Reduction of Incidence, Mortality And Length of Stay With VAP Care in COVID-19 And other Respiratory Infections in Intensive Care Unit By Improving Oral Hygiene-A Systematic Review And Meta Analysis

Pudi Nagaseshu¹, Kavita Kachroo², Greeshma³, Jitendar Sharma⁴

^{1, 2, 3, 4}Health Technology Assessment

^{1, 2, 3, 4} Kalam Institute of Health Technology, Andhra Pradesh MedTech Zone, Visakhapatnam, India

Abstract- The objective of this review was to evaluate Reduction of Incidence, Mortality and Length of Stay with Ventilator Associated Pneumonia (VAP) in COVID-19 and Nosocomial Respiratory Infections in Intensive Care Unit in adults 18 years and over.

Introduction: Inclusion criteria: Patients with nosocomial and respiratory and covid 19 were included with the use of chlorhexidine or other topical agents or devices used for oral hygiene maintenance in ICU patients compared to a placebo product or usual care were included.

Methods: Databases to be searched include PubMed, Google scholar and Cochrane Following the search, titles and abstracts will be screened by two independent reviewers for assessment against the inclusion criteria for the review. The full text of selected citations will be assessed in detail against the inclusion criteria, and studies selected for retrieval will be assessed by two independent reviewers for methodological validity using JBI critical appraisal tools. Studies will not be excluded based on their quality assessment.

Results: 41 Studies met the inclusion criteria for review were taken and those studies were statistically pooled studies and outcomes were measured. All the studies demonstrated the by reducing Incidence, mortality and length of stay.

Conclusion: VAP Care can help reduce the risk of acquiring lung infection as well as improve ICU efficiency by reducing the staff time needed for manual suctioning. VAPCare is a safe system that did not cause any injury or side effects in the patient population, and also performed as intended Prospero Number: CRD42021233859

Keywords- VAP, Mortality, Length of stay and COVID-19

I. INTRODUCTION

The cause of death for Intensive Care Unit (ICU) patients is primarily associated with their critical illness, for which they have been admitted, and secondly hospital acquired illness known as nosocomial infections. Ventilator associated pneumonia (VAP) is a nosocomial infection associated with mechanical ventilation, responsible for 86% of all nosocomial pneumonias inside the hospital. [1] This infection develops within 48 hours or longer after mechanical ventilation is given by means of an endotracheal tube or tracheostomy. It occurs in 9–27% of all intubated patients [2]. In mechanically ventilated patients, the incidence increases with duration of ventilation. The risk of VAP is high in early course of hospital stay, and it is estimated to be 3% per day during the first 5 days of ventilation, 2% per day during 5 to 10 days of ventilation. It results from the invasion of the lower respiratory tract and lung parenchyma by microorganisms. Intubation compromises the integrity of the oropharynx and trachea and allows oral and gastric secretions to enter the lower airways. Patients with VAP, COVID-19 and other respiratory problems were unable to breath on their own hence, they are intubated with endotracheal tube (ETT). Mechanically ventilated patients who suffer from poor oral hygiene are exposed to the harmful accumulation of oral secretions and the initiation of VAP. Proper oral care by qualified care givers can reduce the incidence of VAP. Comprehensive oral care should be considered as a part of the medical treatment when a patient is admitted to the ICU to lower the incidence of VAP. Oral care of ventilated patients in the intensive care units, for prevention of ventilator-associated pneumonia, is an intervention with high clinical relevance, which leads to decrease in morbidity and mortality in the ICU [3].

A.Review question

What is the effectiveness of VAPcare for reducing incidence, Mortality, Length of stay and in adults 18 years and over.

B.Inclusion criteria: Participants

Articles that were considered for inclusion criteria was participants (18 years of age or older) with cardiac diseases, trauma, pneumonia, pulmonary, digestive, nosocomial infections and neurological diseases and covid-19.

C.Intervention

The intervention of interest was considered as Agents used for improved oral hygiene.

D.Comparator

This review considered studies that compared the intervention of oral hygiene with Usual care.

E.Outcomes

This review will consider studies that include the following outcomes in adults with reduction of incidence, mortality and length of stay.

F.Types of studies

Randomized control trail, observational, Retro prospective cohort studies, retrospective studies and prospective studies are included.

II. METHODS

A.Search strategy

The systematic review was conducted by primary electronic database search. Searches were conducted in PubMed, Google scholar and Cochrane data bases. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was developed for this project. Studies published in English language will be included. All the studies in the database from its inception to the present date will be considered.

B.Study selection

Following the search, all identified citations were collated and uploaded into EndNote and duplicates were removed. Titles and abstracts were screened by two Assessment of methodological quality independent reviewers for assessment against the inclusion criteria for the review. The full texts of potentially eligible studies were retrieved and assessed in detail against the inclusion criteria by two independent reviewers. Full-text studies that did not meet the inclusion criteria were excluded. Any disagreements that arose between the reviewers were resolved through discussion.

