

Effect of Salivary Melatonin on Ionizing Radiation Worker and its Effect on Periodontal Disease

DOI: <https://doi.org/10.32007/jfacmedbagdad.6612183>

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Abstract:

Background: The use of ionizing radiation, such as radiotherapy and medical imaging, is common in modern medicine. However, it can have negative effects on the body, such as an imbalance in oxidative stress, which can lead to periodontal or gum disease. Radiographers are particularly at risk of experiencing this due to increased levels of reactive oxygen species. Antioxidant therapy, such as melatonin, may help to minimize oxidative stress and protect tissues.

Objectives: The study aimed to evaluate the impact of radiation on periodontal conditions among radiation workers, as well as to assess the levels of melatonin in their bodies.

Patients and Methods: The study group consisted of 40 men who had worked with ionizing radiation for 5 years or more, while the control group consisted of 40 men who worked as nurses or lab workers. Unstimulated salivary samples were collected from all subjects to measure salivary melatonin levels. Both groups were then evaluated for the plaque index, bleeding on probing, probing pocket depth, and clinical attachment loss.

Results: The results of the study showed that the study group had a higher mean plaque index (1.41 ± 0.484) compared to the control group (1.14 ± 0.524) ($p=0.013$), a higher mean probing pocket depth (4.40 ± 1.463) compared to the control group (2.82 ± 2.328) ($P=0.0002$), and a higher mean clinical attachments loss (2.67 ± 1.461) compared to the control group (1.59 ± 1.919) ($P=0.004$). However, there was no significant difference in the mean gingival bleeding between the two groups. Additionally, the study group had a lower mean salivary melatonin level (34.19 ± 13.849) compared to the control group (42.43 ± 16.783) ($P=0.013$).

Conclusion: This study suggests that radiation exposure may increase the risk of periodontal disease. The results also indicate that both radiation and periodontitis can affect salivary melatonin markers, which may be useful in identifying periodontitis.

Keywords: Antioxidant; Melatonin; Periodontal disease; Radiation; Reactive oxygen species.

J Fac Med Baghdad
2024; Vol.66, No. 1
Received: Jul., 2023
Accepted: Oct, 2023
Published: Aprl.2024

Introduction

Ionizing radiation (IR) is widely used in medicine for both diagnostic and therapeutic purposes (1). Increased oxidative stress in tissues exposed to IR is a key component of the harmful IR action mechanism (2). IR can enter living cells, where it causes the ionization to organic and inorganic substances (3). The key factor for the increased generation of reactive oxygen species (ROS) is the abundance of water in cells. This factor induces IR to radiolysis water molecules (4). ROS interaction with macromolecules causes cell malfunction and apoptotic cell death (2), increased oxidative stress can have both direct detrimental side effects and illnesses that are linked to ROS. Therefore, it is crucial to find prophylactic substances that are both safe and effective to shield humans from IR damage (1).

The hormone melatonin (N-acetyl-5-methoxytryptamine) (5), is primarily produced and secreted by the pineal gland in the brains of animals. Because melatonin is a paracrine, autocrine, and

endocrine hormone, it affects cells nearby, tissues far from the source of production, and the cells that produce it directly (6).

Melatonin (MT) has effects beyond controlling seasonal and circadian cycles. Additionally, MT affects the immune system (7) and has anti-inflammatory capabilities (8). Numerous investigations have found that MT has excellent antioxidant effects (9). Since the beginning of the 21st century, MT has been regarded as a radioprotector due to its potent direct and indirect antioxidant properties (10). A chronic inflammatory disease called periodontitis is characterized by elevated host immune response activity and increased infections in the mouth (11). The imbalance in the biofilm community is included in the pathogenesis of periodontitis. Increasing immunological response and elevating inflammatory response using systemic or local inflammatory mediators are examples of this. An abundance of neutrophils moves toward the site of inflammation as a result of the increased infections. Proteases are produced as a result, and reactive oxygen species are also created. As a result, increased oxidative stress

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results from a large number of neutrophils battling the pathogens (13). Oxidative stress is linked through several mechanisms to cell and tissue damage. These include protein or enzyme oxidation, lipid peroxidation, and DNA damage (14). Human salivary oxidative stress and persistent periodontitis are connected (15). Numerous substances with antioxidant effects were successfully used in treating periodontitis (16). MT has aided in immune response regulation and periodontal tissue protection (17). The objective of this study was to investigate the MT's ability to shield periodontal tissue from the oxidative damage brought on by ionizing radiation.

