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Efficacy of Noninvasive Positive Pressure Ventilation for Improving the Respiratory Function, Use of Accessory Respiratory Muscles, Quality of Sleep and Nutrition of Cystic Fibrosis Patients

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Abstract

Background: Respiratory failure secondary to recurrent respiratory infections is the most common cause of death in Cystic fibrosis (CF).
Objectives: To assess the efficacy of noninvasive positive pressure ventilation (NIPPV) on respiratory function, use of accessory respiratory muscles, ease of physiotherapy for respiratory clearance, quality of sleep and nutritional status in CF patients with respiratory failure.
Methods: All CF patients admitted to the pediatric department of Masih Daneshvari hospital, Tehran from March 2015 to January 2016 were studied. The inclusion criteria were clinical evidence of respiratory distress and signs of respiratory acidosis. The exclusion criteria were nausea and vomiting, not tolerating NIPPV, need for intubation, pneumothorax, presence of giant bullous emphysema or decreased level of consciousness. Baseline spirometry and venous blood gas (VBG) was obtained before and after NIPPV. A simple questionnaire was filled out for the nutritional status, sleep quality, ease of physiotherapy for airway clearance and the volume of secretions after NIPPV compared to baseline. Paired samples t-test and Wilcoxon Signed Rank test in SPSS version 16 were used for the before and after comparison of numerical and ordinal variables, respectively.
Results: Out of a total of 53 CF hospitalized patients 17 met the inclusion criteria. There were 10 (58.8%) males and 7 (41.1%) females with a mean age of 11 ± 4.57 (10 - 25) years, mean weight of 31.85 ± 10.11 (13 - 48) kg and mean BMI of 14.16 ± 2.71 (5.9 - 18). The mean Saturation of peripheral oxygen (SPO_2), respiratory rate (RR) and mean partial pressure of CO_2 (PCO_2) of patients before the intervention were 75 ± 13.25% (52 - 90%), 32 ± 11.17 (22 - 55) mmHg and 55.20 ± 17.62 (30.3 - 108), mmHg respectively. A significant difference was noted after the intervention in SPO_2, venous PCO_2 and RR compared to baseline ($P < 0.05$). The change in sleep quality ($P = 0.001$), nutritional status ($P = 0.001$) and ease of physiotherapy for respiratory clearance ($P = 0.008$) after NIPPV was statistically significant while the change in use of accessory respiratory muscles ($P = 0.785$) and the volume of secretions ($P = 0.1$) was not significant.
Conclusions: NIPPV in CF patients with respiratory failure can improve the respiratory function, sleep quality and nutritional status of patients. Also, NIPPV enhances airway clearance during respiratory physiotherapy.

Keywords: Cystic Fibrosis, Noninvasive Positive Pressure Ventilation

1. Background

Cystic fibrosis is a relatively common disease with a prevalence of 1/2500 live births in Caucasian race. Despite the involvement of various organs, respiratory infections and respiratory failure are the most common causes of death in CF patients (1). Comprehensive studies on the prevalence of CF in Iran are not available (2-5); however, its prevalence in the Middle East has been reported to be 1/2850 to 1/5800 (6, 7). Respiratory failure in CF patients is characterized by impairments in gas exchange and arterial blood gases (ABG) (8). Moreover, airway obstruction due to progressive inflammation and progressive sputum production results in dyspnea, airway hyperinflation,

