Revista da Escola de Enfermagem da USP
ISSN: 0080-6234
reeusp@usp.br
Universidade de São Paulo
Brasil

Campos de Carvalho, Emilia; Capellari Cárnio, Evelin; Youssef Khouri, Vivian; Guilherme, Caroline; Benedita dos Santos, Claudia; Aparecida Pace, Mariangela

Exame da cavidade bucal de pacientes com câncer: avaliação clínica e dosagem indireta de óxido nítrico

Revista da Escola de Enfermagem da USP, vol. 47, núm. 1, febrero, 2013, pp. 101-106
Universidade de São Paulo
São Paulo, Brasil

Available in: http://www.redalyc.org/articulo.oa?id=361033324013

Examination of the oral cavities of patients with cancer: clinical evaluation and indirect measurement of the nitric oxide level

EXAME DA CAVIDADE BUCAL DE PACIENTES COM CÂNCER: AVALIAÇÃO CLÍNICA E DOSAGEM INDIRETA DE ÓXIDO NÍTRICO

EXAMEN DE LA CAVIDAD ORAL DE LOS PACIENTES CON CÁNCER: VALUACIÓN CLÍNICA Y MEDICIÓN INDIRECTA DE ÓXIDO NÍTRICO

Emilia Campos de Carvalho[1], Evelin Capellari Cárnio[2], Vivian Youssef Khouri[3], Caroline Guilherme[4], Claudia Benedita dos Santos[5], Mariangela Aparecida Pace[6]

ABSTRACT

This observational study aimed to verify the association between the clinical state of the oral cavity (based on the Index of Decayed, Missing, and Filled Teeth and the Simplified Oral Hygiene Index) and the indirectly determined nitric oxide level in patients with oncologic and hematologic diseases. This study included 20 hospitalized patients who were in the evaluation phase prior to starting chemotherapy and who had been diagnosed with leukemia (35%), lymphoma (50%) or myeloma (15%). Fifty percent of these patients had normal oral health (no injury or trauma), and most had satisfactory (35%) or typical (35%) hygiene, but 30% had poor or very poor hygiene. The indirectly measured levels of nitric oxide ranged from 13.34 to 257. The nitric oxide level was not associated with other parameters, and there was great variability in its level. Further studies are necessary given the potential of using this indicator in the early detection of oral diseases.

DESCRIPTORS

Nitric oxide
Oral hygiene
Drug therapy
Nursing care

RESUMO

Neste estudo buscou-se verificar associação entre avaliação clínica da cavidade oral (pelos Índices de dentes Cariados, Perdidos e Obturados e Índice de Higiene Oral – Simplificado) e a determinação indireta de óxido nítrico em pacientes com patologias onco-hematológicas. Trata-se de estudo observacional, no qual foram incluídos vinte sujeitos internados, diagnosticados com Leucemia (35%), Linfoma (50%), Mieloma (15%), em avaliação para início de quimioterapia, sendo que 50% apresentaram normalidade da condição bucal (sem lesões ou traumas); a maioria apresentou higiene satisfatória (35%) ou regular (35%), porém, 30% tiveram higiene deficiente ou péssima. A expressão indireta do óxido nítrico variou de 13,34 a 257. O óxido nítrico não apresentou associação com os outros parâmetros; houve grande variabilidade de seus valores. Novos estudos são necessários, em especial pela potencialidade deste indicador na detecção precoce de alterações bucais.

DESCRITORES

Óxido nítrico
Higiene bucal
Quimioterapia
Cuidados de enfermagem

RESUMEN

Este estudio observacional buscó verificar la asociación entre evaluación clínica de la cavidad oral (por medio de el índice de dientes cariados, perdidos y obturados y el índice de higiene oral simplificado) y la determinación indirecta de óxido nítrico en pacientes con enfermedades oncohematológicas. Estudio observacional, que incluyó a 20 pacientes hospitalizados, con diagnóstico de leucemia (35%), linfoma (50%), mieloma (15%), bajo evaluación para el inicio de la quimioterapia, de los cuales el 50% tenía salud bucal normal (sin lesión o trauma). La mayoría mostró higiene satisfactoria (35%) o regular (35%), pero el 30% tenía mala o muy mala higiene. La expresión indirecta del óxido nítrico varió de 13,34 hasta 257. El óxido nítrico no presentó asociación con otros parámetros, hubo gran variabilidad de los valores. Se necesitan más estudios, en particular, el potencial de este indicador para la detección precoz de las enfermedades bucodentales.

