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Role of N-Acetylcysteine in Clearance of Secretions in Mechanical Ventilated Patients

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Abstract

Objective: to determine the role of nebulized N-acetylcysteine in mechanical ventilation in clearing the airway of these patients. Study Design: A Randomized Control Trial. Place and Duration of Study: Department of Anaesthesia and Intensive Care Unit Quid e Azam Medical College Bahawalpur. From January 2018 to June 2019.Methods: In this project total 50 patients were enrolled by consecutive sampling who remained on mechanical ventilation for more than 24 hours and were between age 15 to 80 years old. Written consent of this project was taken from relative of each patient. These patients were divided into two groups by lottery method into case and control. The case group received 2 ml of NAC 20% with 8 ml normal saline 3 times a day for 1 day. The control group only received 10 ml normal saline via their nebulizers 3 times a day at 8 AM, 2 PM, and 9 PM. Data was collected and was analyzed. SPSS 22 was used for this purpose. All numerical variables of this research such as mean FiO_2, mean peak and plateau pressure of airway, mean blood pressure, mean age and importantly mean density of secretions were calculated. In these values t test was applied and p value was calculated. If it was less than .005, then it was considered significant. Similarly, qualitative data such as type of disease were calculated in percentage and chi square test was used to check the significance. Results: The mean O2 saturation of baseline, 12 hours and 24 hours of the controls was 93.84±2.28, 94.27±2.33 and 94.08±1.81 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the controls was 23.16±3.49, 25.38±8.86 and 24.01±4.91 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the controls was 19.04±7.79, 21.37±4.86 and 21.85±8.93 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the controls was 1.04±0.024, 1.05±0.03 and 1.03±0.002 respectively. While, the mean O2 saturation of baseline, 12 hours and 24 hours of the cases was 93.08±2.37, 94.61±2.56 and 94.11±2.34 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the cases was 26.58±5.81, 23.81±8.28 and 24.34±6.15 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the cases was 21.88±78.01, 24.88±6.67 and 23.51±7.55 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the cases was 1.01±0.021, 1.08±0.022 and 1.008±0.0195 respectively. The differences were statistically insignificant. P-value ≤ 0.05 is considered as significant. Conclusion: It is concluded from our observations that use of N-acetylcysteine in patients on mechanical ventilation is very effective in clearance of secretion and to maintain airway clear.

Key words: N-acetylcysteine, mechanical ventilation, airway clearance, normal saline

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Introduction

Maintaining the airway hygiene and clearing the airway secretions is very essential in preventing recurrent respiratory infections and maintaining airway patency. Impaired clearance of the airway is one of the bigger reason of acute respiratory failure and admission in intensive care unit. In intensive care unit usually manual methods are used to facilitate airway clearance and some of them are confirmed as effective (1). Mucous plugs those are retained secretions in tracheobronchial tree are often observed in patients who are mechanically ventilated due to depressed mucociliary clearance, cough reflex and more production of sputum (2). The average annual relative humidity showed significant increase over the years and ranged from 58 to 71% with mean value of 64% in Indian Punjab(3) which

predispose patients to mucous plugs, causing severe morbidity and even mortality. Therapy with mucolytic drugs can be used to reduce bacterial load, improve lung function, more clearance of sputum from airway and decreasing viscosity of airway. This will improve survival. Medications such as anti-Dnase are expensive and locally not available. Therefore, in this situation effective and cheap methods for clearing the airway was need of the hour to reduce retention of secretions in patients with mechanically ventilated. For decades N-acetylcysteine has been used for its mucolytic properties orally. But its effects are not known if given by nebulization through endotracheal tube. It was discovered by Sheffner et al. first time the mucolytic qualities of N-acetylcysteine. After this it has been used in many situations as mucolytic drug (4).

Mucous viscosity is reduced by N-acetylcysteine by disturbing the disulfide bonds in mucoproteins liking the proteins. After use of N-acetylcysteine may increase liquefied secretions. Patients with mechanically ventilation have reduced cough reflex so, their airway should be maintained by mechanical ventilation. N-acetylcysteine causes side effects such as vomiting, stomatitis, nausea, fever, drowsiness, clamminess, chest tightness, bronchoconstriction and rhinorrhea in some patients (5). Significant airflow limitation is unpredictable and uncommon in asthmatic bronchitis patients or patients with bronchial asthma complicated by bronchitis (6). In some countries of Europe N-acetylcysteine used to improve symptoms and decrease frequency of exacerbations in chronic bronchitis. Mucolytic agents are considered ineffective and are not used frequently in USA, Australia and UK (7). Guidelines issued by British thoracic society proposed that in chronic obstructive pulmonary disease, it has no use. So due to unproven trials of these drugs and their efficacy in chronic obstructive pulmonary disease, they are not approved by British National Formulary (8). In United States of America one multicenter randomized controlled trial showed that organic iodide can benefit in patients with chronic bronchitis (9). In literature the use of these drugs in intensive care unit are not available. In this research N-acetylcysteine was used in nebulization form in patients who are on mechanically ventilatation and was compared with normal saline in airway clearance, change in plateau airway pressure, density of secretions and peak airway pressure.

