Original Study

THE EFFECT OF ORAL DECONTAMINATION PLAN ON THE OCCURRENCE OF VENTILATOR ASSOCIATED PNEUMONIA IN ICU PATIENTS: A DOUBLE-BLIND CLINICAL TRIAL

Khaky B,[1] Yazdannik A,[2] Mahjoubipour H,[3] Attari F[4]

1. Research Student, School of Nursing and Midwifery, Isfahan University of Medical Sceinces, Isfahan, IRAN.
2. Assistant Professor, School of Nursing and Midwifery, Isfahan University of Medical Sceinces, Isfahan, IRAN.
3. Department of Anesthesiology and Research Center, Isfahan University of Medical Sceinces, Isfahan, IRAN.
4. Research Student, School of Nursing and Midwifery, Isfahan University of Medical Sceinces, Isfahan, IRAN.

ABSTRACT

Aim: Oral colonization and microaspiration of secretions to the lower respiratory tract are two important processes in infectious pathogens associated with mechanical ventilation. In ICU patients, hospital pneumonia is the most common and deadly hospital infection. The purpose of this study was to investigate the effect of using Nanosil mouthwash in the form of an oral decontamination plan on the clinical pulmonary infection score, which indicates the incidence of ventilator associated pneumonia.

Materials & Method: This research is a clinical, interventional, two-group, randomized, double blind trial. Eighty patients undergoing mechanical ventilation, who were admitted less than 48 hours ago and were eligible for inclusion in the study, were selected and randomly assigned to the two control and experimental groups. An oral decontamination plan using Nanosil mouthwash was carried out for 5 days, every 8 hours, for a duration of 3-5 minutes for the experimental group, and the same plan was carried out for the control group using chlorhexidine mouthwash. On the first and fifth days, the Modified Clinical Pulmonary Infection Score (MCPIS) will be completed to measure ventilator-associated pneumonia and the expected outcome of the occurrence or non-occurrence of ventilator-associated pneumonia will be analyzed.

Results: There was no significant difference in terms of age, sex, background disease, history of smoking, MCPIS initial score, SOFA score and GCS score between the two groups ($p > 0.05$). In both groups, the mean score of SOFA and GCS increased significantly within five days ($p < 0.05$). Also, after five days from the start of the study, the mean score of MCPIS (1.2 ± 0.1 *vs.* $3.5 \pm 0.3, p < 0.001$) and pneumonia incidence (2.7% vs 23.7%, p=0.008) decreased significantly in both groups. However, the mortality rate on the first and fifth days was equal in both groups ($p > 0.05$).

Conclusion: The use of Nanosil mouthwash in the form of an oral decontamination plan for ICU patients reduces the incidence of ventilator associated pneumonia, but further studies and more samples are required to solidify the results.

Key words: : Oral care, oral decontamination, ventilator associated pneumonia, ICU

Introduction

Infections acquired from the treatment environment are always one of the major health problems in Iran. The incidence and mortality of these infections have increased, resulting in significant increase in hospitalization costs.[1] ICU patients are usually in critical condition and there are numerous risk factors that make them susceptible to a range of infections.[2] The use of artificial airway and mechanical ventilation in patients with spontaneous breathing problems can lead to several complications, the most important of which is ventilator-associated pneumonia.[3] Pneumonia is an inflammatory state of the lung with bacterial, viral or fungal origin. Pneumonia contracted from hospital after a urinary tract infection is the second most common infection in hospitals.[4] Ventilator-associated pneumonia (VAP) is a subtype of acquired pneumonia from hospitals. It refers to a state in which pneumonia starts 48 to 72 hours after the creation of an artificial airway.[5]

The most obvious risk factor is the endotracheal tube that crosses the natural barriers of aspiration. Tracheal intubation prevents bulk aspiration, but actually intensifies microaspiration due to the accumulation of secretions above the tube cuff.[6] The incidence of VAP has been reported differently based on the type of hospital or care unit, the type of received antibiotic and the characteristics of the studied population.[7] VAP leads to increased therapeutic costs, increased mechanical ventilation and hospitalization time in ICU. Its raw mortality rate is reported to be 50-70%. There are many risk factors associated with VAP, such as the use of nasogastric tubes, endotracheal intubation, re-intubation, aspiration, aspiration of oral and subglottic secretions, coma, intestinal nutrition, pH alteration factors, etc. The colonization of bacteria in oropharynx is an important risk factor for the incidence of VAP.[8]