C.Data extraction

Data were extracted from studies included in the review by two independent reviewers The data extracted included specific details about the interventions, populations, study methods and outcomes of significance to the review question. Any disagreements that arose between the two reviewers were resolved through discussion.

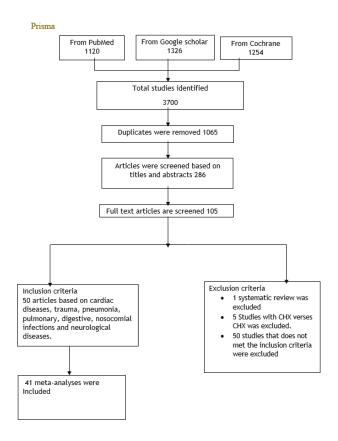
D.Data synthesis

Quantitative data will, where possible, be pooled in a random-effects meta-analysis model. All Effect sizes will be expressed as continuous and dichotomous data odds ratio or risk ratios for categorical data and the weighted mean difference, with 95% confidence intervals of the effect sizes will be estimated. All studies will be pooled to estimate an adjusted relative risk with 95% confidence intervals, irrespective of the study design used and the binary effect measure used. When statistical pooling is not possible, the findings will be presented in a narrative form, including tables and figures to aid in data presentation, where appropriate.

III. RESULTS

A.Study inclusion

A total of 3700 articles were identified by the search strategy of different databases like PubMed, Google scholar and Cochrane of which 2635 were removed based on duplicates, 286 articles were removed based the title and abstract. The full texts of 105 articles were screened, of which 50 articles met the inclusion criteria and were included in this review and 41 meta-analyses were included.



B.Methodological quality

Studies meeting the inclusion criteria were appraised for methodological quality. Based on the limited number of articles identified that met the inclusion criteria for this review and all studies were included, and any risk of bias was considered during data synthesis.

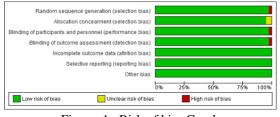


Figure. 1. Risk of bias Graph



Figure. 2. Risk of bias Summary

C.Critical Appraisal: Characteristics of included studies

The 41 included studies in the review are Randomized control trail, observational, Retro prospective

cohort studies, retrospective studies and prospective studies. Included studies explain about mortality studies on length of stay and other complications. These studies are appropriate for the study questions and the population being studied.

D.Review Findings: Incidence of VAP

The meta-analysis was conducted for those included studies for incidence of VAP and studies were compared with agents used for improved oral hygiene and usual care. The studies which are included in the review are randomized control trails. The main results of the meta-analysis comparing agents used for improved oral hygiene and usual care/placebo with antiseptics such as Chlorohexidine (CHX) Povidone, Saline, Tooth brushing and antibiotics (Iseganan) are summarized. Furthermore, subgroup analyses were conducted to explore the effects on the incidence of VAP.

Nine studies with CHX with three different concentrations 0.12%, 0.2% and 2% are compared with the usual care [4-12]. Ten studies were compared with CHX and not brushing/placebo[13,14,15,16,17,18,19,7,20, 21]. Four studies with Saline verses usual were compared [22, 23, 24, 25]. Ten studies were compared with CHX verses Placebo/ usual care [10, 4, 25,18, 27, 28, 24, 29 30, 31]. Four studies compared with povidone and placebo [25,26, 32, 33] Five studies with tooth brushing verses no tooth brushing/placebo [34, 5, 35, 36, 37]. Six studies were compared with antibiotics (Iseganan) verses placebo/ usual care [38, 39, 40, 41, 43, 44] and finally seven studies with other diseases associated like cardiothoracic and trauma were also compared [8, 9, 4, 10, 25, 12, 5].

