

# Effectiveness of Oral Hygiene with Chlorhexidine Mouthwash with 0.12% and 0.2% Concentration on Incidence of Ventilator Associated Pneumonia (VAP) in Intubated Patients – A Parallel arm Double Blind Randomized Controlled Trial

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Received: October 2020

Accepted: November 2020

## ABSTRACT

**Background:** Patients on mechanical ventilation are on higher risk of developing pneumonia due to multiple factors. Incidence of Ventilator associated pneumonia (VAP) varies from 9 to 27 % for mechanically ventilated patients. Various mouth wash with different concentration are used for oral care to prevent VAP. Aim of this study was to find out the most efficacious concentration of chlorhexidine mouth wash to prevent VAP, with minimum adverse events. **Materials and Methods:** This double-blind randomized study included 140 patients in critical care unit requiring mechanical ventilation for more than 48 hours. The study was approved by the Institutional Ethics Committee and written informed consent was sought from the patients or next kin relative for comatose cases. Consenting patients were assigned to either group using block randomization and SNOSE allocation in two groups of 70 each. Group I and Group II received oral care with chlorhexidine 0.12% and chlorhexidine 0.2% respectively. The diagnosis of VAP was made by using CPIS. A score of  $\geq 6$  considered VAP. **Results:** In intervention group 7 VAP, 30 discharges, 11 LAMA (Left against Medical Advice), 8 deaths were reported while 2 VAP, 36 discharges, 9 LAMA, 11 deaths were reported in control group. On comparing the above-mentioned indicators and analysis of data we found a significant difference in VAP incidence but the safety, ICU stay, hospital stay, days on ventilator and mortality of both groups was similar. We found no significant relationship between incidence of VAP and oral microbial load. **Conclusions:** Oral hygiene with Chlorhexidine 0.12% is less effective than Chlorhexidine 0.20% for prevention of VAP in mechanically ventilated patients.

**Keywords:** Chlorhexidine, Mouth wash, Ventilator associated pneumonia, Oral care, oral hygiene.

## INTRODUCTION

Aspiration of colonized oropharyngeal secretion in to the lung along the space between trachea and endotracheal tube is the main presumed mechanism of VAP development in mechanically ventilated patients.<sup>[1]</sup> Apart from this other mechanism which are reported by CDC include inhalation of aerosolized organism, hematogenous spread and translocation of bacteria from gastrointestinal wall.<sup>[2]</sup> Colonization of oropharyngeal secretion with pathogenic bacteria is primarily due to poor oral hygiene and collection of tissue debris.<sup>[1,2]</sup> Antimicrobial, lubricating and buffering properties with optimal flow and secretion of saliva is normal

natural defense mechanism in our oral cavity which prevent colonization of pathogenic organism. This natural defense of saliva hamper in mechanically ventilated patients. Based on several studies on selective decontamination of oral cavity by using various antiseptic agents, it is found that by reducing oropharyngeal bacterial load, the incidence of VAP can significantly be reduced.<sup>[3]</sup>

Although multiple studies have investigated the effect of different topical antiseptic solution for oral care in VAP prevention but chlorhexidine has given better result in this context.<sup>[3,4]</sup> Chlorhexidine has broad spectrum antimicrobial properties, at low concentration it acts as bacteriostatic while at higher concentration the action is bactericidal. Most of the studies show that oral hygiene with chlorhexidine (0.2% and 0.12%) in intubated patients have low incidence of VAP as compared to placebo or povidone iodine.<sup>[3,5,6]</sup>

Several studies which were done in dental practice shows reduction in oral microbial load following chlorhexidine mouth wash.<sup>[6-10]</sup> The aim of this study

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was to add on evidence to support use of Chlorhexidine oral prophylaxis in endotracheal intubated patient to reduce incidence of VAP in Indian context. In this study we had to find the most efficacious strength of chlorhexidine used as mouth wash while minimizing the side effects.

### **Objectives**

The primary objective of this study was to compare the effectiveness of oral prophylaxis of chlorhexidine 0.12% against chlorhexidine 0.20%, measured in terms of incidence of VAP

Secondary outcome was to understand the difference in duration of mechanical ventilation, duration of ICU stay and hospital stay, all-cause mortality rate, side effect (stomatitis) of chlorhexidine 0.12% against chlorhexidine 0.20%, and correlation between oral microbial load and incidence of Ventilator associated pneumonia.