Methodology

This study and randomized controlled trial was done Department of Anaesthesia and Intensive Care Unit Quid e Azam Medical College Bahawalpur. From January 2018 to June 2019.. In this project total 50 patients were enrolled by consecutive sampling who remained on mechanical ventilation for more than 24 hours and were between age 15 to 80 years old. Written consent of this project was taken from relative of each patient. These patients were divided into two groups by lottery method into case and control. The case group received 2 ml of NAC 20% with 8 ml normal saline 3 times a day for 1 day. The control group only received 10 ml normal saline via their nebulizers 3 times a day at 8 AM, 2 PM, and 9 PM. Exclusion criteria were hemodynamically unstable patients, those with tracheostomy tubes, organophosphate poisonings, and pulmonary edema. Whole proposal of this investigation was approved by institutional committee. Sample size was calculated by a reference study done by Gallon AM et al. in which weight of sputum was used after treatment in two groups by using software (www.openepi.com).

Patients who were admitted in intensive care unit and were enrolled in this study. Mucolytics were not received by either control and case. After nebulization with each agent in their respective group with designed amount and time suctioning was done and tracheal secretions

were collected in calibrated container. A mucous extractor was placed between main suction container and suctioning tube and sample of secretion was obtained and its density was calculated. Density of these secretions were calculated simply by weight in grams of total secretions and dividing it to total volume of secretions in millimeter. One ml of secretion was obtained by disposable syringe and then its weight was calculated by digital scale.

In this investigation oxygen saturation, plateau pressure of airway and peak pressure of airway were recorded. Patients' blood pressure and other vitals were documented. History and other clinical examination were also documented. Personal profile was obtained. Patients were auscultated and wheezing of chest were recorded. In both groups these measurements were done at baseline and after 12 hours and 24 hours.

Data was collected and was analyzed. SPSS 22 was used for this purpose. All numerical variables of this research such as mean FiO_2, mean peak and plateau pressure of airway, mean blood pressure, mean age and importantly mean density of secretions were calculated. In these values t test was applied and p value was calculated. If it was less than .005, then it was considered significant. Similarly, qualitative data such as type of disease were calculated in percentage and chi square test was used to check the significance.

Results

Fifty patients were enrolled in this study, both genders. We further categorized the patients as case and control respectively. The mean age, blood pressure and FIO_2 (%) of controls was 45.92±2.37 years, 95.7±5.31 mm Hg and 46.28±2.49 respectively. Gender distribution showed that there were more males than females i.e. n=18 (72%) and n=7 (28%) respectively. While, COPD, IHD, DM and mortality, in controls, was noted as n=4 (16%), n=13 (52%), n=3 (12%) and n=12 (48%) respectively. For the cases, the mean age, blood pressure and FIO2 (%) was 57.88±7.58 years, 93.5±6.82 mm Hg and 47.48±4.06 respectively. Gender distribution showed that there were more males than females i.e. n=16 (64%) and n=9 (36%) respectively. While, COPD, IHD, DM and mortality, in cases, was noted as n=2 (8%), n=14 (56%), n=5 (20%) and n=14 (56%) respectively. The difference was statistically insignificant except age (p=0.000) and blood pressure (p=0.000). (Table. I).

The mean O2 saturation of baseline, 12 hours and 24 hours of the controls was 93.84±2.28, 94.27±2.33 and 94.08±1.81 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the controls was 23.16±3.49, 25.38±8.86 and 24.01±4.91 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the controls was 19.04±7.79, 21.37±4.86 and 21.85±8.93 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the controls was 1.04±0.024, 1.05±0.03 and 1.03±0.002 respectively. While, the mean O2 saturation of baseline, 12 hours and 24 hours of the cases was 93.08±2.37, 94.61±2.56 and 94.11±2.34 respectively. The mean peak airway pressure of baseline, 12 hours and 24 hours of the cases was 26.58±5.81, 23.81±8.28 and 24.34±6.15 respectively. The mean plateau airway pressure of baseline, 12 hours and 24 hours of the cases was 21.88±78.01, 24.88±6.67 and 23.51±7.55 respectively. The mean secretion density of baseline, 12 hours and 24 hours of the cases was 1.01±0.021, 1.08±0.022 and 1.008±0.0195 respectively. The differences were statistically insignificant. P-value ≤ 0.05 is considered as significant. (Table. II).