Fluctures Eubersone	Incidenc	e-Oral Hy	giene Total	IncidenUsual care/P Events	lacebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Study or Subgroup 1.1.1 Antiseptic-Chlo	orhexidine (0.12%)	Total	Events	Total	weight	IV, Rahuoth, 95% Ci	IV, Raildoin, 95% CI
De Risco 1996		3	173	9	180	0.9%	0.35 [0.10, 1.26]	
Houston 2002		4 18	270	9	291 74	1.1%	0.48 [0.15, 1.54]	
Pobo 2009 Scannapieco 2009 Subtotal (95% CI)		7	58	12	59	1.7%	1.22 [0.66, 2.23] 0.59 [0.25, 1.40] 0.70 [0.39, 1.24]	
Subtotal (95% CI)			574		604	6.3%	0.70 [0.39, 1.24]	-
Total events	- 0.12 ChP	32 - 4.66 df	= 2 /P =	45				
Heterogeneity: Tau ^a = Test for overall effect	t Z = 1.23 (P	= 0.22)		0.207,1 - 00.0				
1.1.2 Antiseptic-Chlo	orhexidine (0.063						
Fourrier 2000	of freedome (5	30	15	30	1.7%	0.33 [0.14, 0.80]	
Fourrier 2005 Subtotal (95% CI)		13	114	12	114	2.1%	0.33 [0.14, 0.80] 1.08 [0.52, 2.27] 0.62 [0.19, 1.95]	
Total events		18	144	27	144	3.7%	0.62 [0.19, 1.95]	
Heterogeneity: Tau*	= 0.52; Chi*	= 4.05, df	= 1 (P =					
Test for overall effect	t Z = 0.82 (P	= 0.41)						
1.1.3 Antiseptic-Chic	orhexidine (2%)						
Koeman 2006		13	127	23	130	2.4%	0.58 [0.31, 1.09] 1.11 [0.73, 1.67]	
Mac Naughton 2004		32 5	91 102	28 12	88 105	3.4%	1.11 [0.73, 1.67] 0.43 [0.16, 1.17]	
Tantipong 2008 Subtotal (95% CI)			320		323	1.4%	0.73 [0.41, 1.29]	-
Total events		50		63				
Heterogeneity: Tau ^a Test for overall effect	= 0.15; Chi [*] 7 = 1.09 (P	= 4.72, df = 0.28)	= 2 (P =	0.09); I* = 58%				
1.1.4 Antiseptic-Chlo Caboy 2010	orhexidine r	ot brushi	ng verse 17	es placebo 6	23	0.4%	0.23 [0.03, 1.70]	
Chen 2008		16	60	28	60	3.0%	0.57 [0.35, 0.94]	
Derisco 1996 Grap 2004		5	173	17	180	1.4%	0.31 [0.12. 0.81]	
Grap 2004 Grap 2011		6	23 21	4 10	11 18	1.3%	0.72 [0.25, 2.03] 0.60 [0.29, 1.25]	
Jacomo 2011		19	87	11	73	2.3%	1.45 [0.74, 2.84]	
Ozcaka 2012		12	29	22	32	3.1%	0.60 [0.37, 0.98] 0.88 [0.45, 1.71]	
Panchabhai 2009 Sebastian 2012		14 12	88 41	15 14	83 45	2.3% 2.4%	0.88 [0.45, 1.71] 0.94 [0.49, 1.79]	
Segers 2006 Subtotal (95% CI)		35	485	67	469	3.6%	0.51 [0.34, 0.75] 0.66 [0.51, 0.84]	
Subtotal (95% CI)		127	1024	194	994	22.0%	0.66 [0.51, 0.84]	•
Total events Heterogeneity: Tau ^a	= 0.05: Chi ²	127 12.88.d	f = 9 (P :	= 0.17); I ^a = 30%				
Test for overall effect	t Z = 3.29 (P	= 0.001)						
1.1.5 Antiseptic-Sali	ine rinse ver	Ses usua	d care					
Caruso 2009		14	130	31	132	2.7%	0.46 [0.26, 0.82]	
Hu 2009		.4	25	10	22	1.4%	0.35 [0.13, 0.96]	
Seguin 2006 Xu 2007		12 10	31 62	13	31 44	2.6%	0.35 [0.13, 0.96] 0.92 [0.50, 1.69] 0.44 [0.22, 0.88]	
Subtotal (95% CI)			248		229	8.8%	0.54 [0.36, 0.82]	◆
Total events Heterogeneity: Tau ^a :		40		70				
Test for overall effect	= 0.05; Chi* t Z = 2.93 (P	= 4.30, 01	= 3 (b =	0.23); P = 30%				
1.1.6 Antiseptic-Chlo								
1.1.6 Antiseptic-Chic Bellisimo 2009	orhexidine v	erses Pk 16	64	17	69	2.6%	1.01/0.56 1.830	
Berry 2011		1	71	4	78	0.4%	1.01 [0.56, 1.83] 0.27 [0.03, 2.40]	
Bopp 2006		0	130	1	3 132	0.2%	0.44 [0.03, 7.52]	
Caruso 2009 Chacko 2017		5	12	7	132	1.8%	0.46 [0.26, 0.82] 0.71 [0.31, 1.63]	
Claudia 2017		28	45	17	45	3.3%	1.65 [1.06, 2.55]	
Grap 2004		4	7	3	5 49	1.5%	0.95 [0.36, 2.49] 0.57 [0.29, 1.14]	
Scannapieco 2009 Seguin 2006		12	31	13	31	2.6%		
Tantipong 2008 Subtotal (95% CI)		5	58	10	52 476	1.4%	0.45 [0.16, 1.23] 0.78 [0.55, 1.11]	
Total events		99	520	115	476	18.7%	0.78 [0.55, 1.11]	-
Heterogeneity: Tau* :	= 0.14; Chi*	= 17.71, d	f= 9 (P =	= 0.04); l ^a = 49%				
Test for overall effect	t Z = 1.37 (P	= 0.17)						
1.1.7 Antiseptic-Pov	idone verse	s Usual c	are					
Chua 2004 Feng 2012		6 18	22 71	8 29	20 68	1.7% 3.1%	0.68 [0.29, 1.62] 0.59 [0.37, 0.97]	
Seguin 2006		18	36	29	62	3.1%	0.59 [0.37, 0.97]	
Seguin 2006 Seguin 2014		28	78	21	72	3.2%	1.23 [0.77, 1.96] 0.71 [0.44, 1.16]	
Subtotal (95% CI) Total events		58	207	83	222	9.9%	0.71 [0.44, 1.16]	-
Heterogeneity: Tau ^a = Test for overall effect	= 0.14; Chi*:	= 7.43, df	= 3 (P =					
Test for overall effect	t Z = 1.38 (P	= 0.17)						
1.1.8 Tooth brushing	verses No							
Lorente 2012 Munro 2009		2	217	24	219	0.8%	0.08 [0.02, 0.35] 1.04 [0.78, 1.40]	
Munro 2009 Needle man 2011		48 5	97 10	45 11	95 18	4.1% 2.1%	1.04 [0.78, 1.40] 0.82 [0.40, 1.68]	
Pobo 2009		15	74	18	73	2.6%	0.82 [0.45, 1.50]	
Prendergast 2012 Subtotal (95% CI)		8	38 436	10	40	1.8%	0.84 [0.37, 1.91] 0.72 [0.43, 1.19]	
Total events		78		108	445	11.4%	0.72 [0.45, 1.19]	
Heterogeneity: Tau ^a Test for overall effect	= 0.20; Chi*	= 11.73, d	f=4 (P:	= 0.02); I* = 66%				
Test for overall effect	C Z = 1.27 (P	= 0.20)						
1.1.9 Antibiotics very	ses Placebo	>						
Abele 1997 Reromans 2001		13	58 87	23	50 78	2.7%	0.49 [0.28, 0.86]	
Bergmans 2001 Kollef 2006		52	362	62	347	3.8%	0.80 [0.57, 1.13]	
Lagger 1994		1	33	4	34	0.4%	0.26 [0.03, 2.19]	
Rios 2005 Rodriguez 1990		15	47	13	49 15	2.5%	1.20 [0.64, 2.25]	·
Rodriquez 1990 Subtotal (95% CI)			600		573	11.9%	0.05 [0.00, 0.77] 0.57 [0.35, 0.95]	•
Total events		90		137				
Heterogeneity: Tau ^a Test for overall effect	= 0.20; Chi ^a t Z = 2.17 (P	= 13.63, d = 0.03)	== 5 (P	= 0.02); P = 63%				
			4073		4045	100.0%	0.0010.00.0	
Total (95% CI) Total events		592		842	4010	100.0%	0.69 [0.60, 0.79]	•
Heterogeneity Tau ^a :	= 0.10: Chi ²	= 92.16. d	f= 47 (P	< 0.0001); P = 49%				0.01 0.1 1 10
Test for overall effect Test for subgroup dif	t Z = 5.25 (P	< 0.0000	1) df = 0.4	P = 0.96) IP = 0.96				Incidence-oral Hygiene IncidenUsual care/Placebo
st ini sondroup di	ences: C	··· = £.49.	$\omega = 0.0$					