DESCRIPTORES

Óxido nítrico
Higiene bucal
Quimioterapia
Atención de enfermería

[1] RN. Full Professor, University of São Paulo at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil. ecdcava@usp.br [2] RN. Associate Professor, University of São Paulo at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil. carnioec@eerp.usp.br [3] Dentist. PhD Student in Clinical Medicine of University of São Paulo at Ribeirão Preto Medical School. Ribeirão Preto, SP, Brazil. vivikhouri@yahoo.com.br [4] RN. PhD Student of University of São Paulo at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil. carolg@usp.br [5] Statistician. Associate Professor, University of São Paulo at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil. cbsantos@eerp.usp.br [6] Dentist. M.Sc. Researcher, Nursing and Communication Group, University of São Paulo at Ribeirão Preto College of Nursing. Ribeirão Preto, SP, Brazil. maripace@eerp.usp.br

Português / Inglês
www.scielo.br/reeusp

Received: 04/09/2012
Approved: 06/15/2012

INTRODUCTION

The clinical evaluation of patients' oral cavities has been a challenge to health teams. In patients undergoing hematopoietic stem cell transplantation (HSCT), this evaluation represents a crucial component of care and an interdisciplinary approach is valued because published studies[1-2] found high frequencies of complications and discomfort, including oral mucositis, in patients who underwent HSCT. This fact justifies the recommendations regarding the need to prevent and note the occurrence of this inflammation process, as well as the need to include this knowledge in undergraduate health care curricula, especially in nursing.

This clinical evaluation includes extra- and intra-oral examinations, the assessment of the oral mucosa, the condition of teeth and prostheses, the need for immediate dental treatment, the presence of prostheses and the evaluation of oral hygiene and related instructions.

In the literature, criteria are highlighted for the examination of lesions (presence, condition, location and types) and affected structures. There are criteria for both extra-oral examination, such as those of the World Health Organization (WHO)[3], and intra-oral examination to determine tooth condition and number and the hygiene level[4]. In epidemiological oral health surveys, the *Decayed, Missing, and Filled Teeth* (DMFT index) and the Simplified Oral Hygiene Index (OHI-S index) is used for permanent teeth. This index represents the proportion of decayed, missing and filled teeth. It is the most widely applied index around the world and remains a basic reference point for the diagnosis of dental conditions and the formulation and assessment of oral health programs.

In epidemiological oral health surveys, the Decayed, Missing, and Filled Teeth (DMFT index) and the Simplified Oral Hygiene Index (OHI-S index) is used for permanent teeth.

Oral hygiene assessments can also be performed using the Simplified Oral Hygiene Index - OHI-S, which is used to indicate the extent of residues (biofilms) on representative tooth surfaces. The OHI-S consists of the Simplified Debris Index (DI-S) and the Simplified Calculus Index (CI-S). Both indices can be used individually, but when combined, they make up the OHI-S. Hygiene can be considered satisfactory (a score from 0 to 1), typical (1.1 to 2), deficient (2.1 to 3) or very poor (3.1 to 6)[4].

Another oral condition assessment guide is the BRUSHE[5], the name of which is based on the terms bleeding, erythema or plaque, ulceration, saliva, halitosis, external and debris factors. Although recommended for intensive care units (ICUs), this guide can be useful in any care setting.

In some individuals, however, such as patients who develop mucositis after chemotherapy, oral changes are not always identified during their initial or preclinical phases. Therefore, we intended to determine, for these patients and in this context, whether oral health could be assessed using an indirect measure of the nitric oxide (NO) level in saliva because the role of NO in the pathogenesis of oral and periodontal diseases has been analyzed.