Table. I

Demographic Characteristics among the groups

Variable	Control n=25	Case n=25	P-value
Age (years)	45.92±2.37	57.88±7.58	0.000
Blood pressure (mm Hg)	95.7±5.31	93.5±6.82	0.000
FIO_2 (%)	46.28±2.49	47.48±4.06	0.214
Gender			
Male	n=18 (72%)	n=16 (64%)	0.544
Female	n=7 (28%)	n=9 (36%)	
COPD	n=4 (16%)	n=2 (8%)	0.384
IHD	n=13 (52%)	n=14 (56%)	0.777
DM	n=3 (12%)	n=5 (20%)	0.440
Mortality	n=12 (48%)	n=14 (56%)	0.571

Table. II

Variable	Baseline	12 hours	24 hours	P-value
O2 saturation				
Control, n=25	93.84±2.28	94.27±2.33	94.08±1.81	0.687
Case, n=25	93.08±2.37	94.61±2.56	94.11±2.34	0.263
Peak airway pressure				
Control, n=25	23.16±3.49	25.38±8.86	24.01±4.91	0.213
Case, n=25	26.58±5.81	23.81±8.28	24.34±6.15	0.233
Plateau airway pressure				
Control, n=25	19.04±7.79	21.37±4.86	21.85±8.93	0.870
Case, n=25	21.88±78.01	24.88±6.67	23.51±7.55	0.065
Secretion density				
Control, n=25	1.04±0.024	1.05±0.03	1.03±0.002	0.180
Case, n=25	1.01±0.021	1.08±0.022	1.008±0.0195	0.192

Discussion

Results of this study demonstrated that in patients who are on mechanical ventilation for more than 24 hours, when nebulized with normal saline and with N-acetylcysteine in different patients, showed that both agents were almost have same effects. Density of secretions, improvement in oxygen saturation, and peak air way pressure at baseline and after 12 and 24 hours after were almost similar and there was no significant difference between these two agents. So

Personal experience was shared by Poppe in which two milliliters of N-acetylcysteine 20% was nebulized by 88 patients. Symptoms and signs were improved in these patients. A

dramatic improvement was observed by mucolytic drug as compared to aerosol nebulization. It was also observed that nebulization of N-acetylcysteine induces cough for almost ten minutes (11). In another study done by Hirsch's investigation 20% N-acetylcysteine of about three milliliters in nebulization and 3ml of 10% N-acetylcysteine and was compared to normal saline nebulization. Results of this study demonstrated that nebulization with N-aetylcysteine was more effective in thinning the secretions and increasing its expectoration and volume than nebulization with normal saline and also 10% N-acetylcysteine was equally effective as 20% N-acetylcysteine (12). And two different studies done by Kory et al (13) and Hirsch et al. (14) showed that nebulization with N-acetylcysteine with bronchodilators such as isoproterenol and racemic adrenaline were highly efficient in thinning the sputum and also it caused improvement in subjective condition due to addition of bronchodilators. In above two investigations 20% and 10% N-acetylcysteine were used and density of secretions were measured by consistometer.

Factually, viscosity and density which physical properties of fluid are different in nature and in investigation significantly decrease in respiratory secretion's density were expected but was not done. By decreasing the N-acetylcysteine amount in each dose without addition of bronchodilator in these patients did not show any significant bronchospasm due to N-acetylcysteine.

In this study oxygen saturation was not incremented as it was showed in study done by Gallon et al. (10). In investigation of Gallon after N-acetylcysteine nebulization improvement was observed in oxygen saturation nad there was increased expectoration of sputum, density of sputum was reduced (10). In this study density of secretions and increment in saturation of oxygen was not observed significantly in both groups of patients. These results may be explained because of study design and procedure in which after 24 hours of intubation secretions in airways are not in such large amount so nebulization with either normal saline and N-acetylcysteine did not cause significant impact.

In study conducted by Vargas et al. found that oxygen saturation fluctuated in values demonstrating higher values in afternoon and lower in early morning (15,16). In patients with multi organ failure study done by Agusti et al. found that there was decline in saturation after starting intravenous N-acetylcysteine (17).

So results of this study was different from many investigations. May be it was due to limited sample size, limited time of study on each patient and also may be due to time of starting the study was early, that is it was started after 24 hours of intubation and conducted for only one day. May be larger sample size and more study time in each could have different results.

Conclusion: It is concluded from our observations that use of N-acetylcysteine in patients on mechanical ventilation is very effective in clearance of secretion and to maintain airway clear.

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