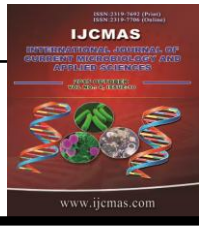
International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 4 Number 10 (2015) pp. 723-732**
http://www.ijcmas.com



Original Research Article

Oral Care as a Preventive Measure of VAP; Miswak Versus Chlorhexidine and Toothbrush, A Prospective, Controlled, Randomized, Non-Blind Study

Soad F. Hafez[1], Ahmed M. El-Mehalawy[2]*, Ali M. Sadek[3] and Hesham S. Bahy[2]

[1]Medical microbiology, Faculty of Medicine, Alexandria University, Alexandria, Egypt
[2]Critical Care Medicine, Faculty of Medicine, Alexandria University, Alexandria, Egypt
[3]Oral Medicine, Faculty of Dentistry, Alexandria University, Alexandria, Egypt
**Corresponding author*

Keywords

VAP,
Oral care,
Chlorhexidine,
Miswak
(Sewak)

Clinical Trials.gov Identifier:
NCT02288390

A B S T R A C T

Colonization of the oral mucosa and dental plaque is considered an important reservoir of respiratory pathogens. Aim of the study is to evaluate the effect of Miswak in mechanically ventilated patients regarding oral care, bacterial colonization and occurrence of VAP in comparison to 0.12% Chlorhexidine plus toothbrush. Forty patients were randomized into 2 groups. Dental plaque score calculation and swabs of Oropharynx and teeth were collected on admission. For group I, Miswak stick was used 4 hourly for oral care. For group II, 0.12% Chlorhexidine/ toothbrush were used 4 hourly. Effectiveness of oral care, colonization by potential respiratory pathogens and rate and time to VAP were monitored. At the end of the study, dental plaque score and oral hygiene showed no significant differences between both groups(P = 0.31 and 0.082 respectively). Dental plaque and oropharyngeal colonization was significantly lower in Miswak group(P=0.041 and 0.031 respectively). *S.viridans* was more frequently isolated in group I (P = 0.439). Miswak caused insignificant reduction of VAP (P = 0.37, RR of 0.71, RRR of 0.29 and ARR of 0.10), longer time to VAP (P= 0.106), lower mortality (P= 0.301) and more ICU discharge (P= 0.34). Group II had significantly shorter mechanical ventilation (MV) days (13.50±4.04 vs 11.13±3.04 days, P= 0.035). Miswak is as effective as combined Chlorhexidine/ toothbrush in improving oral care and dental plaque score. Miswak caused significantly lower incidence of oropharyngeal and dental bacterial colonization. Also, trends for preservation of normal flora, lower occurrence of VAP, less ICU stay and lower mortality, but, significantly longer MV days.

Introduction

Ventilator associated pneumonia (VAP) carries high morbidity and mortality. [1] Oropharyngeal (OPH) and dental plaque colonization has an emerging role in pathogenesis of VAP.[2, 3] Control of dental plaque colonization requires mechanical removal of the plaque by the toothbrush. [4]

Chlorhexidine (CHX) poses antiplaque effect and an antiseptic effect. [5] CHX oral

care showed significant reduction of VAP in cardiac surgery patients,[6] however, subsequent trials did not show consistent benefit.[7, 8] Moreover, there is no difference in mortality, duration of mechanical ventilation (MV) or intensive care unit (ICU) stay.[9] CHX was at times associated with adverse effects including the risk of emergence of resistant strains.[10-12] Natural therapies would ideally reduce plaque levels without affecting the overall biological equilibrium within the oral cavity.[13]

Miswak, the twig of Arak (Salvadora perscia) tree, is commonly used for oral hygiene in Middle East and Africa. Miswak is composed of a compact group of minute natural fibres that represent a natural toothbrush.[14] Miswak contains several natural chemical compounds essential for good oral and dental hygiene together with bactericidal and antiseptic effects.[15] Miswak was proven effective for oral hygiene in ambulant people and was even WHO recommended. [16-18]

The aim of this study was to evaluate the role of Miswak for oral hygiene in mechanically ventilated patients and its effect on dental plaque and OPH colonization, and the subsequent effect on the occurrence of VAP in comparison to toothbrush with 0.12% Chlorhexidine mouth wash.

Patients and Methods

The study protocol was approved by the Faculty of Medicine local ethical committee, reference number 010102. The study included 40 mechanically ventilated patients admitted, between July 2007 and May 2008, to the Critical Care Medicine department, Alexandria University, Egypt. The patients were randomized into 2 groups by the conventional method of randomization according to day of admission.

