Correlation between number of dental amalgam restorations and severity of oral mucositis after head-neck radiotherapy

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Abstract – Background: Head and neck radiotherapy causes side effects such as stomatitis. In vitro studies demonstrated local dose enhancement due to backscatter radiation near metal restorations. The aim of this study was to analyze correlation between number of amalgam restorations with severity of oral mucositis in patients with head and neck radiotherapy.

Method and materials: This cross-sectional study was accomplished on 80 patients under head and neck radiotherapy referred to Cancer Institute (Tehran, Iran) in 2014–2015. Severity of mucositis and pain were measured by three examinations according to WHO criteria and visual analogue scale. Descriptive statistics and Spearman’s correlation coefficient test used to analyze the data by IBM SPSS statistics V22.0.

Results: There was no significant correlation between the number of amalgam restorations and severity of mucositis and pain on second and third examinations. However, severity of mucositis and pain were found to be significantly correlated with radiation dose per session (p = 0.013, rs = 0.276), (p = 0.032, rs = 0.240) and total radiation dose (p < 0.001 rs = 0.393), (p < 0.001, rs = 0.445) on second and third examinations respectively.

Conclusion: This study showed that number of dental amalgam restorations have no impact on aggravation of oral mucositis caused by head and neck radiotherapy.

Introduction

Oral mucositis is a side effect of head and neck radiotherapy [1], and is described as an inflammation, erythema, ulceration and finally pseudo membrane formation in the oral mucosa [2]. Due to severe oropharyngeal pain caused by mucositis it is necessary to take analgesic drugs [3,4]. Mucositis may also reduce quality of life arising from oral pain, bleeding, dysphagia, infections, anorexia, impairment of liquid and food intake, which eventually leads to severe weight loss, dehydration, and in severe cases, hospitalization [4].

Mucositis is very important due to its high prevalence [5]. The incidence of oral mucositis caused by head and neck radiation varies from 80% to 97% [6]. The severity of radiation-induced oral mucositis is dependent on age, gender, fraction size, radiation portals, fractionation, concurrent chemotherapy, type of cancer, type and location of radiotherapy, radiation dose per session and total radiation used [7,8]. One of the factors that may be related to the frequency and severity of oral mucositis is the number of metal restorations and other non-removable metal components in the mouth [9].

There is not enough information about the effect of metal restorations on the occurrence of oral mucositis after head and neck radiotherapy [8]. In addition, few clinical studies addressing this field accomplished so far. Prevention and management of mucositis are dependent to detection of predisposing factors; hence, we decided to conduct a clinical study to determine the correlation between the number of amalgam restorations and the number of quadrants containing amalgam restorations with the severity of oral mucositis induced by head and neck radiotherapy.

Methods and materials

This cross-sectional study was accomplished on 80 consecutive patients under head and neck radiotherapy referred to Cancer Institute of Imam Khomeini Hospital (Tehran, Iran) in 2014–2015. Inclusion criterion was patients...
undergoing head and neck radiotherapy. Edentulous patients, those having fixed or removable prosthesis, orthodontic brackets, metallic restorations except dental amalgam, mandibular plates and other metallic intra osseous components were excluded from the study. All patients were examined every week during their course of radiotherapy, but the severity of mucositis and pain were measured on three occasions. The first visit was performed on the first week of radiotherapy and data such as age, sex and number of amalgam restorations were recorded. The second visit accomplished on the middle of radiotherapy course, and the third visit was done on the last week of radiotherapy or the week after finishing radiotherapy. On each examination degree of mucositis was determined clinically according to WHO criteria (grade 0: no complaint. grade 1: mild soreness and erythema. grade 2: painful erythema, edema and ulcers, able to eat solid foods. grade 3: painful erythema, edema and ulcers, unable to eat solid but able to eat liquid foods. grade 4: unable to eat any food and need to intravenous feeding) [10].

In addition, the severity of pain was measured on each examination by means of a 100-cm visual analog scale (VAS). The patients were requested to describe their pain intensity by selecting a number between 0 and 100. The severity of pain was divided into three levels as: mild pain: 0 ≤ VAS < 30, moderate pain: 31 ≤ VAS ≤ 69 and Sever pain: 70 ≤ VAS ≤ 100 [11].

Information regarding total radiation dose and radiation dose per session were retrieved from patient’s medical records. All patients were recommended to rinse their mouth by water regularly and use a soft, high protein, high calorie and non-irritating diet. Meanwhile, patients with stomatitis were prescribed mouthwash chlorhexidine 0.2% or nystatin suspension 100,000 u/mL in case of oral candidiasis according to already approved treatment protocols at Cancer Institute. Meanwhile, all potential sources of dental infection had to be removed or treated accordingly before starting radiotherapy [12].