There are two strategies for dealing with VAP: Prevention and treatment. Due to high incidence rate and numerous physiological and economic effects, the best strategy is prevention of infection and control of related risk factors.[9] Many studies have shown that some interventions have reduced the incidence of VAP.[4] The reduction of VAP incidence means a significant reduction in hospitalization period and treatment costs, and ultimately a significant impact on mortality in ICU.[10] Infection prevention plans play a key role in preventing VAP incidence in hospitals. These plans include: Developing policies, team consultation on the best operational options, risk assessment, training, communication, and facilitating quality improvement projects to reduce VAP.[2] Endotracheal tube is an important risk factor for VAP, therefore a basic preventive measure is non-intubation or at least minimizing intubation cases. Successful use of non-invasive ventilation with the help of a mask eliminates

many of the issues related to endotracheal tube. Also, strategies that reduce the duration of the usage of ventilation device will have a great effect in preventing VAP by stopping daily intake of sedatives and separation protocols.[8]

Oral care is considered as one of the nursing care standards in ICU. Nurses are directly responsible for and involved in the management of airway secretions of the patient under mechanical ventilation, and there are numerous nursing practices that may lead to a reduction in VAP incidence.[9] Oral decontamination plan is a set of standard decontamination measures to prevent the spread of microbes through the oral mucosa into the digestive and respiratory systems. Nanosil (Sanosil) mouthwash is a formulation that combines hydrogen peroxide and a small amount of silver ion. Due to its anti-microbial properties as well as oxygen release, hydrogen peroxide prevents the proliferation of anaerobic microbial population effective in periodontal diseases. Oxygen released from hydrogen peroxide damages the protective membrane of bacteria and viruses and enables Nanosil to penetrate into it and eliminate microorganisms.[10]

Materials & Method

The present study is a double blind clinical trial (Iranian Registry of Clinical Trials Number: IRCT2017091636194N1) with a pretest and posttest design, involving the control and intervention groups. The statistical population included patients who were recently admitted to the ICU of Amin Clinic in Isfahan (Iran) from November 2016 to May 2017. Inclusion criteria: Age condition over 18 years and under 70 years,[11,12] lack of clear trauma in the jaw and face, having an endotracheal tube and having the patient under mechanical ventilation,[12] absence of pneumonia or respiratory infections at the time of admission to the hospital, maximum 48 hours after the start of intubation,[13] and having no ban in using Nanosil or chlorhexidine and having no allergies. From the 97 patients evaluated, 80 were initially enrolled in the study and were randomly assigned using minimization software into two control and intervention groups (40 patients each).

Measurement Tools

The variables considered by the software included sex, age, performance score of the systems, SOFA score, GCS, and history of smoking.

The SOFA (Sepsis related Organ Failure Assessment) is one of the severity classification systems that is used to evaluate the severity of a disease in patients admitted to the ICU. Using this scoring system, one can have a preventive model of consequences, estimate their incidence, and compare the clinical outcomes of a group with another one. Grading is based on determining the performance of body systems or their failure rate. Six different factors including respiratory, cardiovascular, hepatic, hematological, renal and neurological systems are used in this scale. Each section is scored between 0 and 4, and ultimately these scores are summed to calculate the degree of illness and the risk of mortality. In fact, SOFA is predicting the results. The SOFA scores less than 9 estimate mortality possibility to be about 20%, scores between 10-12 indicate about 40% possibility, the scores 13-14 indicate a possibility of 60%, 15 indicates a possibility of over 80%, and scores over 16 point to a possibility of about 95%.[14]

The Glasgow Coma Scale (GCS) is a tool for measuring the level of consciousness in people over the age of five. The tool consists of three components: The first part involves opening the eyes in four levels, the second part relates to verbal response in five levels, and the third part relates to motor response in six levels. The maximum and minimum GCS score is 15 and 3, respectively. If patients are under mechanical ventilation and intubation, it is not possible to evaluate their verbal response. Therefore, in assessing the level of consciousness, the GCS score of these patients is from the lowest score of 2t to 10t.

