if all the readiness criteria were met the spontaneous breathing test (SPONT/PSV) was performed, and the tracheal tube was removed if the test was successful. In the control group, extubation was performed based on the physician's clinical judgment. Duration of mechanical ventilation and extubation failure rates were compared between groups.

Results: The percentage of extubation failure was higher in the control group than in the intervention (26.4% vs. 11.7%, respectively, P=0.04). The two groups were not significantly different in terms of the percentage of reintubation (11.7% vs. 5.8%), and only the percentage of using noninvasive mechanical ventilation (NIMV) was higher in controls (14.7% vs. 5.8%, respectively, P=0.05). No significant difference was observed between the two groups in terms of the median duration of mechanical ventilation in patients with successful extubation (P=0.12). Likewise, the long-term outcomes, i.e. the length of stay in PICU and hospital were not different in the two groups (P>0.05).

Conclusion
According to the results, daily SPONT/PSV test reduce extubation failure more than physician's clinical judgment in pediatric population. However, type of extubation protocol did not affect mortality, the duration of mechanical ventilation and stay in the PICU.

Key Words: Children, Extubation, Spontaneous Breathing Test, Ventilation.

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1- INTRODUCTION

Although mechanical ventilation can be a lifesaver in severe cases of respiratory failure (1), successful extubation is a major challenge, especially in children (2-5). Both extubation failure and increases in mechanical ventilation duration are associated with increases in mortality and morbidity (6-9). Extubation is performed in the PICU mainly based on clinical judgment rather than a specific protocol (10). Different studies conducted to determine the predicting criteria for successful extubation have till now failed to obtain accurate results (9, 11,12). The SBT has been studied as a method of determining patient readiness for extubation. According to this method, the spontaneous breathing ability of intubated patients is evaluated while providing them with minimum respiratory support (13-17).

Certain criteria for patient readiness have also been investigated as a protocol before performing the SBT to help with successful extubation (18). Using the protocol, including the comparison of the criteria of readiness for weaning from the ventilator and daily SBT with clinical judgement and routine assessments in the ICU have shown many advantages such as reductions in the duration of ventilation and ICU and hospital stay in adults (19); nevertheless, few studies have investigated this subject in children. Two SBT methods were compared in a study, which showed no differences between two groups in terms of extubation failure rates, in line with other studies, and found SBT to be an appropriate extubation method in children (10). Another study comparing two groups with different SBT protocols with a third group without any definite protocols obtained similar results (8). Only one clinical trial conducted in 2011 to investigate a protocol involving the evaluation of readiness for extubation and daily SBT compared to the conventional method found mechanical ventilation to

significantly decrease in the intervention group (15). No studies have yet been conducted in Iran to investigate the effect of these protocols. The present randomized clinical trial was therefore designed to evaluate the effect of a protocol, involving the evaluation of the criteria of readiness for extubation and daily SBT, on the duration of mechanical ventilation and extubation failure rates as the short-term outcomes. Length of stay in the PICU and hospital and mortality were also investigated as the long-term outcomes.

2- MATERIALS AND METHODS

The sample size was calculated using an appropriate formula based on Type I error of 0.05, a power of 80% and the percentage of extubation failure obtained in previous studies (20). After signing written consent forms, the participants were divided into an intervention group and a control group using block randomization with a block size of two. The sixty-eight patients included in the study according to the inclusion and exclusion criteria were randomly divided into the intervention and control groups (n=34 each) .The intervention included an assistant PICU fellow performing the protocol in the intervention group.

In the control group, routine respiratory care was performed. The initial data of the patients collected included age, gender, the reason for hospitalization and intubation, PRISM-II (21), time of intubation, size of the tracheal tube and mode of ventilation, and their laboratory data were related to arterial-blood gas tests before and after intubation. ICU fellows perform the respiratory management of patients in the PICU of Imam Hossein hospital by pediatric attending and in anesthesiology. The attendant decides on ventilator settings and respiratory support reduction and extubation according to the results of arterial blood gas tests performed at least once a day and based on the patient's