When present at low and controlled concentrations, this gas plays a relevant role in biological systems[6]. One of these roles is as a potential bactericide: the production of NO in the gastrointestinal tract has a defensive role in organisms. Neutrophils play a relevant role in the oral cavity mucosa and spontaneously produce NO (without any stimulus). This free radical is part of the defense system against infections and is synthesized through the conversion of L-arginine into L-citrulline during NO synthesis. It affects the proliferation, differentiation and apoptosis of different cell types involved in the healing of lesions [7].

The presence of excessive free radicals in the saliva can favor the occurrence of oral mucosa lesions[6]. Excess NO can contribute to tissue destruction in patients with periodontitis, and higher levels of NO have been found in inflamed periodontal tissue[8].

It is also hypothesized that NO is active in the regulation of saliva secretion, with high salivary NO production levels in individuals with oral mucosal disease[9]. An NO synthesis inhibitor can be useful, especially for the treatment of diseases related to the salivary glands and of some oral mucosal diseases, because these inhibitors favor increased salivation and act as a physiopathological regulator[6]. It should be noted that saliva plays a relevant role in oral health due to its flow, capacity, activity/microbial effects and lubricating effects, among other activities[10-11].

NO is relatively unstable in the presence of oxygen and rapidly autoxidates, making its concentration difficult to measure. The indirect determination of the NO concentration based on the concentration of nitrate has been used successfully[12]. Findings involving salivary NO levels in physiologically normal mucosa and oral mucosal lesions prompted the use of this parameter in this study, which aimed to determine whether clinical oral cavity assessment indicators are associated with the NO concentration determined indirectly using the nitrate concentration in patients with oncologic and hematologic diseases before the start of intravenous chemotherapy.

METHODS

This observational study received approval from the institution's Research Ethics Committee (Protocol 8329/2009), in compliance with ethical requirements. The subjects were patients who were hospitalized during the first semester of 2010 in a clinical unit for patients with oncologic and hematologic diseases at a school hospital in the

interior of São Paulo State. Patients were being assessed prior to starting chemotherapy. They had platelet levels of 20,000 or higher and neutrophil counts of 1,000 or more. In addition, they did not have oral or nasal tubes or catheters, and had a clinical condition that allowed the use of oral hygiene procedures. All subjects received oral hygiene materials (surgical toothbrush, toothpaste containing fluoride and a case in which to store the materials), donated a saliva sample (non-stimulated saliva collection)[13] and were submitted to clinical oral cavity examinations.

The saliva was collected in the morning, before the patients ate and after the oral hygiene process. Each sample was collected in a sterile flask for organic material, covered, stored on ice in a Styrofoam box until transportation to the Physiology Laboratory at EERP-USP and stored in a freezer at -20º C. Then, 1 ml of saliva from each sample was diluted in 4 ml of distilled water and centrifuged. The NO/ozone chemiluminescence technique was used. A script[3] was used to evaluate the oral condition (DMFT) and the level of oral hygiene (OHI-S), and an instrument was used to record sociodemographic data, the diagnosis and treatments.

The data were imported into Statistical Package for Social Sciences (SPSS), version 17.0, and analyzed descriptively. Statistical tests were applied, with significance set at 0.05 ($\alpha = 0.05$). For categorical variables, Fisher's exact test was used, and for quantitative variables, the Kolmogorov-Smirnov was used test to check for the normal distribution of sample means. Student's t-test, Mann-Whitney and Spearman's correlation were also used.

RESULTS

The 20 subjects, ten men and ten women, were patients between 22 and 65 years of age. Sixteen patients were white (80%), three were mulatto (15%), and one was black (5%). Fifteen percent were unemployed, 15% were retired, and 15% were housewives. The following occupations stood out: agricultural worker (5%), hairdresser (5%), operations manager (5%), truck driver (5%), kindergarten aid (5%), bricklayer (5%), teaching aid (5%), clerk (5%), teacher (5%), automotive painter (5%) and independent/retired (5%).