On admission, clinical examination included assessment of disease severity by Acute Physiology and Chronic Health Evaluation (APACHE II) scoring system, [19] oral and dental examinations and dental plaque score calculation. [20]

The preventative VAP bundle was applied to both groups including elevation of the head of the bed, daily "sedation vacations" and minimal dose, daily assessment of readiness to extubate, peptic ulcer prophylaxis, deep venous thrombosis prophylaxis, and oral rather than nasal route for gastric and endotracheal tubes.

For group I, patient's teeth were brushed 4 hourly using a Miswak stick after scraping of half an inch bark from the stick end then Miswak tip was compressed to make it brush like. The end was refreshed daily. For group II, the patient's teeth were brushed 4 hourly using a toothbrush with 0.12% Chlorhexidine. The toothbrush was boiled for one minute every day. For both groups, buccal and lingual surfaces of teeth were brushed in direction away from gingival margin, the patient's tongue was brushed when possible and lip moisturizer was applied as needed.

Patients were monitored for the efficacy of oral care in term of plaque score and halitosis. Colonization of trachea, OPH, and dental plaque by potential respiratory pathogens (PRPs) as *Staphylococcus aureus*, *Pseudomonas, Klebsiella, Proteus, Acinetobacter and E. coli* species was identified by culturing of OPH swab, dental swab and endotracheal tube aspirate (ETA) on inclusion into the study and every 4 days thereafter till ICU discharge, 3 weeks of ICU stay, or death. Secondary endpoints included time to VAP and its incidence, duration of MV, ICU discharge, and mortality rate. No patients were lost to follow-up, discontinued intervention or

excluded from analysis.

VAP was diagnosed when patient developed; new and/or progressive infiltrates in chest radiograph plus two or more of the following; leucocytosis ≥ 12000/mm^3 or leucopenia ≤ 4000c/mm^3, fever > 38^oC or hypothermia < 36^oC, or mucopurulent secretion. The clinically diagnosed VAP was confirmed by quantitative ETA at a cut off value ≥10^5colony forming unit (cfu) /ml.

Statistical analysis

Using Epi Info 7 software at 95% confidence interval and 80% power with experimental to control group equal one and estimated outcome among control group of 50% (based on our previous unpublished data), the minimum sample size was 15 for each group. The results were analyzed using SPSS version 19. Frequency and percentage were utilized for description. Chi-square test was applied to test for the association and/or difference between the two groups.

Results and Discussion

At the time of inclusion, both groups were comparable as regard age, gender, APACHE II score, Glasgow coma scale (GCS), smoking, chronic health diseases, oral hygiene, dental plaque index score, and baseline cultures (table 1). As well, the indications for MV and compliance to VAP bundle throughout study period showed no significant differences.

Dental plaque index score and oral hygiene

At the end of study, the dental plaque index significantly decreased in both groups without intergroup significant differences. Similarly, there was significant improvement of oral hygiene in both groups between admission and the end of the study without significant difference between either group (tables 2, 3).

On the day of admission, three patients had bacterial colonization in each group. The consequently developed colonization was significantly lower and delayed among group I patients. Comparing the overall isolated PRPs from dental, OPH, and ETA samples in both groups, this variance was of highly significance ($\chi2=30.09$, $p<0.001$). Studying isolated dental or OPH colonization was still significant ($\chi2=13.12$, df=6, $p=0.041$and$\chi2=13.84$, df=6, $p=0.031$ respectively). However, isolated tracheal colonization was of insignificant difference ($\chi2=1.81$, df=5, $p=0.875$). On contrary, throughout the study period, *S.viridans* was isolated from dental and OPH swabs more frequently and declined less steadily among group I ($\chi2=0.6$, $p=0.439$) table 4.

VAP started later in group I, moreover, Miswak insignificantly reduced the risk of VAP, relative risk (RR) of 0.71, relative risk reduction (RRR) of 0.29 and absolute risk reduction (ARR) of 0.10. Despite significantly longer duration of MV in Miswak group, there was a trend towards favorable outcome in the form of more ICU discharge and lower mortality (table 5).

The present study displayed bad oral hygiene and plaque index score at time of ICU admission. In agreement, Jones et al [21] reported greater than 73% mean dental plaque coverage on day 1in mechanically ventilated adults. The present study denoted that Miswak and combined CHX/ toothbrush were effective tools for oral hygiene and control of plaque score. Likewise, Al-Otaibi et al [22] found the Miswak to be more effective than toothbrush for reducing plaque and gingivitis when preceded by professional instructions.