## **MATERIALS AND METHODS**

The prospective double-blind randomized control trial was carried out in 35 bedded ICU in tertiary care private hospital in Jaipur, Rajasthan State, India. Participants were recruited from critical care unit if they satisfied inclusion and exclusion criteria for the study.

### **Inclusion criteria**

- Individuals admitted to critical care unit of study site and aged 18 years and above and 75 years or less.
- Individuals requiring mechanical ventilation for 48 hours or more with normal hemodynamic and with or without vasopressor support.

### **Exclusion criteria**

- Diagnosed case of Pneumonia.
- Case of Chronic Obstructive Lung Disease with active Chest Infections.
- Patients who have aspirated/with chest x-rays already showing infiltrates.
- Development of pneumonia within 48 hours of intubation (was considered Community acquired pneumonia (CAP) or Hospital acquired pneumonia (HAP) according to definition).
- Individuals diagnosed with Oral Mucositis.
- Individuals undergoing organ transplantation procedure, or long-term steroid therapy.
- Individuals receiving immunosuppressive therapy or known hypersensitivity to chlorhexidine gluconate.
- Patients already received mechanical ventilation for more than 24 hours.
- Patients who died or discharged or went LAMA within 48 hours of intubation in the ICU.

The study was reviewed and approved by institutional review committee of Apex Hospital Jaipur and was registered with Clinical Trials Registry of India, under registration id CTRI/2019/05/019116. Author NV was involved in

patient recruitment and overseeing data collection and data entry into the data collection software. The study staff, comprising of two critical care nurses administered oral prophylaxis. Another staff, a Critical Care Technician was involved in sample collection and data collection into case report forms. The case report forms were reviewed and authorized by author NV for entry into the data collection software.

**Randomization:** The study was designed as parallel arm, standard control, double blind randomized controlled with allocation ration 1:1 in intervention and control arm. The study used block randomization with block size of four. The randomization list was generated by authors AP and PV; who were not located at study site and allocation concealment was done using Sequentially Numbered Opaque Sealed Envelope (SNOSE). The Envelopes were couriered to study site using secure packaging. The Envelopes were accessible, only to study author PM, who was not involved in data collection or implementation of randomization protocol. The author SJ implemented randomization protocol. The randomization procedure included, assessment of individuals admitted to critical care unit for inclusion and exclusion criteria by critical care physician, once the individual was deemed suitable for inclusion, author SJ would access the sequentially numbered envelopes bundle from author PM and open envelop to write down randomization number and Group A or Group B on participants CRF. The critical care technician would proceed for opening of envelop and individual either of the groups.

### **Sample Size Calculation**

We used the sample size formula for comparing two means, the study by Ronankiet al.<sup>[11]</sup> compared the efficacy of commercially available chlorhexidine mouth rinses in concentration of 0.12% and 0.2% against Streptococcus Mutans and compared the size of means inhibitory zone created in mouth at 24hours. We used the mean inhibitory zone (in mm) and standard deviation to compare the antibacterial effect exerted by two concentrations on oral flora.

We anticipated mean response on the Chlorhexidine 0.12% concentration as 10.2, anticipated mean response on the Chlorhexidine 0.2% concentration as 10.7, standard deviation of response as 0.7, type I error 5%, type II error 80%. Thus, the required sample size is 61 participants in each group, total sample size 122. We enrolled total of 140 participants in the study.

### **Description of the intervention and control**

#### **Intervention**

Chlorhexidine 0.12% was be prepared by diluting commercially available chlorhexidine 0.2% (60 ml 0.2% chlorhexidine + 40ml sterile water).

**Control**

Chlorhexidine 0.2 % was commercially available and purchased in June 2019

**Standard Treatment Protocol**

The oral care practices were aimed to remove microhabitat of the organisms including cleaning of the oral cavity by the nurse with chlorhexidine soaked sterile gauze in intubated patients.

**The procedure was as follows:**

1. Any particulate matter from the oropharyngeal area was rinsed off with sterile water soaked in approximately 15-20 cc of sterile water.
2. The sterile gauze was soaked in 15 ml of chlorhexidine solution.
3. The chlorhexidine soaked sterile gauze was used to swab the entire oropharyngeal mucosa, teeth and part of the endotracheal tube inside the oropharyngeal area.