The Modified Clinical Pulmonary Infection Score (MCPIS) has specifically been used in different studies to investigate the incidence of pneumonia in patients under mechanical ventilation and intubation. It is based on 5 variables: Body temperature (36.5 – 38.4 = 0, 38 – 5 – 38.9 = 1, >39or <36 = 2), white blood cell count (per mm3, 4000-11000=0, <4000 or >11000=1, <4000 or >11000+ band forms 500=2), endotracheal tube secretions in terms of color and smell (Rare=0, Abundant=1, Abundant+ Purulent=2), oxygenation (pao2 to fio2 ratio) (>240 or ARDS=0, 240 and no evidence of ARDS=2), radiographic findings (no Infiltrate=0, diffused=1, Localized=2).

This scale ranges from 0 to 10; a score of more than 5 is a sign of pneumonia, with a sensitivity of 93% and a 100% attribute.

Study Design and Data Collection

Basic information from patients included age, sex, history of smoking and background diseases. Before the intervention, GCS, SOFA and MCPIS scores were calculated and recorded in the control and intervention groups.

In the intervention group, oral care was performed according to a specific schedule including decontamination of oropharynx using Nanosil solution every 8 hours, each time for 3 minutes up to 5 days. In the control group, the same oral care plan was performed with the difference that oral decontamination was done using 0.12% chlorhexidine mouthwash. The oral decontamination plan was carried out for up to 5 days. Exclusion criteria included death before the end of the intervention, extubation prior to the end of the intervention, transfer to other wards or hospitals during intervention, and undergoing any diagnostic and therapeutic procedure in the oral, throat and endotracheal tube before the end of the intervention. Five days after the start of the study, the MCPIS score was evaluated and VAP incidence was checked. The GCS and SOFA scores were also calculated on the fifth day.

Ethical Clearance

This study was conducted in accordance with the Declaration of Helsinki and good clinical practice according to the International Conference on Harmonization guidelines. The study was approved by ethics committee of Isfahan University of Medical Sciences and registered in Iranian Registry of Clinical Trials with number of IRCT2017091636194N1.

Data Analysis

After collecting data, data was analyzed by SPSS software version 18. To compare qualitative data, the chi-square test and Fisher's exact test were used as appropriate. The t-test was used to analyze quantitative data. Also, the probability of mortality rate was calculated by Mann-Whitney and Wilcoxon test. P value less than 0.05 was considered statistically significant.

Results

Of the 97 patients, 80 patients were enrolled in this study and randomly divided into two equal groups. During the study, 3 patients in the case group and 2 patients in the control group were excluded. Finally, data of 37 patients in the case group and 38 patients in the control group were analysed. [Figure 1]

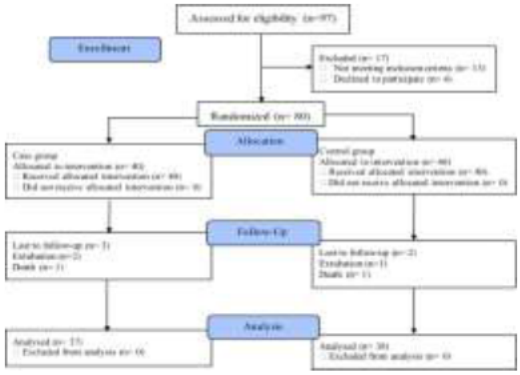

Figure 1: CONSORT flow diagram

There was no significant statistical difference between the mean age in the two groups and they were equal in respect of age (41.6 ± 15.9 *vs.* 44.1 ± 16.5, p=0.49). 67.5 percent of samples in the control group and 72.5 percent of samples in the case group were male (p=0.63). In the control group, 30 percent and in the case group 35 percent of the patients had cigarette addiction (p=0.63).

Variables		Case Group	Control Group	p value
Age (Mean ± SD)		41.6 ± 15.9	44.1 ± 16.5	0.49
Gender	Male (%)	29 (72.5%)	27 (67.5%)	0.63
	Female (%)	11 (27.5%)	13 (32.5%)	
Underling disease (%)		22 (55%)	25 (62.5%)	0.50
Smoking (%)		14 (35%)	12 (30%)	0.63
MCPIS (Mean ± SD)		1.4 ± 0.2	1.1 ± 0.2	0.31
SOFA (Mean ± SD)		7.5 ± 2.4	7.3 ± 2.5	0.75
GCS (Mean ± SD)		5.0 ± 1.7	5.1 ± 1.7	0.90

MCPIS: Modified Clinical Pulmonary Infection Scale; SOFA: Sequential Organ Failure Assessment; GCS: Glasgow Coma Scale