clinical conditions, including eliminating the causes of intubation, appropriate ventilation and oxygenation, and stable vital signs. In the control group, routine respiratory care was performed as described. In the intervention, an assistant PICU fellow performed respiratory care according to the protocol. At least one arterial-blood gas test was also performed once a day in this group. Respiratory supports were reduced if possible as follows: with appropriate oxygenation, PEEP was reduced by one cmH2O every two hours to reach five cmH2O. In addition, FiO2 was reduced by 10% every 15 minutes to reach 0.4 or lower while maintaining SatO2 above 94%. PIP was also reduced by two cmH2O every two hours to reach 20 cmH2O or lower in case with the appropriate ventilation criteria, including proper chest dilation, a high expiratory tidal volume, and low PCO2 levels. Based on these criteria, the hourly respiratory rate was reduced by four to reach a maximum of 10. At a volume control mode, the tidal volume was reduced by 5 ml every two hours to reach 5 ml/kg in case with the appropriate ventilation criteria.

After reducing the settings of the device, the patients were prepared for the SBT if they met all the following criteria: recovery or elimination of their underlying causes for respiratory failure and intubation, temperature <38.5 ºC, a minimum hemoglobin level of 8, ability to swallow secretions, having gag or cough reflexes during suctioning the secretions, having an acceptable level of consciousness, i.e. GCS score (Glasgow Coma Score) ≥8 after discontinuing sedations and analgesics (22), correction of electrolytes, absence of new findings in the chest X-ray, no need for increasing the settings of the ventilator over the previous 24 hours, the total discontinuation of sedation and analgesics in at least the previous six hours, no need for vasoactive

agents, an acceptable arterial-blood gas and air exchange with StO2>94%, despite FiO2<40, PIP<20 and PEEP<5 (23). The initial outcomes recorded in both groups included the duration of mechanical ventilation in patients with successful extubation, extubation failure, the need for NIV and reintubation and ventilator-associated pneumonia. The recorded long-term outcomes in both groups also included the length of PICU and hospital stay and mortality in the PICU.

2-2. Laboratory measurements

The history of mechanical ventilation begins with various versions of what was eventually called the iron lung, a form of noninvasive negative pressure ventilator widely used during the polio epidemics of the 20th century after the introduction of the "Drinker respirator" in 1928, improvements introduced by John Haven Emerson in 1931 (24). The ventilator models used at this center included Raphael HAMILTON (SN: 147305) made in Switzerland, MAQUET Servo-i (SN: 147289) and MAQUET Servo-s (SN: 34542) made in Sweden.

2-2-1. Spontaneous breathing test (SBT): The SBT has been studied as a method of determining patient readiness for extubation. According to this method, the spontaneous breathing ability of intubated patients is evaluated while providing them with minimum respiratory support. Oral feeding was discontinued four hours before the test. The ventilator settings used for the test were as follows:

2-2-2. Mode: Spont/PSV, PEEP≤5, FiO2≤40, PS according to ET size (3-3.5:10, 4-4.5:8, ≥5:6) (25).

The respiratory rate, the heart rate, blood pressure, and expiratory tidal volume were recorded at the beginning and end of a 30-minute SBT and at minute 15. Arterial blood gas was taken at the beginning and end of the test. The SBT failure was confirmed in case at least two of the

following conditions were observed during the intervention: respiratory rate being outside the normal range by age, i.e. tachypnea or bradypnea (6 months:20-60; 6 months to two years:15-45; 2-5 years:15-40 and over 5 years:10-35), respiratory distress, VTe<5 ml/kg, SatO2<90%, hypotension based on PALS guidelines (25) or an over 20% increase in blood pressure, impaired consciousness associated with hypoventilation, heart rate outside the normal range by age, i.e. tachycardia and bradycardia (below1year:100-160, 1-3 years:90-150, 3-6 years:70-130, over 6 years:65-120), Pco2>55 mmHg or an increase in Pco2 by at least 10mmHg in patients with chronic pulmonary disease in the final arterial blood gas test (26).

If the test failed, the parameters and mode of the ventilator were set as before the test, and if the clinical criteria were met as described, the test was repeated 24 hours later. All the intervention stages were controlled and recorded for each patient in the intervention group according to the designed checklist, and the results were recorded in a data collection form. This study is a single-blind study that patients were not aware of respiratory care.