To determine correlation between frequency and severity of mucositis and pain with number of amalgam restorations, radiation dose per session and total radiation dose, spearman correlation coefficient was used. Data were analyzed by IBM SPSS statistics V22.0.

### Ethical considerations

All participants of this study signed informed consent forms and their data kept confidential. This study was approved by research deputy of Shahid Beheshti Dental School with the code of ethics IR.SBMU.RIDS.REC.1394.3363.

### Results

In this study 80 consecutive patients under head and neck radiotherapy referred to Cancer Institute of Imam Khomeini Hospital (Tehran, Iran) including 39 women (48.75%) and 41 men (51.25%) with an average age of 38 years and ranging between 6 and 81 years were examined.

Fifteen patients (18.8%) were under chemotherapy simultaneously and 65 others (81.2%). Out of 80 patients, 76 (95%) were under compact radiotherapy and 4(5%) received various radiotherapy.

All patients had mucositis at least in one examination, and the frequency of mucositis was estimated 100% in the entire period of radiotherapy. Relative frequency for mucositis in 3 examinations is shown in Table I. According to Table I, on the first, second and third examination the relative frequency of mucositis was 72.5%, 97.5% and 98.8% respectively.

Thirty-six patients (45%) had no amalgam restorations, 11 patients (13.8%) had just one, 13 patients (16.3%) had amalgam restorations in one quadrant, 9 patients (11.3%) in two quadrants, 15 patients (18.8%) in three quadrants and 7 patients (8.8%) in four quadrants. The range of number of amalgam restorations were between 1 and 11 with the mean of 2.

Radiation dose per session was 200 cGy for 61 patients (76. 3%). Total radiation dose was 6000 cGy for 31 patients (38.8%) and 7000 cGy for 11 patients (13. 8%). The range of radiation dose was between 1800 and 7000 cGy with an average of 5498 cGy.

On first examination, 60 patients (75%) had pain, with the maximum pain severity of 60 (VAS).

On second examination, 78 patients (97.5%) had pain, with the maximum pain degree of 93. On third examination, all patients had pain, with maximum pain intensity of 95.

The relative frequency of pain severity in three examinations is presented in Table II.

The correlation between mucositis and pain with radiation dose and number of amalgam restorations is shown in Table III.

According to Spearman correlation coefficient, a significant and positive correlation was found between severity of mucositis and degree of pain on three examinations ($p < 0.0001$, $r_s = 0.878$), ($p < 0.0001$, $r_s = 0.953$) and ($p <0.0001$, $r_s = 0.940$).

Moreover, Spearman’s correlation showed a significant and positive correlation between radiation dose per session and both degree of pain and mucositis on first examination; however, no significant correlation between total radiation dose and severity of pain and mucositis was found. On second

### Table I. Relative frequency of mucositis on three examinations.

<table>
<thead>
<tr>
<th>Grade of mucositis</th>
<th>First examination</th>
<th>Second examination</th>
<th>Third examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>22</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>50</td>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>24</td>
<td>30</td>
</tr>
</tbody>
</table>

### Table II. Correlation between radiation dose per session and mucositis.

<table>
<thead>
<tr>
<th>Radiation dose per session</th>
<th>Mucositis frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 cGy</td>
<td>0.940</td>
</tr>
<tr>
<td>6000 cGy</td>
<td>0.953</td>
</tr>
<tr>
<td>7000 cGy</td>
<td>0.960</td>
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</tbody>
</table>

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<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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</tr>
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and third examinations a significant and positive correlation between the degree of mucositis and severity of pain and with radiation dose per session and total radiation dose was found. However, Spearman’s correlation showed no significant correlation between degree of mucositis and pain with number of amalgam restorations on both second and third examinations.

**Discussion**

This study investigated the frequency and severity of oral mucositis and pain induced by head and neck radiotherapy as well as the correlation between severity of oral mucositis and pain with number of amalgam restorations. In addition, correlation between severity of mucositis and radiation dose per session and total radiation dose was evaluated. Contrary to other studies which were carried out in vitro, this study was performed in vivo and clinically in patients.

The results showed mucositis developed in all patients at least in one examination, and mucositis frequency was 100% in the whole period of radiotherapy. According to several previous studies, the prevalence of mucositis was reported over 80% which was similar to the present study [2–5,7,10,13–23]. The frequency of mucositis in all reviewed studies was consonant with the present study, but some disparities in results might be due to differences in population, diagnostic criteria for mucositis severity and the radiotherapy protocol.

Vera-Lionch studied variables such as age, sex, weight, alcohol and tobacco consumption, primary site, type and the stage of cancer, radiation dose, type of radiotherapy, concurrent chemotherapy and degree of mucositis in 450 patients undergoing head and neck radiotherapy and the overall incidence of mucositis was 83% [15].