Patients and Methods

This case-control study was conducted from February to the end of April 2022 in different hospitals in Baghdad City. The Ethics Committee of the College of Dentistry at the University of Baghdad has authorized the protocol for this cross-sectional study (number 488322/date 19-1-2022). The study sample consisted of 80 men categorized into a study group including 40 men who had at least five years of experience in the field of ionizing radiation so the long-term effect of radiation was expected to be found among them and at the same time avoiding the elevated level of oxidative stress markers due to aging Alhusaini et al (2019) and a control group which included 40 men who were employed as workers in the hospitals' lab without being exposed to ionizing radiation. All participants were between (30 -40) years of age and without a history of any systemic illness, non- smokers, and had not taken an antibiotic at least two weeks prior to the data collection.

Salivary Samples: For each participant, unstimulated salivary samples were collected under standardized conditions at (9- 11 am), Navazesh and Kumar (2008). After collection, the samples were placed in a small chilling box to prevent bacterial growth. Then, the saliva was centrifuged for 15 minutes at 4000 rpm to separate a clear supernatant using a micropipette into an Eppendorf tube to be stored at (- 20 °C) in the freezer for the subsequent analysis of salivary melatonin, Carvalho et al (2010).

Oral examination: After the collection of the salivary sample, the clinical periodontal parameters which were bleeding on probing (BOP), plaque index (PLI), clinical attachments loss (CAL), and probing pocket depth (PPD) were assessed (18).

Biochemical analysis of saliva: The measurement of salivary Melatonin concentration was done using the sandwich enzyme linked immune sorbent assay [ELISA] method by a ready kit (Shanghai yl biont, China).

Statistical Analysis: - The Statistics Package for Social Science (SPSS version -22, Chicago, Illinois, USA) was utilized for the data description, analysis, and presentation. The p-value was considered to be statistically significant when p<0.05 and statistically highly significant when p<0.01.

Results

Table (1) shows the mean values for the periodontal variables studied. The mean plaque index was significantly higher in the study than in the control group (p< 0.05).

The mean gingival bleeding score was higher in the study than in the control group but not significantly so (p>0.05). The mean value of the probing pocket depth was significantly higher in the study than in the control group (p<0.01). The mean clinical attachment loss value was significantly higher in the study than in the control group (p<0.05).

Table 1: The mean values for the plaque index, gingival bleeding, probing pocket depth and clinical attachment loss in the study and control groups

Variables	Study Group			Control Group			Statistical Test	
	Mean	±SD	±SE	Mean	±SD	±SE	t-test	p value
PLI	1.41	0.484	0.071	1.14	0.524	0.082	2.528	0.013
BOP	6.36	3.903	0.569	5.80	3.124	0.488	0.731	0.466
PPD	4.40	1.463	0.213	2.82	2.328	0.364	3.744	0.002
CAL	2.67	1.461	0.213	1.59	1.919	0.300	2.936	0.004

PLI= Plaque Index*= significant at P <0., BOP= bleeding on probing NS= not significant, PPD= pridonatal pocket depth**=highly significant at p<0.01, CAL= clinical attachment loss *= significant at P <0.05

The mean values of the salivary melatonin for the study and control groups are shown in table 2. The mean salivary melatonin was higher among the control than in the study with a statistically significant difference (p< 0.05).