The endotracheal tube was immediately extracted if the test was successful, and the patient was provided with a non-rebreathing face mask with a 10-15 l/min flow and underwent 100% oxygen therapy. Arterial blood gas test was performed two hours after extubation. Extubation failure was confirmed in case at least two of the following symptoms emerged within two days of extubation: respiratory distress, hypoxia with SatO2<90%, respiratory rate outside the normal range by age, i.e. tachypnea or bradypnea (below 6 months: 20-60; 6 months to two years:15-45; 2-5 years:15-40 and over 5 years:10-35), apnea>20 seconds, hypotension based on PALS guidelines (12) or an over 20% increase in blood pressure, impaired

consciousness associated with hypoventilation, heart rate outside the normal range by age, i.e. tachycardia and bradycardia (below1 year:100-160, 1-3 years: 90-150, 3-6 years: 70-130, over 6 years: 65-120), Pco2>55 mmHg or an increase in Pco2 by at least 10mmHg in patients with chronic pulmonary disease accompanied by pH<7.3,the symptoms of upper airway obstruction.

The causes of extubation failure included upper airway obstruction; impaired lower airway, neurological causes, and heart failure were recorded. In case of the absence of contraindications for NIMV, Bi-level positive airway pressure (BiPAP) was applied with minimum settings as EPAP: 5 and IPAP: 8-10, and tittered up to EPAP: 8-10 and IPAP: 15-22 and until clinical and laboratory symptoms of respiratory failure disappeared. The patient was reintubated if respiratory failure symptoms persisted after two hours of monitoring (27). The post-extubation oxygen supply method, the criteria of extubation failure, NIMV, and reintubation protocols were the same in the control group.

2-3. Intervention

In the intervention group, if all the readiness criteria were met the spontaneous breathing test (SPONT/PSV) was performed, and the tracheal tube was removed if the test was successful. The intervention included an assistant PICU fellow performing the protocol in the intervention group.

2-4. Ethical consideration

All parents of patients signed consent forms. Ethical code is IR.MUI.MED.REC.1398.072. Trial code is IRCT20190219042766N1.

2-5. Inclusion and exclusion criteria

Included children were all eligible candidates. The excluded patients comprised those requiring intubation for

the obstruction of their upper airways, neuromuscular diseases, cyanotic heart diseases, and primary pulmonary hypertension as well as those with a tracheotomy, chronic mechanical ventilation, and spontaneous extubation and those who would have died before they had been extubated.

2-6. Data Analyses

To survive normal distribution, the Kolmogorov-Smirnov test was performed on the quantitative data, and the data with a non-normal distribution and the discrete quantitative data were reported as median and percentile and were compared using the Mann-Whitney test. The continuous quantitative data with a normal distribution were reported as mean and standard deviation and were compared using the t-test. The qualitative data were reported as percentage and compared using the Chi-square test or Fisher's exact test when the cell sizes were expected to be small (cell sizes <5). The data were analyzed in SPSS software version 16.0, and P<0.05 was set as the level of statistical significance

3- RESULTS

The sixty-eight patients included in the study according to the inclusion and exclusion criteria were randomly divided into the intervention and control groups (n=34 each). Males accounted for 47% of all participating patients and the median age of all patients was 17.5 months. The most frequent causes of admission in the PICU included neurological diseases (36.5%, n=25), and pneumonia (33.5%, n=23). Six out of the 68 patients were intubated in other centers and referred to the PICU. The most frequent (94.1%, n=64) ventilator mode used was the pressure mode, i.e. PSIMV-PC. **Table.1** summarizes the patients' demographic information and initial clinical conditions by group. The two groups were not significantly different in terms of demographic information and initial

clinical conditions. The most frequent cause of admission in the PICU was pneumonia (44.1%) in the intervention group and neurological diseases (41.2%) in the controls. The number of admissions to the PICU for post-operative care was higher in the control group (17.6%) than in the intervention group (2.9%), although the difference was statistically insignificant. Acute respiratory failure was the most frequent cause of intubation in both groups. In the intervention group, the SBT failed in only one patient, and the test was successful the second time, while the other patients were successfully extubated after their first test. Extubation failed in 13 (19%) out of the 68 patients in both groups, of whom only six needed reintubation, which accounted for 46.1% of the patients with extubation failure and 8.8% of the total number of patients.

The remaining 7 (10.2%) patients underwent NIMV and did not require reintubation. According to the initial outcomes, the percentage of extubation failure was 11.7% (n=4) in the intervention and 26.4% (n=9) in the control group, suggesting a significant difference between the two groups (P=0.04). However, no significant differences were observed between these groups in terms of the percentage of reintubation, and the only difference was related to the percentage of using NIMV (**Table.2**).