The average amount of chlorhexidine solution used per oral care provision is about 15 ml and was repeated 8 hourly till extubation. Clinical parameters (heart rate, temperature and blood pressure spo<sub>2</sub>, RR) were recorded hourly. Investigations included daily TLC and DLC; Chest X ray done on baseline then after every 48 hours and when indicated. Endotracheal secretion was sent at baseline (after intubation) then at 48 hours, at 96 hours and after 4 days as clinically indicated.

Evaluation of microbial load count -Oral secretion or saliva 1 ml was sent at base line (after intubation before oral care),at 48 hours, at 96 hours and after 4 day at the time of ET secretion sampling (after 30 min of oral care) for bacterial count (colony forming unit/ ml or CFU/ml) and microscopy at the department of Microbiology in our institute. Evaluation of microbial load done by using bacterial count (colony forming unit/ ml or CFU/ml).As per our routine protocol Arterial Blood Gas analysis was done twice a day in intubated patients or clinically indicated. Every intubated patient was suctioned tracheally with close suction device. There was strict adherence to VAP BUNDLE including elevation of head end of bed (30 to 45 degree), daily sedation interruption and extubation assessment, ET tube cuff pressure was maintained as per standard protocol and was checked in every shift. Standard infection control procedures were enforced.

All intubated patients received chest physiotherapy 8 hourly by physiotherapist unless contraindicated.All intubated resumed gastric feeding as soon as possible by nasogastric tube. We used injection pantoprazole once daily as ulcer prophylaxis. Antibiotics used as per hospital antibiotics policy.Clinical Pulmonary Infection Score (CPIS) is calculated according to parameters showed in [Table 7].

**Outcomes**

Diagnostic criteria's for VAP was based on CPIS Score. CPIS SCORE >6 OR 6 was consider VAP.

**Duration of study:** Data collection phase of the study lasted from June 2019 till Jan 2020, posted approval of study by research ethical committee.

**Data collection and analysis**

Data was collected on paper forms and entered electronically into CSpro 7.2 (US Census Bureau) software. Data was analyzed using STATA 14 (STATA corp.) We used Intention to Treat analysis. Clinical Endpoints – Diagnosis of VAP, Discharge from ICU, Death, Left Against Medical Advice (LAMA). We used per protocol analysis for the study; all the 140 were analyzed irrespective of outcome of their treatment.

**RESULTS**

Baseline characteristics of study participants are presented in [Table 1]. 140 participants eligible for enrolment criteria were provided with written informed consent and randomized on a 1:1 basis, i.e. 70 intervention arm (Chlorhexidine 0.12%) and 70 control arms (Chlorhexidine 0.20%). A total 78.57% were males and 21.43% were females with a mean age of 47 years in intervention group and in control group 68.57% were males and 31.43% were females with a mean age of 48.5 years. Clinical characteristics did not differ significantly among groups. Comparison of the 140 participants in this sample analysis who were enrolled indicated no significant difference in baseline variables (Gender, personal and medical history, Diagnosis of Current Episode Related to Respiratory System, Days admitted to the hospital, Days admitted in ICU, Days on ventilator and mortality).

[Table 2] presents the Day wise Clinical and Laboratory Parameters across both the study groups. Comparison of day wise participants data in the sample analysis did not see significant differences about CPIS score, Total Leukocyte Count, Presence of organisms (gram negative bacteria, gram positive bacteria, fungi) and Oral Microbial load among the intervention and control groups.

Outcome measurements across the both study groups are shown in the [Table 3]. A total of 140 participants were enrolled in the both groups, 70 in group 1 and 70 in group 2. In intervention group 7 Ventilator Associated Pneumonia, 30 discharge, 11 LAMA, 8 deaths were diagnosed. On the other hand, 2 Ventilator Associated Pneumonia, 36 discharge, 9 LAMA, 11 deaths were found in control group. Comparison of above-mentioned indicators analysis data we found significance difference in both groups. We also performed the subgroup analysis between the groups in which 20 participants underwent tracheostomy in group 1 and 24 participants in group 2. We also found that significant difference between Mean APACHE Score 15.8 (6.7) in group 1 and 18.4 (6.8) in group 2. [Table 4] presents Subgroup analysis for Participants underwent tracheostomy.

[Table 5] presents 15% LAMA cases with outcome were observed in group 1 and 13% LAMA cases with outcome were observed in group 2.

