RETROSPECTIVE COHORT STUDY

Prospective Analysis of Incidence of Ventilator-associated Pneumonia Associated with Active and Passive Humidification in SARS-CoV-2 Patients

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Abstract

Aim: Comparison of the incidence of ventilator-associated pneumonia (VAP) in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients requiring mechanical ventilation using active and passive humidification.

Materials and methods: The prospective study was carried out by the Department of Critical Care Medicine in a tertiary care hospital. Subjects were divided into two groups. Baseline demographic data was collected for both groups. In both the groups, the clinical pulmonary infection score (CPIS), which included—temperature, white blood cell (WBC) count, tracheal aspirate quantity, alveolar oxygen pressure (PaO_2)/fraction of inspired oxygen (FiO_2) ratio, chest ray, and any pathogenic bacterial growth from tracheal aspirate, was documented, and the final score was analyzed, which predicted the incidence of VAP. The secondary outcomes studied were the independent variables, such as duration of ventilator support, mortality rate, and endotracheal tube (ETT) patency in both groups.

Results: The intergroup distribution of primary outcome, including the distribution of CPIS parameters, did not differ significantly in both groups; that is, the VAP rate remained the same in both groups. Secondary outcomes, including duration of ventilator support and mortality rate, remained the same, whereas airway occlusion and peak pressure were higher in the patients receiving passive humidification.

Conclusion: The incidence of VAP remained the same in both groups with the use of either active or passive humidification systems. Extended use of both systems resulted in the curtailment of ETT patency, whereas the use of a heated humidifier (HH) lowered the risk for artificial airway occlusion.

Keywords: Active humidification, Passive humidification, Ventilator-associated pneumonia.

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Introduction

The coronavirus disease 2019 (COVID-19) caused by single-strand enveloped virus [severe acute respiratory syndrome coronavirus 2 (SARS- Cov-2)] has severely impacted healthcare systems all over the world. Patients of COVID-19 who require initiation of invasive mechanical ventilation due to respiratory failure are at high risk of developing ventilator-associated pneumonia (VAP), leading to an increase in mortality and morbidity rate.[19] VAP, defined as the infection or pneumonia occurring in patients within 48–72 hours after initiation of mechanical ventilation, is recognized as one of the common nosocomial infections.[1,5,13] Recent studies have documented the incidence of VAP among patients with COVID-19 ranging between 44 and 86%.[13–19]

Various factors have been attributed to the increase in the incidence of VAP rates in SARS-CoV-2 cases, common amongst them being extended prone ventilation with the administration of sedatives and paralytic agents. Aggressive use of immunomodulatory drugs like corticosteroids, lack of adequate staffing, reduced frequency of suctioning due to personal protective equipment (PPE), and lower rigorous use of standard palladium strategies during the pandemic.

In patients initiated on mechanical ventilation, there is a breach of inherent defenses of the upper airway by invasive airway devices leading to loss of natural heat and moisture of the inspired gases. Warm humidified gases are essential for maintaining ciliary function and mucus clearance, a lack of which may lead to the thickening of secretions, increasing resistance to the passage of gases, and may act as a nidus for various respiratory infections. External artificial humidification systems are required to be used in these patients to moisten and warm gases to compensate for this loss. Artificial humidification of these gases can be either active or passive. In active humidification through a heated humidifier (HH), the inspired gases are made to pass over a heated water bath, and in passive humidification through a heat and moisture exchanger (HME), there is a trapping of the patient's own exhaled gas, which is returned to the patient on subsequent inhalations (Tables 1 and 2).