Table.3 presents the reasons for extubation failure by group, suggesting no significant differences between the two groups, and the most frequent reasons included heart failure (5.9%, n=2) in the intervention group and upper airway obstruction (8.8%, n=3) in the controls. As another short-term outcome, duration of mechanical ventilation in the patients with successful extubation was a median of 4 days (25 to 75 percentile: 3-7days), and it was not significantly different between the two groups (P=0.12) (**Table.2**). Ventilator-Associated pneumonia was observed as a

mechanical ventilation complication in 6 (8.8%) patients, i.e. n=3 in each group, there was not a significant difference between the two groups (**Table.2**). According to the long-term outcomes of the study, only two patients died after reintubation, and the total mortality was 2.9% in all the patients with extubation failure, and the two groups were not significantly different in this regard (**Table.2**). The length of PICU stay was a median of 9.5 days in all the study patients (25th to 75th percentile: 6-14.7 days). No significant differences were also observed between these groups in terms of the median length of PICU stay (P=0.3) (**Table.2**). The length of hospital stay was a median of 15.5 days (25th to 75th percentile: 9-25 days). No significant differences were also observed between these groups in terms of the median length of hospital stay (P=0.1) (**Table.2**).

Table-1: The patients' demographic information and initial clinical conditions in two groups.

Variables	Control group (n=34)	Intervention group (n=34)	P-value
Age (month)	20(4.7-85.5)	16.5(6-59)	O.77
Male	16(47.1%)	16(47.1%)	0.59
Weight (kg)	8.9(5.7-20.2)	8.7(6.6-21.7)	0.71
PRISM 2	3(0.75-6)	3(0-9)	0.82
Causes of PICU admission			
Pneumonia	8(23.5%)	15 (44.1%)	0.06
ARDS	1(2.9%)	2(5.9%)	0.5
Neurologic Disease	14(41.2%)	11(32.4%)	0.3
Heart Disease	2(5.9%)	2(5.9%)	0.5
Sepsis	2(5.9%)	2(5.9%)	0.5
Post operation	6(17.6%)	1(2.9%)	0.05
Others	1(2.9%)	1(2.9%)	0.5
Indications for MV			
Acute respiratory failure	19(55.9%)	21(61.8%)	0.4
Loss of consciousness	15(44.1%)	13 (38.2%)	0.4
Pressure Ventilator Mode	31(91.2%)	33(97.1%)	0.3
Intubation in other center	3(8.8%)	3(8.8%)	0.5

Values are median (25th percentile and 75th percentile) or numbers (%). PRISM 2: Pediatric Risk of Mortality 2, ARDS: Acute Respiratory Distress Syndrome, MV: Mechanical Ventilation, PICU: Pediatric Intensive Care Unit.

Table-2: Short-term and long-term outcomes in the study and control groups.

Primary Outcome	Control n=34	Intervention group n=34	P-value
Extubation Failure	9(26.4%)	4(11.7%)	0.04
Need for NIV	5(14.7%)	2(5.8%)	0.04
Reintubation	4(11.7%)	2(5.8%)	0.06
Duration of MV in successful extubation	4(2-6) n=25	5(4-8) n=30	0.12
Ventilator Associated Pneumonia	3(8.8%)	3(8.8%)	0.6
Long term Outcome			
Mortality in re-intubation	1(2.9%)	1(2.9%)	0.5
Length of stay in PICU	8.5(5-14.2)	12(6-15)	0.3
Length of stay in Hospital	13.5(8.5-23)	17(10-26)	0.1

Values are median (25th percentile and 75th percentile) or numbers (percentage). NIV: Non-Invasive ventilation, MV: Mechanical Ventilation, PICU: Pediatric Intensive Care Unit.

Table-3: Causes of extubation failure in all patients and two groups.