Table 1: Compare patient's primary data

Also, the frequency of underling disease were 37.5% and 45% in the control and case groups, respectively (p=0.50). the mean score of SOFA, GCS and MCPIS were given in table 1. As you can see, there is no statistically significant difference between the two groups in the mean scores of SOFA, GCS and MCPIS. [Table 1]

In the fifth days, there were not observed significant difference in the mean score of SOFA (6.7 ± 2.5 *vs.* 6.3 ± 2.8, p=0.50) and GCS (7.0 ± 2.1 *vs.* 6.8 ± 2.03, p=0.70) between case and control groups. But, MCPIS score was significantly higher in control group (3.5 ± 0.3 *vs.* 1.2 ± 0.1, p<0.001). [Table 2]

Variables	Case Group	Control Group	p value
MCPIS (Mean ± SD)	1.2 ± 0.1	3.5 ± 0.3	<0.001
SOFA (Mean ± SD)	6.7 ± 2.5	6.3 ± 2.8	0.50
GCS (Mean ± SD)	7.0 ± 2.1	6.8 ± 2.03	0.70
Pneumonia (%)	1 (2.7%)	9 (23.7%)	0.008

MCPIS: Modified Clinical Pulmonary Infection Scale; SOFA: Sequential Organ Failure Assessment; GCS: Glasgow Coma Scale

Table 2: Compare the mean of MCPIS, SOFA, GCS and frequency of pneumonia in fifth day

Also, paired t-test showed that the mean score of MCPIS in the test group did not show significant difference between the two times (p=0.54). But, paired t-test showed that the mean score of MCPIS in the control group on the fifth day of study were significantly higher than the first day of study (p <0.001). For all patients in case and control groups, the mean score of SOFA and GCS was significantly improve after the five days follow up (p<0.05). [Table 3]

Variables		First Day	Fifth Day	p value
Case Group	MCPIS (Mean±SD)	1.4 ± 0.2	1.2 ± 0.1	0.54
	SOFA (Mean±SD)	7.5 ± 2.4	6.7 ± 2.5	0.04
	GCS (Mean±SD)	5.0 ± 1.7	7.0 ± 2.1	<0.001
Control Group	MCPIS (Mean±SD)	1.1 ± 0.2	3.5 ± 0.3	<0.001
	SOFA (Mean±SD)	7.3 ± 2.5	6.3 ± 2.8	0.02
	GCS (Mean±SD)	5.1 ± 1.7	6.8 ± 2.03	<0.001

MCPIS: Modified Clinical Pulmonary Infection Scale; SOFA: Sequential Organ Failure Assessment; GCS: Glasgow Coma Scale

Table 3: Compare the mean of MCPIS, SOFA, GCS before and after intervention

Ventilation association pneumonia were observed in 1 patient of case group (2.7%) and 9 patients of control group (23.7%). Oral care with Nanosil solution significantly better than Chlorhexidine reduced the incidence of ventilation association pneumonia (p=0.008). [Table 2]

Finally, the Mann-Whitney test showed that there was no significant difference between the two groups in the mortality rate on the first and fifth day of study (p> 0.05). Wilcoxon test showed that the mortality rate in both groups

on fifth day was significantly lower than the first day ($p < 0.05$). [Table 4]

Time	Probability of Mortality	Case Group Frequency (%)	Control Group Frequency (%)	Z	p
First Day	0-10%	21 (52.5%)	16 (40%)	1.02	0.31
	15-20%	13 (32.5%)	17 (42.5%)		
	40-50%	6 (15%)	6 (15%)		
	50-60%	0	0		
Fifth Day	0-10%	26 (70.3%)	23 (60.5%)	0.74	0.46
	15-20%	7 (18.9%)	12 (31.6%)		
	40-50%	4 (10.8%)	1 (2.6%)		
	50-60%	0	2 (5.3%)		
Wilcoxon Test	Z	1.99	2.19	-	

Table 4: Frequency distribution of mortality rate in two groups on the first and fifth day of intervention

Discussion

VAP is the most commonly diagnosed infectious disease in Intensive Care Unit.[15,16] The incidence of this complication varies according to hospitals and facilities and is reported to be between 13 and 51 people per 1,000 ventilators per day.[7] VAP is associated with prolonged hospitalization,[17] longer mechanical ventilation,[6] increased hospital costs and a doubling of the risk of death.[18] CDC recommend oral hygiene as the best preventing strategy for VAP.[19] Therefore, finding more effective mouthwash can reduce the incidence of VAP.