impaired ventilation and perfusion (VQ mismatch), respiratory distress and use of accessory respiratory muscles, which gradually decrease maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) and cause respiratory muscle fatigue and impaired blood gas exchange at the level of alveoli and consequent blood gas impairment (8, 9). Long term hypoxia gradually increases the pulmonary artery pressure and leads to cor pulmonale (10). At present, mask NIPPV is used to assist respiration of patients with acute respiratory failure (11). In this technique, patient's respiration is assisted by use of devices similar to ventilators with predetermined pressures and volumes during inhalation and exhalation via different oral and nasal masks. Hodson et al. (12) and Pipr et al. (13) showed that NIPPV reversed hypercapnia and decreased respiratory muscle fatigue by increasing alveolar ventilation. The suggested mechanism for the efficacy of NIPPV is increased alveolar ventilation and decreased hypoventilation and respiratory work (11, 14). Also, NIPPV enhances the clearance of pulmonary secretions in CF patients; however, its exact mechanism has yet to be fully understood (10). In general, use of NIPPV has been documented in respiratory physiotherapy guidelines for CF patients especially when the respiratory muscle weakness is due to fatigue (15). Considering the advantages of using NIPPV in pulmonary patients and high prevalence of respiratory failure in CF patients, NIPPV may be helpful in these patients (16).

2. Objectives

This study sought to assess the efficacy of NIPPV in decreasing pulmonary secretions and improving the respiratory function, quality of sleep and nutrition of CF patients in a tertiary referral center for respiratory diseases.

3. Methods

All CF patients presenting to Masih Daneshvari hospital in Tehran from March 2015 to January 2016 were evaluated. Parents or legal guardians of patients signed written informed consent forms prior to the inclusion of patients in the study. The inclusion criteria were CF patients with the criteria of acute or chronic respiratory failure including clinical evidence of respiratory distress (tachypnea and use of accessory respiratory muscles), evidence of respiratory acidosis including a pH $<$ 7.35 or $PCO_2 \geq$ 45 mmHg or clinical evidence of long-term hypoxemia or hypercapnia. Patients with the following signs/symptoms were excluded from the study:

1. Nausea and vomiting
2. Not tolerating NIPPV
3. Requiring intubation based on consultation with an anesthesiologist
4. Occurrence of pneumothorax
5. Giant bullous emphysema
6. Decreased level of consciousness

All patients were subjected to baseline spirometry according to the American Thoracic Society guidelines and their forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and FEV1/FVC were recorded. Also, since frequent blood gas monitoring was required, VBG was obtained instead of ABG to decrease patients' pain and discomfort, and pH and PCO_2 were also recorded.

Patients' medical history was taken and a simple questionnaire was filled out to assess the use of accessory respiratory muscles, sleep quality and nutritional status of patients as reported by patients themselves or their companions and categorized as poor, moderate and good. The arterial oxygen saturation rate was recorded using a contact pulse oxymeter at rest.

For NIPPV, a standard oronasal mask with a suitable size for each patient was used. A Resmed S9 VPAP Auto machine with Bi level positive airway pressure (BIPAP) option was used by an experienced nurse under the supervision of a pediatric pulmonologist. The inhalation and exhalation pressures were adjusted according to the published guidelines, patient's comfort and blood gas status (13). The NIPPV was performed overnight, during sleep and four times a day, each time for two hours under supervision of a nurse. The NIPPV was performed for 72 hours as such. The mask was removed from the face for respiratory physiotherapy or eating. The same techniques including positional drainage, stimulating an effective cough and massage of the chest wall were used for all patients. The ease of physiotherapy for airway clearance and the volume of secretions were also recorded by the attending physician and physiotherapist. The data were analyzed using SPSS version 16. Paired samples t-test was used to analyze the changes in RR, PCO_2 and SPO_2 after the intervention compared to baseline. Changes in ordinal variables including the use of accessory respiratory muscles, sleep quality, nutritional status, volume of secretions and ease of physiotherapy for respiratory clearance were analyzed after the intervention compared to baseline using Wilcoxon Signed Rank test.