Figure. 3. Forest plot showing the incidence for agents for oral Hygiene and usual care

E.Mortality of VAP

The main results of the meta-analysis comparing agents used for improved oral hygiene and usual care/placebo with antiseptics such as Chlorohexidine (CHX) Povidone, Saline, Tooth brushing and antibiotics (Iseganan) are summarized. Furthermore, subgroup analyses were conducted to explore the effects on mortality of VAP. Eight studies with CHX and usual care[4, 5, 11, 13, 6, 12, 31, 45].

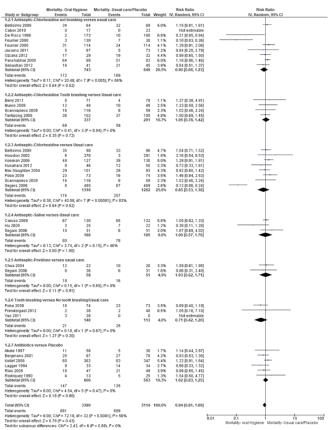


Figure. 4. Forest plot showing the mortality for agents for oral Hygiene and usual care

Nine studies were compared with CHX and not brushing/placebo [31, 21, 7, 8, 9, 14, 15, 16, 17]. Three studies with Saline verses usual were compared [23, 24, 25]. Nine studies were compared with CHX verses not brushing/usual care [31, 8, 9, 21, 7, 14, 15, 16, 17]. Two studies compared with povidone and placebo [25, 33] Three studies with tooth brushing verses no tooth brushing/placebo [34, 5, 46]. Six studies were compared with antibiotics (Iseganan) verses placebo/ usual care [39, 40, 41, 43, 44, 38, 42].