Four patients indicated that they used tobacco or twist tobacco. None of the patients reported a drinking habit. The following medical diagnoses were identified: acute myeloid leukemia (1), acute myeloid leukemia with the t(8;21) translocation (1), acute promyelocytic leukemia (1), M3 acute myeloid leukemia (1), acute lymphocytic leukemia (1), pro-B acute lymphocytic leukemia (1), B-cell prolymphocytic leukemia (1), non-Hodgkin Lymphoma (3), mantle-zone non-Hodgkin lymphoma (2), marginal-zone non-Hodgkin lymphoma (1), multiple myeloma (3), Hodgkin lymphoma (1), splenic relapse of Hodgkin's lymphoma (1), Burkitt lymphoma (1) and anaplastic large T ALK + cell lymphoma (1).

Oral condition: In the clinical evaluation, 50% of subjects had no dental lesions, traumas or infections (Table 1). The following abnormalities were observed in the other subjects (50%): a dental infection (15%), sores (10%), gingivitis (5%), traumatic lesions (15%) and the joint occurrence of a traumatic lesion and an infection (5%). Twenty-five percent of the subjects had prostheses, 10% of which were fixed, 10% partial and 5% full superior. The sample distribution was homogeneous with regard to the oral condition based on the presence or absence of lesions (p=1/Fisher's exact test).

The subjects were also evaluated with using the DMFT index. These evaluations revealed an average of four decayed teeth (median=2 decayed teeth, SD=5, minimum=0 decayed teeth, maximum=16 decayed teeth) and seven missing teeth (median=4 missing teeth, SD=8, minimum=0 missing teeth, maximum=26 missing teeth).

Oral Hygiene: Using the OHI-S, hygiene was considered predominantly satisfactory (35%) or typical (35%); deficient and very poor hygiene conditions were also observed (30%). The median OHI-S score was 1.58 (mean=1.58, SD=1.03, minimum=0.16, maximum=4). Given the relevance of this parameter for these patients, from a clinical viewpoint, the deficient and very poor scores were considered undesirable; hence, oral hygiene was considered unsatisfactory in 30% of participants (Table 1).

Table 1 - Distribution of subjects according to oral condition and oral hygiene - Ribeirão Preto, 2010

	Oral condition in subjects without injuries or traumas	Oral condition in subjects with injuries or traumas	Total
Satisfactory or typical hygiene	7	7	14
Deficient or very poor hygiene	3	3	6
Total	**10**	**10**	**20**

Oral Hygiene and Condition

For the OHI-S, the mean score of the 14 subjects with a satisfactory/typical OHI-S score was 1.06 (SD=0.64, minimum=0.16, maximum=2.0, median=1.07). Among the seven subjects in this group who did not have oral lesions or traumas, the values were as follows: median=0.83, mean=1.05, SD=0.72, minimum=0.16 and maximum=2 (p=0.958/ Kolmogorov-Smirnov test). In the group with lesions and traumas, the values were as follows: mean=1.09, minimum=0.33, maximum 1.83, SD=0.63 and median=1.32 (p=0.751/ Kolmogorov-Smirnov). No significant difference between these two groups was found with respect to the mean OHI-S score (p=0.914/t-test).

Among the six subjects with a deficient/very poor mean OHI-S score, the values were as follows: mean=2.80, minimum=2.16, maximum=4.00, SD=0.69 and median=2.74. For the three subjects in this group without

lesions or traumas, the values were as follows: mean=2.87, minimum=2.13, maximum=4.00, SD=0.99 and median=2.49. For the three subjects in this group with lesions or traumas, the values were as follows: mean OHI-S score=2.72, SD=0.48, minimum=2.16, maximum=3.00 and median=3.00. No statistically significant difference was found between the groups with respect to the median OHI-S score (p=0.825/Mann-Whitney).

Regarding the oral condition, for the ten subjects without oral traumas or injuries, the mean OHI-S score was 1.60 (SD=1.16, minimum=0.16, maximum=4.0, median=1.65). This group had a normal distribution with respect to the different levels of hygiene, (p=0.983, Kolmogorov-Smirnov test). Similarly, among the ten subjects with abnormal oral conditions (lesions and traumas), the mean OHI-S score was 1.58 (SD= 0.97, minimum=0.33, maximum=3.00, median=1.58, p=0.940, Kolmogorov-Smirnov test). No statistically significant difference was observed between the mean OHI-S score of the two groups (ten subjects with lesions or traumas and ten subjects without lesions or traumas; p=0.970/t-test). Regarding the assessment of the oral condition, variations in the satisfactory/typical oral hygiene indices were observed in the group without lesions and traumas and in the group with these alterations.