The results of our study indicated that the both of Nanosil mouthwash and Chlorhexidine mouthwash reduced the risk of VAP. However, Nanosil mouthwash was more effective than Chlorhexidine and dramatically save the MCPIS score and reduced the incidence of VAP.

In a study by Meinberg *et al* in 2012 in the intensive care unit, 28 patients were treated with 2 percent Chlorhexidine gel, brushing teeth 4 times a day, and 24 patients were also treated with placebo gel with brushing 4 times a day. The results of their study also showed no statistically significant difference between the results of the two groups, as well as the ineffectiveness of Clorhexidine mouthwash.[20] In the study of Lorente *et al*, benefited from a high statistical size, 217 patients were under oral care with Chlorhexidine gel of 0.12 percent with brushing three times a day, and 219 patients were also under oral care with only Chlorhexidine gel of 0.12 percent three times a day. The results showed that there was no statistically significant difference between the two groups in terms of pneumonia reduction.[21] In a systematic review study conducted by El-Rabbany *et al* in 2015, they investigated 28 performed researches about Chlorhexidine and the impact of oral health on the prevention of pneumonia. The results of their investigation showed that the role of Chlorhexidine is still debatable and requires greater studies for confirmation.[22]

So far, no clinical studies have compared the efficacy of Nanosil and Chlorhexidine mouthwashes on preventing VAP. In a laboratory study conducted by Kariminik *et al*, they investigated the effect of Chlorhexidine and Nanosil mouthwashes and some antibiotics on streptococcus mutans bacterium isolated from dental plaque in a laboratory environment. The results of their study showed that this bacterium and most of its products have most susceptibility to Nanosil mouthwash.[23] Isfahanian *et al* study was conducted for the laboratory comparison of the antibacterial effect of two mouthwashes of Nanosil and Chlorhexidine; in this laboratory-comparative study the sampling of supragingival and subgingival plaques of 15 patients was done, and the number of bacteria was determined in two aerobic and anaerobic fluid environments by spectrophotometer. The results concerning Chlorhexidine showed that there was no significant difference between cultivated colonies in both aerobic and anaerobic environments, but in the case of Nanosil mouthwash, the number of developed colonies, especially in the anaerobic environment, has been severely reduced.[24]

The lesser effect of Chlorhexidine in the present study may be due to this principle that this substance has a small antimicrobial spectrum. In other words, Chlorhexidine primarily affects Gram-positive organisms, while Gram-negative microbes are the most common organisms in the oral-pharyngeal cavity of critically ill patients.[25] Whereas, Nanosil component such as hydrogen peroxide and silver ions by destroyed bacterial and viral protective membranes and bacterial inactivation have a broad spectrum antibacterial effect. Our results confirm the pervious in-vitro studies that shown the Nanosil mouthwash has a stronger antibacterial effect on oral bacteria.[23,24]

Conclusion

The results of this study showed that Nanosil is more effective than Chlorhexidine in the prevention of VAP occurrence, and its reduces VAP incidence in critically ill patients hospitalized in the intensive care units.

Acknowledgements

We are grateful to official members of ICU departments of Amin Hospital for their help.

Conflict of interest

The Authors declare that there are no conflicts of interest.

Reference

1. Vincent J, Abraham E, Moore F, Kochanek P. Textbook of critical care nursing. London: Saunders; 2011.
2. Rebmann T, Greene LR. Preventing ventialator Associated Pneumonia : an executive summary of the association for professionals in infection control and epidemiology, Inc, elimination guide. Am J Infect Cont 2010;38(8):647-649.
3. Pileggi C, Bianco A, Flotta D, Nobile CG, Pavia M. Prevention of ventilator associated pneumonia, mortality and all intensive care unit acquired infections by topically applied antimicrobial and antiseptic agents: a meta analysis of randomized controlled trials in intensive care units. Crit Care 2011;15(3):R155.
4. Muscedere J, Dodek P, Keenam S, Fowler R, Cook D, Heyland D. Comprehensive evidence-based clinical