F.Length of hospital stay

The main results of the meta-analysis comparing agents used for improved oral hygiene and usual care/placebo with antiseptics such as Chlorohexidine (CHX) Povidone, Saline, Tooth brushing and antibiotics (Iseganan) are summarized. Furthermore, subgroup analyses were conducted to explore the effects on length of ICU stay for VAP. Three studies with tooth brushing verses no tooth brushing/placebo [37, 34, 5]. Six studies show antiseptics verses usual care [7, 8, 9, 12, 13, 25]. Two studies were included antibiotics verses usual care [40, 41, 42] Three studies were included for Chlorohexidine verses usual care/placebo [16, 31, 45].

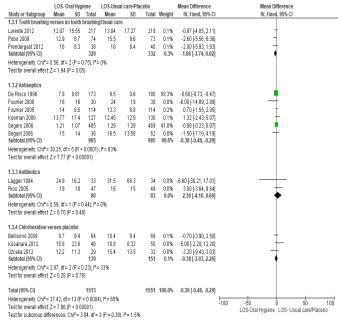


Figure. 5. Forest plot showing the Length of stay for agents for oral Hygiene and usual care

IV. DISCUSSION

VAP is the most frequently occurring nosocomial infection in the ICU and is associated with increased morbidity and mortality VAP is a main source of concern in critically ill patients. Most VAP is caused by microorganisms that are present in the oropharynx [48] and aspiration of pathogenic bacteria from the oropharynx is, therefore, the main pathophysiologic mechanism involved. According to some studies, respiratory pathogens isolated from the lung are often genetically indistinguishable from strains of the same species isolated from dental plaque and the tongue [49]. Therefore, it seems logical that improved oral care may reduce the risk of nosocomial respiratory infection. In this regard, authors have investigated the utility of some oral decontamination by the application of antibiotic or antiseptic agents. With respect to oral decontamination with chlorhexidine in critically ill patients, some studies have reported a reduction in positive dental plaque cultures [4, 9]. Standardized protocols which include the use of an antiseptic agent, can potentially reduce the risk for patients in acute care settings of developing VAP [49]. Thus, the CDC supports interventions to improve oral health, and subsequent reduction in the colonization of dental plaque with respiratory pathogens which may result in the development of VAP. Regular oral care with chlorhexidine is standard of practice for patients receiving mechanical ventilation in many hospitals. Our updated review of the evidence, however, suggests that caution is warranted. Although chlorhexidine does seem to protect against postoperative lower respiratory tract infections. chlorhexidine oral care may provide sufficient oral

decontamination in patients but is inadequate to overcome the infectious hazard of an endotracheal tube. In the sub analysis of seven studies with 665 patients, the oral application of antiseptics (chlorhexidine 0.12–2%, povidone, saline and antibiotics) did significantly reduce the incidence of VAP However, reduction was found in the mortality and ICU stay with the oral application of antiseptics and antibiotics. Oral hygiene with antiseptics and antibiotics it might paradoxically decreasing the time of patients, resources, and organizational focus available for more robust interventions that are more likely to reduce incidence, decrease length of stay, and decrease mortality.

V. CONCLUSION

VAPCare is a promising new technology that has shown good safety and effectiveness in secretion clearance and oral hygiene management. By ensuring consistency and compliance to airway suctioning protocols, VAP Care can help reduce the risk of acquiring lung infection as well as improve ICU efficiency by reducing the staff time needed for manual suctioning. VAPCare is a safe system that did not cause any injury or side effects in the patient population, and also performed as intended. VAPCare effectively automates secretion clearance and oral lavage, and can bring consistency to this process, which is today entirely dependent on the nurses' skill and time availability. Nursing time saving is another potential benefit of VAPCare. Administration of antiseptics in different concentrations alongside the suction of oropharyngeal secretions and mechanical debridement gave good results in the lowering of the accumulation of the pathogens responsible for the VAP. The results obtained showed that, among patients undertaking antiseptics, antibiotics and toothbrushing there was a significant reduction in the incidence of VAP, mortality and length of ICU stay in ICU.

VI. LIMITATION

Although there is no published data on VAPcare, it needs to be investigated through further research.