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Table 1: Intergroup distribution of demographic data of cases studied

			Active humidification group (n = 20)		*Passive humidification group (n = 20)*		
Serial no.	*Parameters*		*n*	*%*	*n*	*%*	*p-value*
a.	Age (years)	<40	1	5.0	2	10.0	0.898^{NS}
		40–49	5	25.0	6	30.0	
		50–59	5	25.0	4	20.0	
		60–69	6	30.0	4	20.0	
		>70	3	15.0	4	20.0	
b.	Sex	Male	18	90.0	16	80.0	0.661^{NS}
		Female	2	10.0	4	20.0	
c.	Comorbidities	Nil	5	25.0	4	20.0	0.129^{NS}
		HTN	5	25.0	8	40.0	
		DM	1	5.0	2	10.0	
		HTN + DM	9	45.0	3	15.0	
		Other	0	0.0	3	15.0	

p-value by Chi-squared test; *p*-value of <0.05 is considered to be statistically significant; ***p*-value of <0.001, NS, statistically nonsignificant; (Gaudet A & group, 2020)[13]

Table 2: Intergroup distribution of primary outcome including the incidence of VAP using CPIS score

Serial no.	*CPIS score parameter*		*Active humidification group (n = 20)*		*Passive humidification group (n = 20)*		
			n	*%*	*n*	*%*	*p-value*
a.	WBC count	0	9	45.0	6	30.0	0.560^{NS}
		1	8	40.0	9	45.0	
		2	3	15.0	5	25.0	
b.	Tracheal secretions	0	4	20.0	0	0.0	0.107^{NS}
		1	6	30.0	7	35.0	
		2	10	50.0	13	65.0	
c.	PaO_2/FiO_2 ratio	0	1	5.0	0	0.0	0.999^{NS}
		2	19	95.0	20	100.0	
d.	X-ray chest findings	1	19	95.0	12	60.0	0.020*
		2	1	5.0	8	40.0	
e.	Culture growth	0	6	30.0	4	20.0	0.421^{NS}
		1	2	10.0	5	25.0	
		2	12	60.0	11	55.0	
f.	Overall score	0–6	6	30.0	5	25.0	0.999^{NS}
		7–12	14	70.0	15	75.0	

*p-value of <0.05 is considered to be statistically significant; NS, statistically nonsignificant; (Gaudet A & group, 2020)[13]

Many studies conducted during the pre-COVID era comparing the efficacy of either of these humidification systems have failed to elicit any benefit of one system over the other.[8–11] The goal was to compare the incidence of VAP using both humidification systems in cases diagnosed with SARS-CoV-2. We tried to ascertain if the type of humidification has any role in the prevention of VAP in this subset of cases. The independent variables included were the duration of intensive care unit (ICU) stay, mortality rate, and artificial airway patency. Despite extensive research, there is a lack of standardized criteria for the diagnosis of VAP; we used the commonly used clinical pulmonary infection score (CPIS), which includes—temperature, leucocyte count and morphology, amount of tracheal secretions and their character, alveolar oxygen pressure (PaO_2)/fraction of inspired oxygen (FiO_2) ratio, findings of pulmonary infiltration and progression on chest X-ray, and growth of any pathogenic bacterial growth from the tracheal aspirate. Whereas the CPIS score of >6 or 6 suggests VAP Table 3.

Materials and Methods

The prospective study was carried out by the ICU Department in a tertiary care hospital located in Pune, India. The Institutional Ethics Committee approval was obtained. Disclaimer concurrence was achieved by Disaster Mental Health Research Center Code

Table 3: Intergroup distribution of secondary outcome measures

			Active humidification group (n = 20)		*Passive humidification group (n = 20)*		
Serial no.	*Outcome*		*n*	*%*	*n*	*%*	*p-value*
3A) Secondary outcomes—clinical outcomes							
a.	Mortality	Survived	20	100.0	20	100.0	0.999^{NS}
		Expired	0	0.0	0	0.0	
b.	No. of days on a ventilator	<10 days	8	40.0	13	65.0	0.245^{NS}
		10–20 days	7	35.0	5	25.0	
		>20 days	5	25.0	2	10.0	
3B) Airway dynamics:							
	Airway patency						
a.	PIP (cms of H_2O)	<40	2	10.0	0	0.0	0.002**
		40–50	17	85.0	9	45.0	
		>50	1	5.0	11	55.0	
b.	Pplats (cms of H_2O)	<30	6	30.0	2	10.0	0.127^{NS}
		30–35	4	70.0	16	80.0	
		>35	0	0.0	2	10.0	
c.	Visual inspection	Not block	20	100.0	1	5.0	0.001***
		Partially block	0	0.0	19	95.0	

p-value by Chi-squared test; *p*-value of <0.05 is considered to be statistically significant; ***p*-value of < 0.01; ****p*-value of <0.001; NS, statistically nonsignificant; (Gaudet A & group, 2020)[13]