Linda S Elting studied 2 groups of patients including 126 patients with oral or oropharyngeal cancer, and 65 patients with laryngeal or hypopharyngeal cancer. The results of this study were the most similar ones to ours in terms of frequency of mucositis (99% vs 100%). The intensity and frequency of mucositis and pain, the impact of mucositis on weight loss and quality of life, the use of analgesics and other treatments were investigated in this study. The risk of mucositis in this study was 99% in patients with oral or oropharyngeal cancers and 98% in patients with laryngeal or hypopharyngeal cancer [17].

A review study determined risk factors related to both patients and radiotherapy method. Risk factors related to patients included: location of tumor, age, oral health, nutritional status, functional status of kidneys and liver, and risk factors associated to radiotherapy were reported radiation patterns, portal radiations and radiation dose. The prevalence of mucositis was above 90% [7].

There was a significant and positive correlation between radiation dose per session and severity of mucositis and pain on first examination in the present study. Whereas no significant correlation was found between total radiation dose and severity
of mucositis and pain in the first examination. The reason was probably due to receiving lower total radiation dose on first examination, which was cumulated on second and third examinations, as one study showed that the first signs of mucositis in patients with head and neck radiotherapy would appear after 10 Gy and severe signs would occur after 30 Gy [10]. On the other hand, radiation causes destruction of cellular structures and vascular changes, therefore increasing radiation dose lead to more intensity of oral mucositis and pain [6,13]. That is why, on second and third examinations a significant and positive correlation was demonstrated between severity of mucositis and pain with both radiation dose per session and total radiation dose.

In a study on 326 patients, it was shown that severe oral mucositis was associated with different risk factors and 136 (41.7%) patients had grade 3 mucositis. Moreover, male sex, oropharyngeal cancer, low hemoglobin levels, low leukocytes or lymphocytes, concurrent chemotherapy, and oral feeding were shown to be significantly associated with a higher frequency of severe oral mucositis [23].

These studies investigated lots of variables but none of them investigated the effect of amalgam restorations on severity and frequency of mucositis. The present study, showed no correlation between the number of amalgam restorations with severity and frequency of oral mucositis after head and neck radiotherapy.

Obviously, oral cavity as a vital and physiological environment with vascular circulation is different from in-vitro conditions such as a phantom head. Hence, our results are not comparable with previously mentioned studies accordingly. In addition, in the present study patients were examined repeatedly and any erythema or infection in the oral cavity were detected and treated immediately.

Few experimental in vitro studies investigated dose distribution and enhancement near different dental materials such as:

- Chin revealed that additional radiation was absorbed by water which caused radiation attenuation. This study tested, dose distribution by radiotherapy near 23 dental materials and reported 2% dose enhancement adjacent to amalgam and also found that increased distance from metal restorations led to decreased radiation distribution [24].

- Kinhikar described the effect of mandibular titanium plates and screws on dose enhancement and showed 10% radiation dose enhancement. This study didn’t evaluate radiation dose enhancement near amalgam [25].

- Serichetaphongse evaluated back- and forward-scattered doses from nine contemporary dental materials and revealed that atomic number and density of materials have a direct relationship with backscattered dose and an inverse relationship with forward-scattered dose [26].

One study showed that radiation dose distribution is dependent on both dental material and electron beam energy. Amalgam and higher energy showed the most dose distribution [27]. As present study indicated there was a significant and positive correlation between radiation dose per session and total radiation dose and severity of mucositis and pain, but there was not any correlation with amalgam restorations.

An in vitro study showed the highest back scattering radiation for Ni-Cr alloy and the lowest for ceramics [28]. Another in vitro study reported the effect of metal-containing topical agent on surface dose enhancement during radiotherapy. The results showed no significant difference in surface dose enhancement between metal containing topical agent and nonmetal-containing topical agent in each thickness [29].

All of previous studies were done in vitro, which justifies the difference between our results and previous ones. Vital oral environment, vascular circulation and healing ability of oral tissue and also capability of saliva to absorb radiation lead to different results in our study [24].

**Conclusion**

Although, the degree of mucositis and severity of pain were correlated with radiation dose; the number of amalgam restorations had no impact on frequency and severity of oral mucositis in patients under head-neck radiotherapy.

**Conflict of interest**

There was no conflict of interest in this manuscript.

**Funding**

The full cost of the study was paid by the authors.

**Ethical approval**

This study was approved by research deputy of Shahid Beheshti Dental School with the code of ethics IR.SBMU.RIDS. REC.1394.3363.

**Informed consent**

All participants of this study signed informed consent forms and their data kept confidential.

**Authors contribution**

Maryam Baharvand designed the method and edited the manuscript. Marzieh Alimohammadi as a co responder performed an oral examination, searched for related articles, designed tables and now she is submitting the manuscript. Marzie Kamali performed the data analysis. Soheila Manifer and Ali Kazemian got the information, set up the database and drafted manuscript.

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