Table.1 Basic characteristic of both groups on inclusion

	Group I	Group II	T	P
Age (years) mean ± SD	38.10±19.759	45.65±19.381	1.488	0.230
Gender (%)				
Male	45	40	0.102	0.5
Female	55	60		
APACHE II (Mean ± SD)	16.8±5.053	17.56±5.675	1.68	0.21
GCS (Mean ± SD)	12.40±4.057	9.70±5.302	1.771	0.78
Smokers (%)	45	50	2.66	0.264
Chronic health disease (%)				
COPD	25	30		0.12
DM	25	20		0.31
Renal failure	25	20		0.29
Hepatic failure	15	10		0.31
Dental plaque index score (%)				
1	40	10		
2	20	35		0.085
3	40	55		
Oral hygiene (%)				
Accepted	10	15		0.084
Bad	90	85		
Tracheal colonization (No)	2	3		0.50
Dental swabs (No)				
S. viridans	19	20		
Klebsiella	3	2		0.75
Candida	2	2		
Pseudomonas	1	0		
Oropharyngeal swabs (No)				
S. viridans	19	19		
Klebsiella	2	3		0.36
Candida	2	2		

GCS, Glasgow coma scale; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; *S. viridans.Streptococcus viridans*.

Table.2 Comparison between both groups regarding dental plaque index score on admission and at the end of the study

	Group I		Group II		P
	No.	%	No.	%	
On admission					
1	8	40	2	10	
2	4	20	7	35	**0.085**
3	8	40	11	55	
At the End					
0	16	80	14	70	
1	3	15	4	20	**0.31**
2	1	5	2	10	
P	**0.001***		**0.001***		

Table.3 Comparison between both groups regarding oral hygiene on admission and at the end of the study

	Group I		Group II		P
	No.	%	No.	%	
On admission					
Accepted	2	10	3	15	**0.084**
Bad	18	90	17	85	
At the end					
Accepted	20	100	19	95	**0.082**
Bad	0	0	1	5	
P	**0.0001***		**0.0001***		

Table.4 Comparison between both groups as regard results of culture of dental swab, oropharyngeal swab and endotracheal aspirate throughout the study period in both groups

	Group I			Group II		
Microorganism	**Dental No. (%)**	**OPH No. (%)**	**ETA No. (%)**	**Dental No. (%)**	**OPH No. (%)**	**ETA No. (%)**
S.viridans	42 (32.5)	44 (34.1)	0 (0.0)	30 (10.98)	24 (8.79)	0 (0.0)
K. pneumoniae	5 (3.8)	5 (3.8)	2 (1.55)	9 (3.29)	7 (2.56)	9 (3.29)
Pseudomonas	1 (0.77)	1 (0.77)	3 (2.3)	10 (3.66)	6 (2.19)	6 (2.19)
Candida	6 (4.65)	9 (6.97)	1 (0.77)	7 (2.56)	8 (2.93)	1 (0.36)
Proteus	1 (0.77)	0 (0.0)	1 (0.77)	3 (1.09)	4 (1.44)	2 (0.71)
OSSA	1 (0.77)	3 (1.09)	1 (0.77)	3 (1.09)	4 (1.44)	1 (0.36)
ORSA	1 (0.77)	1 (0.77)	1 (0.77)	3 (1.09)	2 (0.71)	4 (1.44)

OPH, oropharyngeal; ETA, endotracheal aspirate; *OSSA*, Oxacillin sensitive *S. aurous*; *ORSA*, Oxacillin resistant *S. aurous*.

Table.5 Comparison between the two studied groups regarding outcome

	Group I	Group II	P
ICU discharge			
No	13	9	0.34
%	65	45	
Duration of MV (days)			
mean± SD	13.50±4.04	11.13±3.04	0.035*
Incidence of VAP			
No	5	7	0.37
%	25	35	
Time to VAP (days)			
Range	8-13	4-12	
mean± SD	10.50±2.38	9.13±2.95	0.106
Mortality			
No	7	11	0.301
%	35	55	

As well, Batwa et al[23] described that Miswak was as effective as a toothbrush for reducing plaque on buccal teeth surfaces. Other studies reported the Miswak extract to improve gingival and bleeding indices. [24, 25]

Darout et al [26] noted that the periodontal status of Miswak Sudanese users is better than that of toothbrush users. In contrary, Norton and Addy [27] studied the oral hygiene and gingival health of adult Ghanaians who used chewing sticks, toothbrushes, or a combination of both.

Plaque and gingivitis scores were higher in the chewing stick users. However, they attributed this result to the difference in gender as men had poorer oral hygiene and gingival health than women.