APPENDIX

Search	Query	Items found
#5	Search ((((endotracheal tube [MeSH Terms]) OR intubation)	943242
	AND oral hygiene) [MeSH Terms]) OR (((((Oral care [MeSH	
	Terms]) AND ((((usual care [MeSH Terms]) OR ((((Placebo	
	[MeSH Terms])	
¥4	Search (Endotracheal tube [MeSH Terms]) OR intubation	73672
#3	Search ((((((((cardiac disease [MeSH Terms]) OR myocardial)	35479
	OR cardiac arrest) AND pneumonia) OR bronchial pneumonia)	
	AND neurologic) OR neurological) AND trauma) OR mental	
	condition) OR psychological condition) AND digestive diseases	
	AND nosocomial infections	
#2	Search ((((Adult [MeSH Terms]) OR person [MeSH Terms])	57251
	AND ventilator) OR breathing machine) OR mechanical	
	ventilator	
#1	Search ((((adult [MeSH Terms]) OR person [MeSH Terms]) OR	1547154
	women) OR men) AND patient	
APPENI Recent	DIX 2 queries in Cochrane	
Search	Query	Items found
1	((Adult) tj.ab,kw OR (person) ti,ab,kw AND (ventilator) ti,ab,kw	11647
	OR (breathing machine) ti,ab,kw OR (mechanical ventilator)	
2	((cardiac disease) tj.ab,kw OR (myocardial) ti,ab,kw OR cardiac	37784
	arrest) ti,ab,kw AND (pneumonia) ti,ab,kw OR (bronchial	
	pneumonia) ti,ab,kw AND (neurologic) ti,ab,kw OR	
	(neurological) ti,ab,kw AND (trauma) ti,ab,kw OR (mental	
	condition) ti,ab,kw OR (psychological condition) AND	
	(digestive diseases)ti,ab,kw AND (nosocomial infection)	
3	(endotracheal tube) ti ab kw OR (intubation) ti ab kw AND Oral	3258

REFERENCES

- Koenig SM, Truwit JD. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev. 2006;19(4): 637–57.
- [2] Chastre J, Fagon JY. Ventilator-associated pneumonia: Am J Respir Crit Care Med. 2002; 165: 867-903.
- [3] Ron Gershonovitch, Noam Yarom and Mordechai Findler Preventing Ventilator-Associated Pneumonia in Intensive Care Unit by improved Oral Care: a Review of Randomized Control Trials SN, Compr. Clin. Med.
- [4] Scannapieco FA, Yu J, Raghavendran K, Vacanti A, Owens SI, Wood K and Mylotte JM. (2009) A randomized trial of chlorhexidine gluconate on oral bacterial pathogens in mechanically ventilated patients. Critical Care 13(4): R117.
- [5] Pobo A, Lisboa T, Rodriguez A, Sole R,Magret M, Trefler S, et al. A randomized trial of dental brushing for preventing ventilator associated pneumonia. Chest. 2009;136(2):433–9.

- [6] Houston S, Hougland P, Anderson J, LaRocco M, Kennedy V, Gentry L. Effectiveness of 0.12% chlorhexidine gluconate oral rinse in reducing prevalence of nosocomial pneumonia in patients undergoing heart surgery. Am J Crit Care. 2002; 11:567-570.
- [7] DeRiso AJ 2nd, Ladowski JS, Dillon TA, Justice JW, Peterson AC. Chlorhexidine gluconate 0.12% oral rinse reduces the incidence of total nosocomial respiratory infection and nonprophylactic systemic antibiotic use in patients undergoing heart surgery. Chest. 1996; 109:1556-1561.
- [8] Fourrier F, Cau-Pottier E, Boutigny H, Roussel-Delvallez M, Jourdain M, Chopin C. Effects of dental plaque antiseptic decontamination on bacterial colonization and nosocomial infections in critically ill patients. Intens Care Med 2000; 26:1239e1247.
- [9] Fourrier F, Dubois D, Pronnier P, et al. Effect of gingival and dental plaque antiseptic decontamination on nosocomial infections acquired in the intensive care unit: a double-blind placebo-controlled multicenter study. Crit Care Med 2005; 33:1728e1735.
- [10] Tantipong H, Morkchareonpong C, Jaiyindee S, Thamlikitkul V. Randomized controlled trial and metaanalysis of oral decontamination with 2% chlorhexidine solution for the prevention of ventilator-associated pneumonia. Infection Control & Hospital Epidemiology 2008;29(2):131–6.
- [11] Macnaughton P, Baily J, Donlin N, Branfield P, Williams A, Rowswell H. A randomised controlled trial assessing the efficacy of oral chlorhexidine in ventilated patients. Intens Care Med 2004;30 (Suppl. 1): S5eS18.
- [12] Koeman M, van der Ven AJ, Hak E, et al. Oral decontamination with chlorhexidine reduces the incidence of ventilatorassociated pneumonia. Am J Respir Crit Care Med 2006; 173:1348e1355.
- [13] Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial. J Am Med Assoc 2006; 296:2460e2466.
- [14] Sebastian MR, Lodha R, Kapil A, Kabra SK. Oral mucosal decontamination with chlorhexidine for the prevention of ventilator-associated pneumonia in children a randomized, controlled trial. Pediatric Critical Care Medicine 2012;13: e305–10.
- [15] Panchabhai TS, Dangayach NS, Krishnan A, Kothari VM, Karnad DR. Oropharyngeal cleansing with 0.2% chlorhexidine for prevention of nosocomial pneumonia in critically ill patients: an open-label randomized trial with 0.01% potassium permanganate as control. Chest 2009;135 (5):1150–6.