Causes of extubation failure	All n=68	Control group n=34	Intervention group n=34	P-value
Upper airway obstruction	4(30%)	3(33%)	1(25%)	0.6
Lower respiratory tract	3(25%)	2(22%)	1(25%)	o.7
Neurologic	2(15%)	2(22%)	0	0.4
Heart failure	4(30%)	2(22%)	2(50%)	0.35

4- DISCUSSION

This study was conducted to compare the criteria of readiness for extubation and daily spontaneous breathing test (SBT) on the duration of mechanical ventilation and extubation failure rates. The present study showed that using an extubation protocol, including the investigation of the criteria of readiness and daily SBT, reduces extubation failure rates (11.7% vs. 26.4%). Although the frequency of reintubation was four in the control group and two in the intervention group, the difference was statistically insignificant, suggesting that using NIMV reduces the risk of reintubation in the controls. The need for NIMV was approximately 2.5 times higher in the control group compared to in the intervention group (14.7% vs. 5.8%), suggesting a statistically significant difference. The percentage of extubation failure was 19% in all the patients, which is consistent with other studies reporting 4.9% (10) to 29% (19) despite proposing different definitions for extubation failure and sometimes only reintubation was identified as extubation failure. The percentage of reintubation in the present study patients was 8.8%, suggesting a low extubation failure rate based on the latter definition. The reasons for extubation failure in all the patients included upper airway obstruction and heart failure, which is inconsistent with other studies finding upper airway obstruction as the most common cause (23, 24). This discrepancy of the results can be explained by the higher number of eligible heart failure patients divided between the two groups in the present study compared to in other studies. Although the causes of extubation failure as confounding variables could have indirectly affected the percentage of extubation failure, the difference between the two groups was insignificant in terms of these causes. Investigating the other outcomes showed that using the protocol does not contribute to the duration of mechanical ventilation. The median duration of mechanical ventilation was five days in the intervention group and four in the control group. This difference can be explained by using strict criteria of readiness before performing the SBT. The physician in the control group might have overlooked these criteria based on his clinical judgment, and extubated the patient; nevertheless, this difference was statistically insignificant. In 2011, Foronda et al. (23) showed that using an extubation protocol based on criteria of readiness, the SBT is associated with reductions in the duration of mechanical ventilation, and that the two groups are not significantly different in terms of their needs for NIMV and reintubation. Randolph et al. (8) compared two groups using different extubation protocols with a third group not using any protocols and found the duration of extubation and extubation failure rate to be the same in all the groups. Another study proposed no significant differences between the protocol group and physician-monitored group in terms of reintubation, and found ventilator-associated complications, including subglottic stenosis and pneumonia, to be the same in all the groups, which is consistent with the present results in terms of mechanical ventilation complications (15). This

discrepancy of results between the present study and the studies by Foronda et al. and Randolph et al. can be attributed to the differences in the study design and protocols used. In terms of the long-term outcomes, using the protocol did not contribute to reducing mortality and length of hospital and PICU stay. None of the similar studies on pediatrics has investigated the long-term outcomes, although studies conducted on adults comparing the use of extubation protocols and daily SBT with clinical judgments and routine ICU examinations in the ICU have demonstrated many advantages. A meta-analysis and review of 17 clinical trials with these objectives showed significant reductions in the duration of mechanical ventilation, length of ICU stay and weaning duration, and reported no effects on mortality (19). These results are inconsistent with the present long-term outcomes, which suggest no effects on the length of hospital and PICU stay.

Given the extent and validity of this meta-analysis, this inconsistency is noteworthy and requires further studies to be conducted to investigate the long-term outcomes in children. The results obtained in this meta-analysis for the short-term outcomes suggested reductions in the duration of mechanical ventilation and no effects on the frequency of reintubation, which is consistent with similar studies on children. The present study and the one by Foronda et al. are the only clinical trials on children comparing a protocol involving the investigation of criteria of readiness for extubation and daily SBT with clinical judgments and routine PICU examinations. Moreover, the present research was the first study addressing the long-term outcomes of using the protocol, including mortality and length of hospital and PICU stay. On the other hand, the present study limitations comprised a small sample compared to other studies, which requires further studies to be performed using larger samples, and failure to blind, which might have affected the physicians' clinical judgments.

5- CONCLUSION

The present study showed that the extubation protocol reduces extubation failure rates, and does not affect mortality and the duration of mechanical ventilation and hospital and PICU stay. Further studies are recommended to be conducted using larger samples to investigate the short-term and long-term outcomes of using these protocols.

6- ACKNOWLEDGMENTS

7- CONFLICT OF INTEREST: None.

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