[Table 6] presents Radiographic Findings at admission

[Figure 1 and Figure 2] presents CPIS Score correlation with Microbial load in Group 1 and Group 2 respectively.

To understand the association between oral microbial load and incidence of VAP we ran logistic regression with VAP as outcome variable. The Odds of developing VAP in the intervention arm was 0.76 (CI -0.82 to 1.13) and odds of developing VAP in

control arm was 0.56 (CI-0.21 to 0.93) for oral microbial load more than 300 indicating no relation between VAP and Oral microbial load.

We also did the chest radiographic findings analysis between the both groups. [Table 6] 67.14% participants normal, 5.71% participants Old Koch's chest, 4.29% participants Haziness, 8.57% participants ARDS and 2.86 % Pleural effusion were reported in group 1 and 77.14% participants normal, 2.86% participants Old Koch's chest, 2.86% participants Haziness, 2.86% participants ARDS and 1.43 % Pleural effusion were reported in group 2.

**Table 1: Presents the baseline characteristics of the study participants**

Variables	Chlorhexidine 0.12% N = 70	Chlorhexidine 0.20% N = 70	P Value
Age (Mean, SD)	47 (16.9)	48.5 (17)	0.37
Gender			
Males (%)	78.57%	68.57%	0.18
Females (%)	21.43%	31.43%	0.23
Education			
Matriculation (%)	28.57%	35.71%	0.34
Higher Secondary (%)	28.57%	15.71%	0.4
Vocational Training (%)	10%	10%	0.8
Graduate (%)	30%	37%	0.12
Post Graduate (%)	2.86%	1.43%	0.49
Personal History			
Tobacco Smoking (%)	22.86%	20%	0.68
Tobacco Smokeless (%)	3.08%	1.47%	0.53
Alcohol Consumption (%)	27.94%	16.42%	0.10
Medical History			
Diabetes (%)	17.14%	11.43%	0.33
Hypertension (%)	24.29%	30.43%	0.24
Coronary Artery Disease (%)	13.04%	12.86%	0.78
Hyperthyroidism (%)	1.45%	0%	
Hypothyroidism (%)	2.94%	2.86%	0.79
Substance Abuse (%)	0%	2.86%	
Depression (%)	1.43%	1.43%	0.65
Anaemia (%)	4.35%	4.29%	0.58
Diagnosis of Current Episode			
Related to Respiratory System (%)	19.71%	9.85%	0.07
Number of days admitted to the hospital (mean, SD)	10 (6.8)	9 (7%)	0.18
Number of days admitted in ICU (mean, SD)	8.9 (6.6)	7.8 (4.2)	0.45
Number of days on ventilatory (mean, SD)	5.2 (3.7)	4.1 (2.1)	0.32
Tracheostomy (%)	32%	30%	0.48

**Table 2: Day wise Clinical and Laboratory Parameters across both the study groups**

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
<b>Chlorhexidine 0.12% (Intervention – Group 1)</b>										
CPIS Score (mean, sd)	2.1 (1.4)	1.8 (1.5)	1.3 (1.3)	1.3 (1.5)	1.5 (2.2)	1.4 (2.0)	1.4 (1.4)	1.8 (1.2)	2.7 (1)	2.3 (1.6)
Total Leukocyte Count (mean, sd)	15532 (7405)	13802 (7003)	12103 (5503)	11050 (4157)	11551 (4887)	11847 (7907)	11870 (7433)	13214 (6565)	12756 (7479)	10663 (4468)
Presence of micro-organism in ET secretion	27%		20%		33%		50%		33%	
Oral Microbial load (mean, sd)	203 (150)		219 (140)		228 (138)		233 (136)		175 (50)	
<b>Chlorhexidine 0.20% (Control – Group 2)</b>										
CPIS Score (mean, sd)	2 (1.4)	2.1 (1.7)	1.5(1.8)	1.2 (1.1)	1 (1.4)	1 (1.8)	0.9 (0.7)	1 (1.5)	0.5 (0.8)	1 (1.2)

Total Leukocyte Count (mean,sd)	14606 (7403)	14415 (7158)	13570 (7614)	11771 (6550)	11254 (5651)	11033 (4681)	10533 (3484)	9320 (2578)	8985 (2585)	9450 (3480)
Presence of micro-organism in ET secretion	26%				32%		50%		50%	
Oral Microbial load (mean, sd)	257 (165)				239 (129)		166 (57)		300 (173)	