Nitric Oxide

The indirectly determined levels of salivary NO in the study subjects were as follows: mean= 95.92, minimum= 13.34, maximum= 268.96 and mean= 50.11.

Oral Condition and Nitric Oxide

Among the ten subjects without oral lesions or traumas, the mean NO level was 133.36 (minimum=19.42, maximum=268.96, median=114.34, SD=104.16, p=0.686/ Kolmogorov Smirnov). Similarly, among the ten subjects with abnormal oral conditions, i.e., with lesions or traumas, the mean NO level was 58.49 (minimum=13.34, maximum=170.25, median=49.5, SD=43.83, p=0.155/ Kolmogorov Smirnov).

The differences in mean NO levels in relation to the oral condition were not statistically significant (p=0.058/ t-test). Clinically, however, higher NO levels were observed in the first group. These findings may be due to the small number of study subjects, resulting in a low statistical test power.

Oral Hygiene (OHI-S) and Nitric Oxide

The 14 subjects with satisfactory/typical OHI-S scores (70% of the sample) had a mean salivary nitric oxide level of 110.97 (minimum=19.42, maximum=268.96, median=51, SD=94.59). Among the participants with unsatisfactory OHI-S scores (deficient/very poor, 30% of the sample), the mean nitric oxide level was 60.80 (minimum=13.34, maximum=170.25, SD=56.68).

When the association between the OHI-S score and the nitric oxide level was assessed, no associations were observed (p= 0.88/Spearman); i.e., there was no linear correlation, as shown in Figure 1.

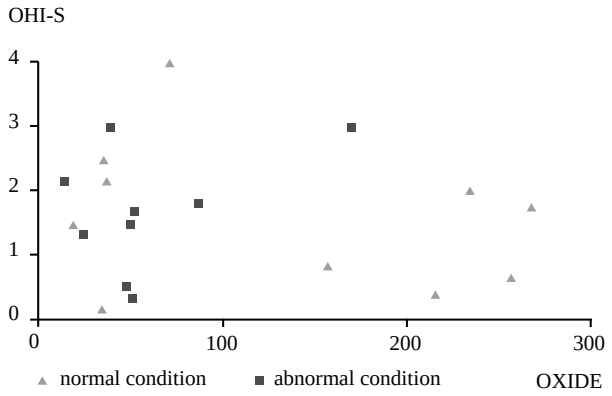

Figure 1 - Scatter plot of the nitric oxide level (OXIDE) vs. the Simplified Oral Hygiene Index (OHI-S) score, which respects the subjects' oral condition

Correlations among Oral Condition, Nitric Oxide and Oral Hygiene

For the ten subjects without oral lesions or traumas, the mean NO level was 133.37 (minimum=19.42, maximum=268.96, median=114.34, SD=104.16, p=0.686/ Kolmogorov-Smirnov test). Seven of them (70%) had a satisfactory/typical OHI-S score, and the mean NO level for these seven patients was 170.21 (SD=104.19, minimum=19.42, maximum=268.96). The other three, who had unsatisfactory OHI-S scores (deficient or very poor), had a mean NO level of 47.37 (SD=20.25, minimum=34.69, maximum=70.73, median=36.70). No statistically significant differences were found with respect to the mean NO levels in the group of patients without oral condition alterations between those with satisfactory/typical OHI-S scores and those with deficient/very poor OHI-S scores (p=0.210/ Mann Whitney).

Regarding the OHI-S score, the ten subjects with abnormal oral conditions (presence of lesions or traumas) had a mean NO level of 74.24 (minimum=13.34, maximum=170.25, median=49.5, SD=43.83, p=0.058 (t-test)); the differences between the groups with distinct OHI--S scores were not statistically significant. Seven (75%) of them had satisfactory/typical oral hygiene levels, and the mean NO level for these seven patients was 51.73 (SD=18.57, minimum=24.15, maximum=87.60, median=49.74). Three patients had non-satisfactory oral hygiene levels and a mean NO level of 74.24 (SD=84.14, minimum=13.34, maximum=170.25, median=39.13). The mean NO levels in the group with altered oral conditions were different between the patients with satisfactory/ typical OHI-S scores and those with deficient/very poor OHI-S scores, but this difference was not statistically significant (p=0.569/ Mann-Whitney).