- [16] Özçaka Ö, Başoğlu OK, Buduneli N, Taşbakan MS, Bacakoğlu F, Kinane DF. Chlorhexidine decreases the risk of ventilator associated pneumonia in intensive care unit patients: a randomized clinical trial. J Periodontal Res. 2012;47(5):584–92.
- [17] Jacomo AD, Carmona F, Matsuno AK, Manso PH, Carlotti AP. Effect of oral hygiene with 0.12% chlorhexidine gluconate on the incidence of nosocomial pneumonia in children undergoing cardiac surgery. Infection Control &Hospital Epidemiology 2011;32(6):591–6.
- [18] Grap MJ, Munro CL, Hamilton VA, Elswick RK Jr, Sessler CN, Ward KR. Early, single chlorhexidine application reduces ventilator-associated pneumonia in trauma patients. Heart & Lung 2011;40(5):e115–22.
- [19] Grap MJ, Munro CL, Elswick Jr RK, Sessler CN, Ward KR. Duration of action of a single, early oral application of chlorhexidine on oral microbial flora in mechanically ventilated patients: a pilot study. Heart Lung 2004; 33:83e91.
- [20] Chen QL, Ye XF, Jiang YZ, Yan MQ. Application of new oral care method to orotracheal intubation. Fujian Medical Journal 2008;30(5):155–7.
- [21] Cabov T, Macan D, Husedzinovic I, Skrlin-Subic J, Bosnjak D, SestanCrnek S, Peric B, Kovac Z and Golubovic V. (2010) The impact of oral health and 0.2% chlorhexidine oral gel on the prevalence of nosocomial infections in surgical intensive-care patients: a randomized placebo-controlled study. Wien KlinWochenschr 122(13–14): 397–404.
- [22] Xu J, Feng B, He L, Shen H, Chen XY. Influence of different oral nursing methods on ventilator-associated pneumonia and oral infection in the patients undergoing mechanical ventilation. Journal of Nursing Science 2007;7(22):56–7.
- [23] Hu X, Chen X. Application of improved oral nursing method to orotracheal intubation. Chinese Journal of Mis diagnostics 2009;9(17):4058–9.
- [24] Caruso P, Denari S, Ruiz SAL, Demarzo SE, Deheinzelin D. Saline instillation before tracheal suctioning decreases the incidence of ventilator-associated pneumonia. CriticalCare Medicine 2009;37(1):32–8.
- [25] Seguin P, Tanguy M, Laviolle B, Tirel O, Malledant Y. Effect of oropharyngeal decontamination by povidoneiodine on ventilator-associated pneumonia in patients with head trauma. Critical Care Medicine 2006;34(5):1514–9.
- [26] Seguin P, Laviolle B, Dahyot-Fizelier C, Dumont R, Veber B, Gergaud S, et al. Effect of oropharyngeal povidone-iodine preventive oral care on ventilatorassociated pneumonia in severely brain injured or cerebral

hemorrhage patients: a multicenter, randomized controlled trial. Crit Care Med. 2014;42(1):1–8

- [27] de Lacerda Vidal CF, Vidal AK, Monteiro JG Jr, Cavalcanti A, Henriques APC, Oliveira M, et al. Impact of oral hygiene involving toothbrushing versus chlorhexidine in the prevention of ventilator associated pneumonia: a randomized study. BMC Infect Dis. 2017;17(1):112.
- [28] Chacko R, Rajan A, Lionel P, Thilagavathi M, Yadav B, Premkumar J. Oral decontamination techniques and ventilator associated pneumonia. Br J Nurs. 2017;26(11):594–9
- [29] Bopp M, Darby M, Loftin KC, Broscious S. Effects of daily oral care with 0.12% chlorhexidine gluconate and a standard oral care protocol on the development of nosocomial pneumonia in intubated patients: a pilot study. J Dent Hyg 2006; 80:9.
- [30] Berry AM, Davidson PM, Masters J, Rolls K, Ollerton R. Effects of three approaches to standardized oral hygiene to reduce bacterial colonization and ventilator associated pneumonia in mechanically ventilated patients: A randomised control trial. International Journal of Nursing Studies 2011;48(6):681–8.
- [31] Bellissimo-Rodrigues F, Bellissimo-Rodrigues WT, Viana JM, Teixeira GC, Nicolini E, Auxiliadora-Martins M, Passos AD, Martinez EZ, Basile-Filho A and Martinez R. (2009) Effectiveness of oral rinse with chlorhexidine in preventing nosocomial respiratory tract infections among intensive care unit patients. Infection Control and Hospital Epidemiology 30(10): 952–8.
- [32] Feng S, Sun X, Chen Y. Application of different mouthwashes in oral nursing for patients with orotracheal intubation. China Medicine and Pharmacy 2012;8(2): 100–1.
- [33] Chua JVDE, Sison CMC, Berba RP. The efficacy of povidone-iodine oral rinse in preventing ventilatorassociated pneumonia: a randomized, double-blind, placebo-controlled (VAPOR) trial: preliminary report. Philipp J Microbiol Infect Dis 2004; 33:153e161
- [34] Prendergast V, Jakobsson U, Renvert S, Hallberg IR. Effects of a standard versus comprehensive oral care protocol among intubated neuroscience ICU patients: results of a randomized controlled trial. Journal of Neuroscience Nursing 2012;44(3):134–46.
- [35] 35.Needleman IG, Hirsch NP, Leemans M, Moles DR, Wilson M, Ready DR, et al.Randomized controlled trial of toothbrushing to reduce ventilator-associated pneumonia pathogens and dental plaque in a critical care unit. Journal of Clinical Periodontology 2011;38(3):246– 52.
- [36] Munro CL, Grap MJ, Jones DJ, McClish DK, Sessler CN. Chlorhexidine, toothbrushing, and preventing ventilator