IHR_2022_Mar_NM_454. The study was conducted between 1st February 2021 and 31st December 2021. All patients satisfying the inclusion criteria included in our study were divided into two groups—HH being the active humification group and HME being the passive humification group alternately within 24 hours of intubation.

Inclusion Criteria

All COVID reverse transcription polymerase chain reaction positive cases admitted to the ICU who were mechanically ventilated for >5 days duration were assigned to either HH or HME within 24 hours of intubation.

Exclusion Criteria

- Patients <18 years of age.
- Immunosuppressed patients with human immunodeficiency viruses and white blood cell (WBC) count <1000 cells/mm^3 solid or with hematological malignancies.
- Any known contraindication to the application of HH or HME.
- Patients admitted with advance directives for palliative care.

Data Collection

All patients satisfying the inclusion criteria were included in the study from 1st February 2021 to 31st December 2021. After obtaining informed consent, the subjects were assigned active or passive humification groups alternately. The HHs used were from Fisher and Paykel RT380 circuits with a humidified base with a temperature of 37°C and provided 100% relative humidity. The HME filters used were Covidien Hygroster mechanical filters; these filters were changed every 48 hours intervals or as per requirement.

Routine checks of ventilatory parameters and suctioning (close suction catheters), which were carried out every 4 hours or as per clinical indication by respiratory therapists, and changing of the endotracheal tube (ETT) or HME filters were noted accordingly.

Primary dependent variables included demographics, clinical, laboratory, and microbiological data on admission, the subsequent trends and independent variables, which included total duration of ventilatory support, type of humidification system used and days of application, ETT tube dimensions, respiratory system-lung compliance, airway resistance, incidents of ETT blockage, and clinical outcomes were collected by a team of respiratory therapists and senior registrars, and patient daily monitoring charts were entered into a computerized database. CPIS scores were calculated and interpreted by two independent ICU consultants. The manuscript was reviewed by all the authors, and it upholds the correctness, accuracy, and completeness of the data and the adherence of the study to the protocol submitted.

Outcome

Incidence of VAP between both the groups based on CPIS score, clinical outcomes, length of ventilator support, and patency of airway delivery device were recorded.

Statistical Analysis

The intergroup statistical comparison of the distribution of categorical variables was tested using the Chi-squared test or Fisher's exact probability test if >20% of cells have an expected frequency <5. The entire data was statistically analyzed using Statistical Package for the Social Sciences (SPSS version 24.0, IBM Corporation, United States of America).

Results

Characteristics on Admission

- During the study period, a total of 40 patients meeting the inclusion criteria were included.
- The total number of patients receiving active humidification (HH)—($n = 20$) and the total number of patients receiving passive humidification (HME)—($n = 20$).
- The distribution of demographic characteristics such as age, gender, and comorbidity status among the cases studied did not differ significantly between the two study groups (p-value >0.05 for all).

Incidence of VAP

Distribution of CPIS parameters such as WBC, tracheal secretions, PaO_2/FiO_2 ratio, and culture growth status did not differ significantly between the two study groups (p-value of >0.05 for all). The distribution of CPIS parameters, such as chest X-ray findings, differs significantly between the two study groups (p-value of <0.05). A significantly higher proportion of cases in the passive group had higher chest X-ray score compared to the active group (p-value of <0.05). Overall, VAP incidence did not differ between the group.