No significant differences were found with respect to the median NO level for subjects with satisfactory/typical OHI-S scores between those subjects with and without lesions or traumas (p=0.142/Mann Whitney). When the difference in the means between the groups with and without oral alterations was evaluated, the T-test indicated that there was a higher mean NO level in the group without oral traumas or lesions and with satisfactory or typical hygiene (p=0.023).

When the median NO levels for subjects with deficient or very poor OHI-S scores were analyzed, no differences were found between the groups with and without lesions or traumas (p=0.827/ Mann Whitney).

Tobacco use has an effect on the NO level. Out of the four subjects who indicated a past smoking habit, three had typical OHI-S scores and deficient hygiene levels; however, no alterations (lesions or traumas) were found when examining the smokers' oral conditions. The mean NO level for smokers was 140.19 (SD=130.38, minimum=19.42, maximum=268.96, median=136.19, p=0.831/ Mann Whitney), and there was no statistically significant difference with respect to other subjects in the group without oral lesions or traumas (mean=128.82, SD=96.27, median=114.34, minimum=34.69 and maximum=257.88). In comparison with the non-smoking patients in the sample, whose mean NO level was 84.86 (SD=74.02, minimum=13.34, maximum=257.88, median=50.30, p=0,705/Mann Whitney), no statistically significant differences were observed between the median values, although smoking subjects' NO levels were higher.

DISCUSSION

Among the subjects, 30% had high NO levels, above 150. One of them reported a history of smoking, was missing most teeth, had an infection in one tooth, had a traumatic lip injury, used an implant and was consuming a predominantly liquid oral diet. Three others were had received chemotherapy previously. One patient had a neutrophil count of 1000, and another had a fever and seven missing teeth. Five patients were diagnosed with lymphoma and one with leukemia. Among the subjects with high NO levels, the majority were immunosuppressed.

Various factors can lead to variations in the NO level; for example, diet contributes to NO production. A diet rich in vegetables (nitrates) plays a protective role against oral and gastric lesions. Cigarettes are rich in nitrites, which organisms can rapidly absorb and eliminate through urine or even saliva[10]. NO production increases during the formation of dental plaque, and cigarette use inhibits the defense against bacterial proliferation[14]. Bacteria also produce NO, and the oral flora is very rich and diversified.

The presence of excessive free radicals in patients' saliva can enhance the occurrence of oral mucosa lesions[6]. In addition, excessive NO contributes to tissue destruction in individuals with periodontitis. Saliva contains a range of inflammatory mediators, including cytokines, enzymes, growth factors and hormonal factors, that can change the NO level by inhibiting or potentiating its expression[15].

When the median NO levels in subjects with deficient or very poor OHI-S scores were examined, no difference was found between the groups with and without lesions or traumas. In a study that indirectly determined the NO levels in patients with implants, higher NO levels were observed in patients whose healing process did not involve any lesions[16].

This study contributes to the body of research investigating[16] the association between oral care and physiological clinical indicators. Large variations in the NO level were found. The clinical conditions, medications used, level of immunodeficiency, history of tobacco use and the type of diet before the examination, all variables that could not be controlled for in the study, may have interfered with the described results. Studies that control for these variables are recommended.

CONCLUSION

The OHI-S, the DMFT and the assessment instrument for traumas, lesions and dental infections were adequate to characterize the oral conditions of the patients.

Great variation was found in the determined NO levels. Significant differences were found between the mean NO levels of subjects with satisfactory/typical hygiene conditions and the mean NO levels of both individuals with lesions or traumas and patients with good oral health. The highest levels were found in patients without oral lesions or traumas and with satisfactory/typical oral hygiene.

Variables that could not be controlled for in the study, the sample size and the use of convenience sampling, without estimates of the statistical power, may have interfered with the described results.