**Table 3: Outcome Measurement across the study groups**

Indicators	Chlorhexidine 0.12% (Intervention – Group 1)	Chlorhexidine 0.20% (Control – Group 2)	Odds Ratio	P value
<b>Diagnosed</b>		<b>Diagnosed</b>		
Ventilator Associated Pneumonia	7	2	4.2	0.03
Discharge	30	36	0.65	0.001
LAMA	11	9	1.3	0.045
Death	8	11	0.68	0.04

**Table 4: Subgroup analysis for Participants undergoing tracheostomy**

Variable	Chlorhexidine 0.12% (Intervention – Group 1)	Chlorhexidine 0.20% (Control – Group 2)	Odds Ratio	P Value
Undergone Tracheostomy (n)	20	24		
Diagnosed with VAP (n)	4	1	5.75	0.058
Mean APACHE Score (SD)	15.8 (6.7)	18.4 (6.8)		0.001
Deaths (n)	1	2	0.75	0.91

**Table 5: Side effects and LAMA cases**

Variables	Chlorhexidine 0.12% (Intervention – Group 1)	Chlorhexidine 0.20% (Control – Group 2)	Odds Ratio	P Value
Left Against Medical Advice (LAMA) (n, %)	14 (20%)	16 (23%)		
LAMA cases with outcome (n, %)	11 (15%)	9 (13%)		
Oral Ulcer (n, %)	1 (1.5%)	0		

**Table 6: Radiographic Findings at admission**

Chest Radiograph findings	Group 1		Group 2	
	N	%	n	%
Normal	47	67.14	54	77.14
Old Koch's chest	4	5.71	2	2.86
Haziness	3	4.29	2	2.86
Normal	44	62.86	51	72.86
ARDS	6	8.57	2	2.86
Pleural effusion	2	2.86	1	1.43

**Table 7: CPIS**

CPIS	Temperature (*C)		Oxygenation (P/F ratio)	
36.5-38.4	0		>240 or ARDS	0
38.5-38.9	1		≤240 or No ARDS	2
≥39.0 or ≤36	2		Pulmonary radiography	
White blood cells count ( $10^3/\mu\text{l}$ )			No infiltrate	0
4-11	0		Diffuse or patchy infiltrate	1
≤4 or ≥11	1		Localize infiltrate	2
Either <4 or ≥11 plus band form ≥500	2		Culture of tracheal aspirate	
Tracheal secretion			Pathogenic bacteria cultured in light quantity or no growth	0
<14	0		Pathogenic bacteria cultured in moderate or heavy quantity	1
≥14	1		Same pathogenic bacteria seen on gram stain	2
≥14 plus purulent	2			

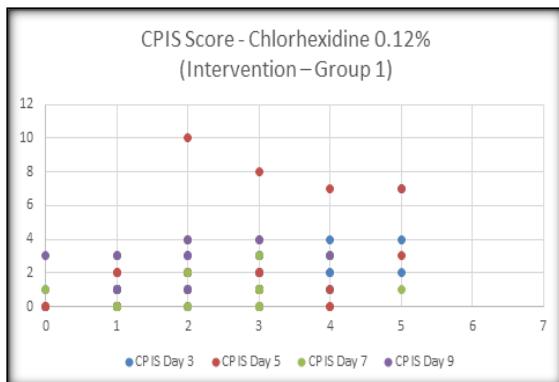


Figure 1: CPIS Score correlation with Microbial load (Group 1)

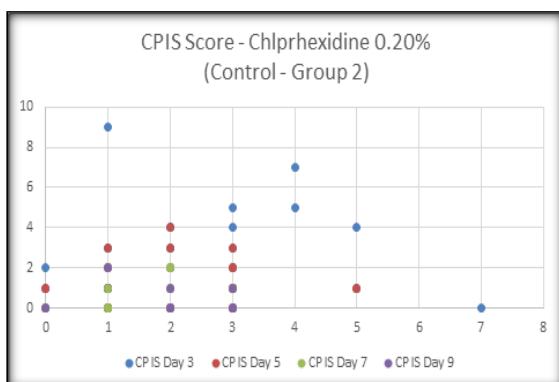


Figure 2: CPIS Score correlation with Microbial load (Group 2)