The present study denoted higher incidence of colonization by PRPs especially gram negative bacteria (GNB) in CHX group compared to Miswak. In agreement, several studies reported lower efficacy of CHX against GNB. Scannapieco et al[28] compared 0.12 % CHX to placebo controlin mechanically ventilated patients. The total number of cfu's recovered from dental plaque as *enterics*, *Pseudomonas* and *Acinetobacter* were not reduced by CHX at any time point. But, *S. aureus* was significantly reduced. Pedreira et al[29] reported that 0.12% CHX was not superior to routine oral care in in mechanically ventilated children in term of normal flora or colonization when *A. baumannii*, *P.aeruginosa*, *K. pneumoniae*, and *Enterobacter* species were the predominant pathogens.

In another study, Koeman et al [30] compared CHX, CHX/ Colistin (CHX/COL), to placebo. CHX/COL provided significant reduction in OPH colonization with both gram-positive and GNB, whereas CHX mostly affected gram-positive bacteria. As noted by Koljalg et al,[31] GNB resistant to ciprofloxacin, imipenem, cefotaxime, ceftazidime, gentamicin and aztreonam appeared to have increased CHX resistance.

Again, Fourrier et al [32] studied gingival and dental plaque decontamination with a 0.2% CHX gel versus placebo in 228 mechanically ventilated patients. Highly

resistant *Pseudomonas*, *Acinetobacter*, and *Enterobacter* species were not eradicated by CHX.

Chelli-Chentouf et al [33] described a strong in vitro and in vivo antimicrobial effect of Miswak methanolic extract against (*Staphylococcus, Streptococcus, Escherichia and Lactobacillus* species) identified from oral cavity of school children. Miswak extract more significantly inhibited the growth of GNB than Gram positive ones.

Superiority of Miswak against GNB colonization noted in the present study can be partly explained by the relative preservation of normal flora *S. viridans*. However, this relative preservation cannot be attributed to lower efficacy of Miswak against gram positive bacteria since both *OSSA* and *ORSA* were isolated at lower rate in Miswak group.

Todar[34] specified that the normal flora occupy available colonization sites, compete for nutritional substances and produce inhibitory substances which make it more difficult for nonindigenous microorganisms to become established.

Moeintaghavi et al [35] compared, in vitro, the antimicrobial activities of various concentrations of miswak extract and CHX mouth wash gainst *S. salivarius* and *S. sanguis*. They described higher efficacy of CHX compared to Miswak.

The only study of Miswak extract in mechanically ventilated patients was carried out by Khezri et al [36] in a double blind randomized trial in year 2011. Eighty patients were randomized into four groups; CHX 0.2 %, Matrica R (chamomile extracts) 10%, Persica TM 10% (contains three medicinal plants, Salvadora Persica, Yarrow and Mint), and normal saline. Immediately before and after mouth rinsing, saliva samples were cultured for *S. aureus* and *S. pneumoniae.* The rate of bacterial colonies decreased after intervention in all groups. CHX was the most effective ($p < 0.001$) followed by PersicaTM (p: 0.008) and Matrica (p: 0.01).Other studies had found Miswak to be active against *S. aureus* and[37]*S. faecalis.*[38, 39]

In the present study, CHX group had significantly shorter mechanical ventilation days. However, Miswak was associated with an insignificant trend for better outcome in the form of VAP timing and occurrence, mortality, and ICU stay.

Fourrier et al [32] observed no differences in the incidence of VAP, mortality, and length of stay when compared 0.2% CHX gel versus placebo for gingival and dental plaque decontamination. Koeman[30] reported that the risk of VAP was significantly reduced in both treatment groups CHX and CHX/ COL compared with placebo, but, there were no differences in duration of mechanical ventilation, ICU stay, or ICU survival. Shi et al [40] conducted a Cochrane Systematic Review that revealed reduction of VAP incidence in adult patients without change in mortality, ICU stay or mechanical ventilation days. However, the children population did not show even a difference in VAP.

In conclusion, using Miswak stick, our clinical study is unique. One cannot always generalize in vitro results to the in vivo situation. Besides, extract may not be equivalent to the crude natural plant product especially it for sure will lack the brushing effect.

Poor oral hygiene and high plaque index scores are common among critically ill patients on ICU admission. In this regard, Miswak was not inferior to the combined effect of 0.12% CHX/ toothbrush. Miswak

was significantly superior to CHX/ toothbrush in term of dental and OPH colonization by PRPs. Miswak was associated with a trend for preservation of normal dental and OPH*S. viridans* flora, reduced occurrence of VAP, a longer time to VAP, lower ICU stay and mortality rate. CHX was associated with a significantly shorter mechanical ventilation days.

Acknowledgement

The authors thank the physicians and nursing staff of the Critical Medicine department.

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