4. Results

During the nine-month period, from 53 CF patients hospitalized in the Pediatric Ward of Masih Daneshvari Hospital; 17 (32.07%) met the inclusion criteria and thirty six patients (67.9%) excluded due to absence of respiratory distress (n = 36), respiratory acidosis (n = 36), hypoxia (n =

24) or long-term hypercapnia (n = 32). There were 10 males (58.8%) and seven females (41.1%). The mean age of patients was 17.11 ± 4.15 years (range 10 - 25 years). The mean weight of patients was 31.85 ± 10.11 kg (range 13 - 48 kg). The mean height of patients was 147.18 ± 15.94 cm (range 117 - 165 cm). The mean BMI was 14.16 ± 2.71 (5.9-18). The mean SPO_2, the mean RR and the mean PCO_2 of patients was 75 ± 13.25 (52 - 90)%, 32 ± 11.17 (22 - 55) mmHg and 55.20 ± 17.62 (30.3 - 108) mmHg, respectively.

Normal distribution of data was checked by Kolmogorov-Smirnov test ($P > 0.05$). The mean pressure used by BIPAP machine in patients was 10.4 ± 3.21 and 6.6 ± 3.4 Cm H_2O for IPAP and EPAP, respectively.

The RR, PCO_2 and SPO_2 values before and after the intervention and their comparison with paired t-test are presented in Table 1. As seen in the the the change in SPO_2, PCO_2 and RR was statistically significant after the intervention compared to baseline ($P < 0.02$). Also, the change in sleep quality ($P = 0.001$), nutritional status ($P = 0.001$) and ease of physiotherapy for respiratory clearance ($P = 0.008$) after NIPPV was statistically significant while the change in use of accessory respiratory muscles ($P = 0.785$) and the volume of secretions ($P = 0.1$) was not significant.

Table 1. The RR, PCO_2 and SPO_2 Values Before and After NIPPV

Variable	Before	After	P Value
SPO_2	75 ± 13.25	91 ± 3.37	0.000
PCO_2	55.2 ± 17.6	46.2 ± 13.01	0.01
RR	32.3 ± 11.1	22.5 ± 2.3	0.004

5. Discussion

The purpose of this study was to evaluate the efficacy of NIPPV as a relatively novel intervention in decreasing pulmonary secretions and improving the respiratory function, quality of sleep and nutrition of CF patients in a referral center for respiratory diseases. The study was addressing the following questions:

1. Is NIPPV able to decrease the RR, PCO_2 and use of accessory respiratory muscles as the hallmarks of respiratory distress and failure?

2. Does NIPPV increase the SPO_2 significantly?

3. Does the use of NIPPV increase the quality of sleep and nutritional status dramatically?

4. Is the airway clearance after NIPPV easier by the way of chest physical therapy?

In the current study, BIPAP option was used for NIPPV and the IPAP and EPAP pressures were adjusted based on patient's tolerance and titration of VBG, and were in agreement with previous studies (17). Our results showed that use of NIPPV in CF patients significantly increased SPO_2 ($P < 0.05$) and caused a significant reduction in PCO_2 and RR of patients ($P < 0.05$). Also, our results showed that use of NIPPV significantly improved the sleep quality, nutritional status and ease of respiratory clearance by physiotherapy ($P < 0.05$); although the effect of NIPPV on use of accessory respiratory muscles and the objective volume of secretions was not significant ($P > 0.05$).

Despite the availability of several studies on the use of NIPPV in different respiratory diseases, no definite consensus has been reached on selection of the mode of machine or inhalation or exhalation pressures in NIPPV (18). This is also true for use of NIPPV for respiratory failure in children. In a review study by Teague et al. (17) on the indications for use of NIPPV in pediatric medicine, the agreed values for inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) in CF patients were reported to be 8 - 18 Cm H_2O and 4 - 10 Cm H_2O, respectively. Flight et al in their nine-year study on hospitalized patients with CF, who had received NIPPV, reported that the lowest IPAP pressure was 2.7 Cm H_2O without applying EPAP; in other words, continues positive airway pressure (CPAP) was used (19). They showed that use of CPAP caused significant improvements in CF patients.