The distribution of mortality and number of days on ventilators did not differ significantly between the two study groups (p-value of >0.05 for all).

Distribution of airway patency parameters, such as peak inspiratory pressure (PIP) and visual inspection, differs significantly between the two study groups (p-value of <0.05 for both). A significantly higher proportion of cases in the passive group had higher PIP and visual inspection scores compared to the active group (p-value of <0.05 for both). The distribution of airway patency parameters like plateau pressure did not differ significantly between the two study groups (p-value of >0.05).

Discussion

We carried out this prospective study to ascertain the role of HH or HME in prohibiting VAP in cases diagnosed with SARS-CoV-2 who were initiated on invasive mechanical ventilation. There was no remarkable difference observed in the incidence of VAP ascertained through CPIS score, mortality rates, or the prolongation of days on ventilators between the cases in the two study groups. The occurrences of ETT blockage were more with a group of patients who were managed with passive humidification.

Various factors have been attributed to the high occurrence of VAP rates in COVID-19 cases common, among them being a prolongation of mechanical ventilation and prone ventilation with the administration of sedatives and paralytic agents, aggressive use of immunomodulatory drugs like corticosteroids, lack of adequate staffing, reduced frequency of suctioning due to PPE and poor use of standard prevention strategies during the pandemic.[16,19] Ours is one of the few papers to study the role of type of humidification in the prevention of VAP in patients with SARS-CoV-2. Though numerous studies have been published in the pre-COVID era comparing the role of either of the humidification system in reducing the incidence of VAP rates, no definitive outcomes on the benefits of either humidification system have been documented. According to the study conducted by Siempos et al.,[8] use of HMEs, when compared with HH, does not show any primacy in decreasing pneumonia and mortality rate.

Endotracheal tube (ETT) blockage is a potentially critical and known drawback of invasive mechanical ventilation characterized by an increase in airway resistance and visible signs of obstruction on pressure and flow tracings. Though our sample size was small, the incidence of ETT blockage was higher, especially in patients with passive humidification; this finding is comparable to other studies conducted during COVID-19, where tube blockage rates of as high as 72% have been documented due to peculiar thick viscous secretions in these patients. According to Hess et al.,[4] and Kola et al.,[6] prolonged invasive mechanical ventilation and the existence of VAP increase the probability of artificial airway occlusion. According to the randomized controlled trials study conducted by Villafane et al.,[2] the author found that after 72 hours, the inner diameter of the ETT decreases by 2.5–6.5 mm with the use of HME, whereas, in HH, it is only decreased by 1.5 mm.

An increase in airway occlusion leads to higher peak pressure, whereas no change in plateau pressures was noted. Airway occlusion due to inadequate humidification leads to frequent tube changing and thus can lead to an increase in VAP rates. According to the study conducted by Morán et al.,[7] in cases with acute lung injury and acute respiratory distress syndrome, the use of HH showed lower PIP as compared to HMEs; thus, humidification also affects respiratory mechanics in the patients receiving mechanical ventilation, which was like the findings in our study.

Frequent tube blockages and the presence of thick tenacious secretions, which are difficult to clear by conventional suctioning techniques needing frequent bronchoscopy interventions, highlight the function of humidification systems in the treatment of mechanical patients of SARS-CoV-2. Though the definitive role of either of the systems is yet to be ascertained, there is a need for constant monitoring to prevent life-threatening complications.

Limitations

The overall sample size was small, that is, 40 patients ($n = 40$), 20 in each group. The study was conducted in a single hospital setup and was patient-specific as it was conducted in the course of the pandemic in the year 2021, that is, only SARS-CoV-2 patients were included.

Conclusion

The incidence of VAP in SARS-CoV-2 patients associated with the use of either active or passive humidification remains the same. Longer duration of the ventilator supports more risk of secondary bacterial infection and hence increase in mortality rate. Extended use of mechanical ventilation results in a decrease of ETT patency, and to a higher extent with the use of HME. Using HH has shown a lower risk for artificial airway obstruction compared with HME.

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