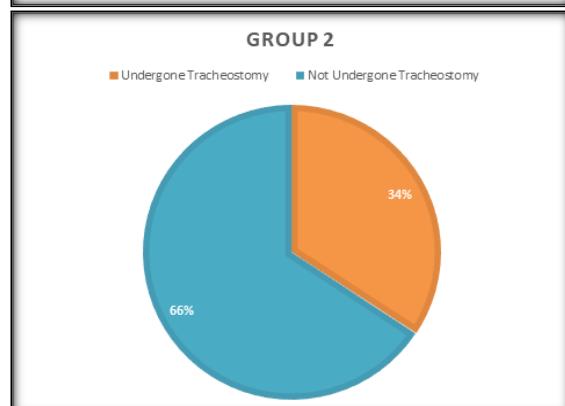
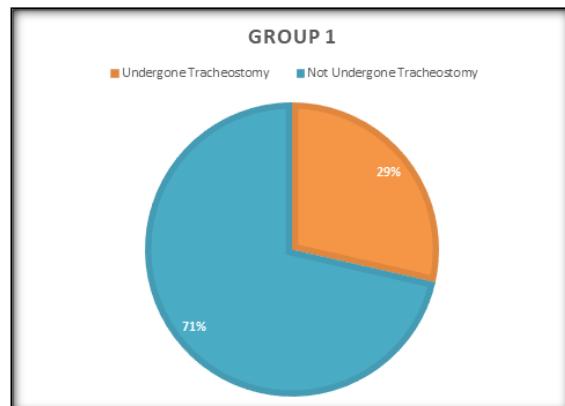


Figure 5: Pie Charts for participants undergone tracheostomy or not undergone tracheostomy, Chlorhexidine 0.12% (Intervention – Group 1), Chlorhexidine 0.20% (Control – Group 2)

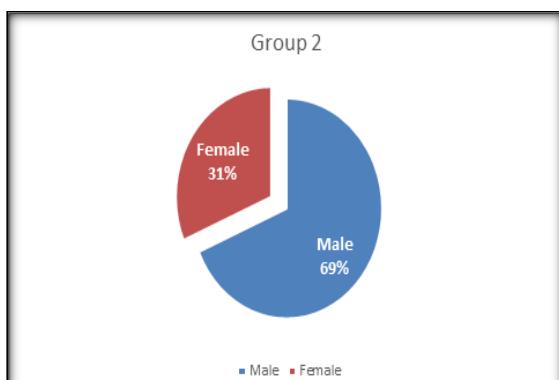
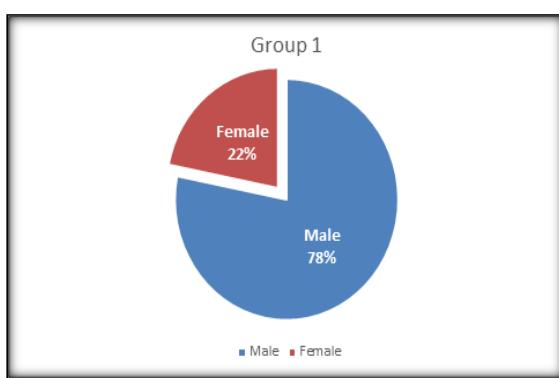


Figure 3: Pie charts for gender, Chlorhexidine 0.12% (Intervention – Group 1), Chlorhexidine 0.20% (Control – Group 2)

## DISCUSSION

VAP is a common nosocomial infection in the (ICU). Based on 2011 survey the average incidence of VAP was found 2.6% on 1000 mechanical ventilation days. The presence of similar clinical finding in many patients in the ICU, make the diagnosis of VAP very difficult. CPIS  $\geq 6$  is used for diagnosing VAP which is based on high sensitivity and negative predictive value in one multi centre randomized VAP diagnostic strategy study.<sup>[9]</sup>

So many previous studies reported that aspiration of oropharyngeal secretion which contains organism is a major cause of VAP and high microbial load is also associated with high incident of VAP in mechanically ventilated patients. Several studies also reported that oral hygiene using Chlorhexidine was more effective in preventing VAP compared to the other drugs or placebo but optimal concentrations remain unknown. Chlorhexidine is active against both Gram positive and gram-negative strain as well as fungi. Chlorhexidine has both bacteriostatic and bactericidal action.