The indirect NO measurements in this study exhibited no association with the OHI-S score in the assessment of oral health. Further research is recommended, and future studies should include more participants and should determine the typical NO levels of healthy patients.

Oral evaluation is a relevant part of a patient's physical examination, especially in clinical situations in which the oral or hygiene conditions will be altered, such as when patients use chemotherapy or have mucositis. Identifying or validating indicators that support this assessment is essential for nursing, particularly for the patients under analysis, who presented with indications for the preliminary assessment of oral cavity conditions. Further research can increase our knowledge of NO levels, which can serve as a predictive indicator of oral lesions in patients with mucositis.

This study exemplifies the use of joint interdisciplinary patient assessments, and the different views will further the use of preventive and educational interventions for patients who will undergo chemotherapy or treatment changes, when necessary, with a view to greater patient safety.

REFERENCES

1. Gondim FM, Gomes IP, Firmino F. Prevenção e tratamento de mucosite oral. Rev Enferm UERJ. 2010;18(1):67-74.
2. Ferreira P, Gamba MA, Saconato H, Gutiérrez MGR. Tratamento da mucosite em pacientes submetidos a transplante de medula óssea: uma revisão sistemática. Acta Paul Enferm. 2011;24(4):563-70.
3. World Health Organization (WHO). Oral health surveys, basic methods. 4th ed. Geneva; 1997.
4. Green RM, Vermillion JR. The simplified oral hygiene index. J Am Dent Assoc. 1964;68(1):7-13.
5. Abidia RF. Oral care in the intensive care unit: a review. J Contemp Dent. 2007;8(1): 1-2.
6. Sunitha M, Shanmugam S. Evaluation of salivary nitric oxide levels in oral mucosal diseases: a controlled clínical trial. Ind J Dent Res. 2006;17(3):117-20.
7. Luo J, Chen AF. Nitric oxide: a newly discovered function on wound d healing. Acta Pharmacol Sin. 2005;26(3):259-64.
8. Ugar-Çankal D, Nurdan O. A multifaceted molecule, nitric oxide in oral and periodontal diseases. Clin Chim Acta. 2006;366(1-2):90-100.
9. Ohashi M, Iwase M, Nagumo M. Elevated production of salivary nitric oxide in oral mucosal diseases. J Oral Pathol Med. 1999;28(8):355-9.
10. Sato EF, Choudhury N, Inoue M. Dynamic aspect of reactive oxygen and nitric oxide in oral cavity. J Clin Biochem Nutr. 2008;42(1):8-13.
11. Pace MA, Watanabe E, Facetto MP, Andrade D. Staphylococcus spp. na saliva de pacientes com entubação orotraqueal. Rev Panam Infectol. 2008;10(1):8-13.
12. Marchi-Alves LM, Carnio EC. Is there any correlation between insulin resistance and nitrate plasma concentration in white coat hypertensive patients? Cardiol Res Pract. 2009;24:376-82.
13. Davies NA, Broadley K, Beighton D. Salivary gland hypofunction in patients with advanced cancer. Oral Oncol. 2002;38(7):680-5.
14. Carossa S, Pera P, Doglio P, Lombardo S, Colagrande P, Brussino L, Rolla G, Bucca C. Oral nitric oxide during plaque deposition. Eur J Clin Invest. 2001;31(10):876-9.
15. Rocha FMS, Siqueira CS, Rocha FSR, Moura CCG, Souza MA, Barbosa DZ. Análise dos níveis de óxido nítrico na saliva de pacientes desdentados totais reabilitados com implantes. Horiz Cient. 2010;4(2):1-20.
16. Lacerda RA, Nunes BK, Batista AO, Egry EY, Graziano KU, Angelo M, et al. Evidence-based practices published in Brazil: identification and analysis of their types and methodological approches. Rev Esc Enferm USP [Internet]. 2011 [cited 2011 Nov 22];45(3):777-86.

Research funded by CNPq

Correspondence addressed to: Emilia Campos de Carvalho
Av. Bandeirantes, 3900 - Monte Alegre
CEP 14040-902 - São Paulo, SP, Brazil