The effect of NIPPV on SPO_2 of CF patients has been evaluated in many previous studies. Kofler et al. reported increased SPO_2 following NIPPV alone compared to the group receiving respiratory physiotherapy (20). In their study, level of SPO_2 in NIPPV group was significantly higher than that in the group receiving respiratory physiotherapy including respiratory exercises and chest wall massage. Moreover, Holland et al. compared the efficacy of NIPPV and standard pharmaceutical therapy plus physiotherapy and reported significantly higher SPO_2 values in NIPPV group ($P = 0.001$) (21). However, these findings were in contrast to the results of Placidi et al. who compared NIPPV with respiratory physiotherapy including stimulation of coughing and found no significant difference (1). Studies on the efficacy of NIPPV for decreasing pulmonary secretions are mainly inconclusive. Fauroux et al. and Holland et al. found no significant difference in respiratory clearance between the NIPPV and respiratory physiotherapy by stimulation of cough (21, 22). However, in the study by Fauroux et al. the fatigue of patients after clearance in NIPPV group was less than that in patients who only received respiratory physiotherapy (22). In a recent study by Rodriguez Horta the effect of NIPPV compared to conventional chest physical therapy and positive expiratory pressure (PEP) on increasing the rate of airway clearance in CF was significant (23). They studied 32 subjects with

the mean age of 31 and used BIPAP mode for NIPPV [IPAP (10-20) Cm H_2O]. Thy reported the significant reduction in lung clearance index (LCI) in NIPPV group.

The efficacy of NIPPV for improving sleep quality of CF patients has been evaluated in a few studies. Young et al evaluated the effect of non-invasive ventilation on sleep quality of eight patients with CF using a sleep questionnaire (24). They did not find a significant difference in sleep quality or PCO2 of patients when awake between the two groups of NIPPV and nasal oxygenation alone; however, significant differences were noted in nocturnal PCO_2, quality of life and nocturnal dyspnea. The findings of Young et al are in contrast to our results. This controversy may be attributed to the difference in the quality of questionnaires used in the two studies. Our questionnaire was qualitative, ordinal and self-reported by patients. Moreover, we did not have a control group. The efficacy of NIPPV was previously evaluated by Young et al. and Milross et al. (22, 25). The study by Young et al was conducted in room air. Milross et al. used NIPPV combined with oxygen. In both studies, arterial PCO_2 significantly decreased compared to the group receiving oxygen alone; this finding was in agreement with our result and was due to the improved respiratory function by NIPPV. Also, studies performing sleep tests such as polysomnography have reported significant improvement of sleep quality in patients receiving NIPPV (25).

Assessment of the effect of NIPPV on use of accessory respiratory muscles was strength of our study since this variable has not been evaluated before in CF patients receiving NIPPV. The results showed that despite the significant improvement in objective indices of respiratory function including reduction in arterial PCO_2 and increased arterial SPO_2, use of accessory respiratory muscles by patients receiving NIPPV was still significantly high. Considering the chronicity of CF and long-term changes in respiratory mechanics of these patients, correction of their respiratory habits and use of diaphragm instead of accessory respiratory muscles require long-term respiratory physiotherapy exercises in addition to the use of NIPPV to improve respiratory indices.

Also, considering the long-term course of CF, future studies with larger sample sizes are required to assess the efficacy of NIPPV in decreasing the need for hospital admissions of CF patients.

5.1. Limitations

Although we tried to carefully prepare the study, we are still aware of its limitations. First of all, the sample size is really small. It should be mentioned that this report is a part of a greater study and we hope to gather more samples in the future. Second, in this study we didn't have any control group and the results are compared to the baseline. It seems that introducing a control group in which the mask of NIPPV is placed but the device turned off would be of value. Third, since the questionnaire was designed to measure sleep quality in our study, it seems not to provide enough evidence compared to polysomnography data as an objective measurements for sleep study.

5.3. Conclusions

Use of NIPPV in CF patients with acute or chronic respiratory failure can improve their respiratory function, nutritional status and sleep quality. Also, this method significantly enhances respiratory clearance during respiratory physiotherapy. Long-term studies on a larger group of patients are required to assess the effect of NIPPV on survival of CF patients.

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