In low chlorhexidine concentrations, this interaction slows the reproduction of the microbes (bacteriostatic). In high concentrations, the interaction causes damage to the cell membrane, kills the microbe (bactericidal). Chlorhexidine is

available in various forms and varying strength 0.2%, 0.12% and up to 5%. Lower concentration 0.10%, 0.12% (9) and 0.2% (6) is used as mouth rinses and higher concentration 2% and 5% is used as a surface disinfectant

Most of the studies used much less Chlorhexidine concentration solution of 0.12% or 0.2% for oral hygiene. Some recent studies reported that oral application of a 0.12 solution of Chlorhexidine was not superior to a placebo for preventing VAP among ICU patients.

In our study we found that oral hygiene with Chlorhexidine 0.12% is less effective than Chlorhexidine 0.20% for VAP prevention in mechanically ventilated (tracheally intubated or tracheostomized) cases.

Our study failed to find a relationship between VAP and Oral microbial load. The reason for this could be low incidence of VAP in our study and low incidence might be because we were using chlorhexidine in both groups. There is no significant difference in Days admitted to the hospital, Days admitted in ICU, Days on ventilator and mortality.

**Limitation-** In the multicenter randomized VAP diagnostic strategy study performed by Luyt et. al. the sensitivity of CPIS Score >- 6 for diagnosing VAP patient with bronchoscopy result was 89% and the specificity 47% and negative predictive value was 84%. CPIS is a preliminary test for VAP diagnosis but it is not a definite diagnostic test alone, this clinical scoring has been used as screening tool.<sup>[10]</sup>

To diagnose VAP for microbiological examination Broncho alveolar lavage (BAL) sampling is more sensitive and specific than tracheal secretion sample. We used tracheal secretion as sample for microbiological examination. Leukocyte count and body temperature changes which are of the CPIS criteria are observed in many diseases.

Aspiration pneumonitis (chemical pneumonitis), alveolar hemorrhage, lung contusion, drug reaction and TRALI can mimic chest x-ray opacity as in pneumonia. Fever and leukocytosis observed in the first 72 hours post operatively can be observed in also pulmonary edema, pulmonary infarction, vascular tissue and atelectasis, this may change CPIS score.

Patient already on antibiotics due to other reason may prevent VAP or delay VAP. Patient on drug paracetamol round the clock as analgesic may interfere with body temperature.

In our study LAMA rate was high that reduces actual days on mechanical ventilator and might interfere with incidence of VAP.

## CONCLUSION

- Chlorhexidine 0.12% is less effective than Chlorhexidine 0.20% for prevention of Ventilator Associated Pneumonia in mechanically ventilated

patients, while the safety of 0.12% and 0.20% is similar.

- There is no significant difference in ICU stay, hospital stay, Days on ventilator and mortality. This study also found no relation between incidence of VAP and oral microbial load.

## Summary:

Chlorhexidine solution has broad spectrum antimicrobial property. It is used as skin disinfectant at higher concentration (1%, 2%) and topical oral antiseptics at lower concentration (0.12% and 0.2%). Most of the larger RCT showed that oral hygiene with chlorhexidine (0.2% and 0.12%) in intubated patients have low incidence of VAP as compared to placebo or povidone iodine but optimal concentration of chlorhexidine was still unknown. Our study was aimed to find out most efficacious concentration of chlorhexidine mouth wash to prevent VAP in mechanically ventilated patients.

It was hypothesized that concentration of chlorhexidine (0.12%) will be similar effective as chlorhexidine (0.2%) in terms of prevention of VAP in mechanically ventilated patients and similar or more safety concern. Our study found that oral hygiene with chlorhexidine 0.12% is not much efficacious for prevention of VAP when compared with 0.2% while having similar safety.

**Abbreviations:** VAP- Ventilator associated pneumonia, HAP- Hospital acquired pneumonia, CAP -Community acquired pneumonia, LAMA- Left against medical advice, CPIS- Clinical pulmonary infection score, ICU- Intensive care unit.

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**How to cite this article:** Vyas N, Mathur P, Jhawar S, Prabhune A, Vimal P. Effectiveness of Oral Hygiene with Chlorhexidine Mouthwash with 0.12% and 0.2% Concentration on Incidence of Ventilator Associated Pneumonia (VAP) in Intubated Patients – A Parallel arm Double Blind Randomized Controlled Trial. *Ann. Int. Med. Den. Res.* 2021; 7(3):AN06-AN13.

**Source of Support:** Nil, **Conflict of Interest:** None declared