practice guidlines for ventilator associated pneumonia. J Crit Care 2008;23(1):126-37.
5. Gillespie R. Prevention and management of ventilator associated pneumonia, the care bundle approach SA J Hospital Infect 2009;25(2):44-51.
6. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. Criti Care Med 2005;33(10):2184-93.
7. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors. J Infect Dev Ctries 2009;3(10):771-7.
8. Kasper D, Fauci A, Houser S, longo D, Jameson J. Harrisons Principles of Internal Medicine. 19th ed. New York: Hill Education; 2015; 2015.
9. Ricart M, Lorente C, Diaz E, Kollef MH, Rello J. Nursing adherence with evidence-based guidelines for preventing ventilator-associated pneumonia. Crit Care Med 2013;31(11):2693-6.
10. Arabi Y, Al-Shirawi N, Memish Z, Anzueto A. Ventilator-associated pneumonia in adults in developing countries: a systematic review. Int J Inf Dis 2008;12(5):505-12.
11. Lacherarde JC, De Jonghe B, Guezennec P, Debbat K, Hayon J, Monsel A *et al*. Intermittent subglottic secration drainage and ventilator-associated pneumonia. Am J Respir Crit Care Med 2010;182(7):910-7.
12. Alimi M, Manzari Z, Mazlom ZR, Moghadam BA, Rouhani H. Evaluation of the effects of oronasal Versus oral disinfections with Chlorhexidine on clinical criteria of ventilator-associated pneumonia. Evidence Based Care J 2016;6(3):19-30.
13. Darvishi Khezri H. The role of oral care in prevention of ventilator associated pneumonia: A literature review. J Shahid Sadoughi University (JSSU). 2014;21(6):840-9.
14. Ferrieira FL, Bota DP, Bross A, Melot C, Vincent JL. Serial Evaluation of the SOFA score. JAMA 2001;286(14):1754-8.
15. Buczko W. Ventilator-associated pneumonia among elderly medicare beneficiaries in long-term care hospitals. Health Care Financ Rev 2009;31(1):1-10.
16. Valles J, Pobo A, Garcia-Esquirol O, Mariscal D, Real J, Fernandez R. Excess ICU mortality attributable to ventilator-associated pneumonia: the role of early vs late onset. Intensive Care Med 2007;33(8):1363-8.
17. Amin A. Clinical and economic consequences of ventilator-associated pneumonia. Clin Inf Dis 2009;49(Suppl 1):S36-S43.
18. Li L, AI Z, Li L, Zheng X, Jie L. Can routine oral care with antiseptics prevent ventilator-associated pneumonia in patients receiving mechanical ventilation? An update meta-analysis from 17 randomized controlled trials. Int J Clin Exp Med 2015;8(2):1645-57.
19. Klompas M, Branson R, Eichenwald EC, Greene LR, Howell MD, Lee G *et al*. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014;35(S2):S133-S54.
20. Meinberg MC, Cheade Mde F, Miranda AL, Fachini MM, Lobo SM. The use of 2% chlorhexidine gel and toothbrushing for oral hygiene of patients receiving mechanical ventilation: effects on ventilator-associated pneumonia. Rev Bras Ter Intensiva 2012;24(4):369-74.
21. Lorente L, Lecuona M, Jiménez A, Palmero S, Pastor E, Lafuente N *et al*. Ventilator-associated pneumonia with or without toothbrushing: a randomized controlled trial. Eur J Clin Microbiol Infect Dis 2012;31(10):2621-9.
22. El-Rabbany M, Zaghlol N, Bhandari M, Azarpazhooh A. Prophylactic oral health procedures to prevent hospital-acquired and ventilator-associated pneumonia: a systematic review. Int J Nurs Stud 2015;52(1):452-64.
23. Kariminik A, Motaghi MM. Evaluation of Antimicrobial susceptibility pattern of Streptococcus mutans isolated from dental plaques to chlorhexidine, nanosil and common antibiotics. Int J Life Sci 2015;9(2):18-21.
24. Esfahanian V, Mohamadi F, Amini SH. An In vitro comparison of antimicrobial effect of nanosil and chlorhexidine mouthrinses. J Islamic Dent Assoc Iran 2012;24(3):238-43.
25. Johnstone L, Spence D, Koziol-McClain J. Oral hygiene care in the pediatric intensive care unit: practice recommendations. Pediatr Nurs 2010;36(2):85.

Corresponding Author

Dr. Ahmadreza Yazdannik
Assistant Professor,
Nursing and Midwifery School,
Isfahan University of Medical Sceinces, Isfahan, IRAN.
Email Id: - yazdannik@nm.mui.ac.ir