associated pneumonia in critically ill adults. American Journal of Critical Care 2009;18(5):428–37.

- [37] Lorente L, Lecuona M, Jimenez A, Palmero S, Pastor E, Lafuente N, et al. Ventilator-associated pneumonia with or without toothbrushing: a randomized controlled trial. European Journal of Clinical Microbiology and Infectious Diseases 2012;31(10):2621–9.
- [38] Abele-Horn M, Dauber A, Bauernfeind A, Russwurm W, Seyfarth-Metzger I, Gleich P, et al. Decrease in nosocomial pneumonia in ventilated patients by selective oropharyngeal decontamination (SOD). Intensive Care Med 1997;23:187-95. [PubMed] [Google Scholar]
- [39] Rodriguez-Roldan JM, Altuna-Cuesta A, Lopez A, Carrillo A, Garcia J, Leon J, et al. Prevention of nosocomial lung infection in ventilated patients: use of an antimicrobial pharyngeal nonabsorbable paste. Crit Care Med 1990;18:1239-42.
- [40] Rios F, Maskin B, Sanez VA. Prevention of ventilator associated pneumonia by oral decontamination: prospective, randomized, double-blind, placebo controlled study. In: Program and abstracts of the American Thoracic Society International Conference (San Diego). 2005. C95. Poster 608.
- [41] Laggner AN, Tryba M, Georgopoulus A, Lenz K, Grimm G, Graninger W, Schneeweiss B, Druml W. Oropharyngeal decontamination with gentamicin for long-term ventilated patients on stress ulcer prophylaxis with sucralfate? Wien KlinWochenschr. 1994; 106:15–19.
- [42] Shi Z, Xie H, Wang P, Zhang Q, Wu Y, Chen E, Ng L, Worthington HV, Needleman I, Furness Oral hygiene care for critically ill patients to prevent ventilatorassociated pneumonia (Review)-cochrane
- [43] Kollef MH, Pittet D, Sanchez Garcia M, Chastre J, Fagon JY, Bonten M, et al. A randomized double-blind trial of iseganan in prevention of ventilator-associated pneumonia. Am J Respir Crit Care Med. 2006; 173:91–7.
- [44] Bergmans DC, Bonten MJ, Gaillard CA, Paling JC, van der Geest S, van Tiel FH, Beysens AJ, de Leeuw PW, Stobberingh EE. Prevention of ventilator-associated pneumonia by oral decontamination: a prospective, randomized, double-blind, placebo-controlled study. Am J Respir Crit Care Med. 2001; 164:382–388.
- [45] Kusahara DM, Peterlini MA, Pedreira ML. Oral care with 0.12% chlorhexidine for the prevention of ventilator critically ill children: associated pneumonia in Randomised.controlled and double-blind trial. International Journal of Nursing Studies 2012;49(11):1354-63.
- [46] Yao LY, Chang CK, Maa SH, Wang C, Chen CC. Brushing teeth with purified water to reduce ventilator associated pneumonia. Journal of Nursing Research 2011;19(4):289–97.

- [47] El-Solh AA, Pietrantoni C, Bhat A, Okada M, Zambon J, Aquilina A, Berbary E (2004) Colonization of dental plaques: a reservoir of respiratory pathogens for hospitalacquired pneumonia in institutionalized elders. Chest 126:1575–1582.
- [48] Bahrani-Mougeot FK, Paster BJ, Coleman S, Barbuto S, Brennan MT, Noll J, Kennedy T, Fox PC, Lockhart PB (2007) Molecular analysis of oral and respiratory bacterial species associated with ventilator-associated pneumonia. J Clin Microbiol 45:1588–1593.
- [49] Tablan, O.C., Anderson, L.J., Besser, R., Bridges, C., Hajjeh, R., 2003. Guidelines for Preventing Health-Care-Associated Pneumonia: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee