

TITLE: FACTORS OF VIRULENCE OF GRAM NEGATIVE BACILLI ISOLATED FROM ORAL CAVITY OF HEAD AND NECK CANCER PATIENTS AND EFFECTS OF ARTIFICIAL SALIVA IN VITRO AND IN VIVO

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ABSTRACT: Head and neck cancer (HNC) is multifactorial and oral microbioma may contribute to the development of oral infections, systemic infections and carcinogenesis. Microbial control may be important during immunosuppression and hyposalivation post-radiotherapy. **This study aimed:** to evaluate the frequency of Gram negative Bacilli (GNB) in saliva from HNC-active patients (n=15), post-radiotherapy patients (n=30) and healthy individuals of control group (n=20); to analyze the main virulence factors of oral GNB isolated from HNC-active patients and to validate the use of artificial saliva for the control of the pathogenic microbiota and for treatment of hyposalivation post-radiotherapy. GNB were quantified by culture methods and serial dilutions of saliva, using Cetrimide and MacConkey Agar. A total 37 GNB isolated from saliva of 10 HNC-active individuals were genotyped by RAPD-PCR using OPA-02 and (GTG)₅ primers. A total 24 genotypes were characterized for resistance to 7 antibiotics by Kirby-Bauer test. The production of gelatinase, phospholipase and nitrite was detected in media containing gelatin, egg and nitrate, respectively. The in vitro antimicrobial spectrum of the artificial saliva was evaluated, spectrophotometrically, against 46 clinical isolates of GNB, *Staphylococcus*, *Streptococci* group mutans, *Lactobacilli* and *Candida* species. In addition, the benefits in relation to use of artificial saliva was analyzed by validated questionnaire. GNB were predominant in HNC-active and post-radiotherapy patients, in comparison of healthy individuals (Mann-Whitney, p<5%). In GNB, there was the frequency of 28% of multiple antibiotic resistance bacilli, 16.67% of phospholipase production strains and 25% of gelatinase production strains. There was high frequency of nitrite production genotypes (84.62%), which is a precursor of carcinogenic nitrosamines. Artificial saliva had broad antimicrobial spectrum in vitro against oral clinical isolates. Clinically, there were improvements in dysphagia, mastication and phonation, after the use of artificial saliva by 19 voluntaries. In conclusion, there is a high incidence of pathogenic GNB, in saliva of HNC-active and post-radiotherapy patients in relation to control. Due to virulence factors, these pathogens can cause local infections, metastatic infections and can influence in the carcinogenesis process. The artificial saliva can contribute for oral microbial control and for oncologic patients' life quality.

Keywords: head and neck neoplasms, radiotherapy, artificial saliva, hyposalivation, microbiota

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