Table 2: Melatonin Levels in Study and Control Group

Variables	Study Groups			Control Groups			Statistical difference	
	Mean	±SD	±SE	Mean	±SD	±SE	t-test	P value
MT	34.192	13.849	2.020	42.432	16.783	2.621	2.523	0.013*

MT=Melatonin *= significant at P <0.05

Discussion

The findings of this investigation demonstrated that the study group had more periodontal disease than the control group, and the Melatonin was lower in the study group compared to the control group.

This agreed with the findings of some studies (18-20), which found that radiologists had greater periodontal characteristics than the control group. The results also agreed with another study, in which periodontal parameters (PLI, BOP, PPD, CAL) were found to be greater in irradiated subjects than in subjects not exposed to radiation and came in accordance with the study (21, 22). They reported that radiation workers had higher periodontal parameters; this finding may be attributable to the employees' decreased salivary flow, which has been linked to an increase in periodontal disease infection by lowering bacterial clearance and having an

impact on microbial homeostasis (23). According to other studies (24), increases in ROS among radiographers may also contribute to the rise in periodontal diseases. The findings that periodontal parameters are more prevalent among diagnostic radiology employers point to the necessity for public preventive programs for them that include the enhancement of dental knowledge, dental health education, and attitude toward both oral hygiene and correct nutrition and food.

The finding of this study agreed with some research works (25- 27), which found that the salivary melatonin level was higher in healthy subjects than in patients with periodontitis. However, the results of the current study disagreed with Lodhi et al (2016) who found that the salivary melatonin level was higher in patients with chronic periodontitis than in healthy subjects.

The explanation for the increased periodontitis among the irradiated workers could be due to the reduced level of Melatonin. This is because periodontal disease is associated with the formation of free radicals. Many of these free radicals arise from pathogenic bacteria and phagocytic cells. It has been suggested that oxidative damage to periodontal tissues has been attributed to an increase in reactive oxygen and nitrogen during periodontal disease (26). Melatonin may lessen this oxidative damage and hence help protect tissue. It has been observed that high levels of free radicals can promote increases in the consumption of Melatonin (29). Therefore, decreased melatonin levels in periodontitis might result from by products or mediators that could interfere with the melatonin levels (30).

Melatonin may support the antioxidative defense directly by scavenging free radicals (27, 31), or indirectly by suppressing the synthesis of enzymes that generate ROS (17).

Another explanation for the protective role of Melatonin on periodontal tissues might be due to some extent to its antimicrobial action against *P. gingivalis*, *Streptococcus mutans*, and *Prevotella intermedia* (32). Melatonin is also a significant immune system regulator since it increases the acquired and innate immunity and stimulates monocytes and neutrophils (26).

Melatonin may change the periodontal destruction by suppressing prostaglandin E2, thereby inhibiting the differentiation of osteoclasts (33). Additionally, it interacts with other biological substances, including calcitonin and some of the proteins that control the process of bone resorption in periodontal disease (15).

Due to its antioxidant qualities and capacity to neutralize reactive species, it may reduce bone resorption at the level of the osteoclast lacuna (34). It boosts the proliferation and differentiation of osteoblasts, promotes type I collagen, osteopontin, bone sialoprotein, and osteocalcin gene expression, and stimulates osteogenic differentiation in bone marrow stem cells (35, 36).

The degree of periodontal disease affects salivary melatonin levels, its level decreases as periodontal disease severity grows, suggesting that MT works to defend the body against microbiological invasion. Therefore, it is helpful in the management of periodontal diseases (37).

Treatment with MT reduces periodontal tissue destruction by reducing inflammatory cytokines and balancing the antioxidant concentration (38). This result also agreed with some studies (13, 30) which reported that MT could offer advantages for managing tumor responses to radiotherapy and reducing radiation toxicity in healthy tissues. MT has strong anti-oxidative properties that minimize radiation-induced oxidative DNA damage and cell death. It can be used as a treatment before radiotherapy increases antioxidant effects by lowering oxidative stress, attenuating strong immune responses, and ameliorating acute effects of radiotherapy (39).

Conclusion

Radiation could be a predisposing factor for periodontal disease. Both radiation and periodontitis affect salivary melatonin markers, which indicates periodontitis.

Authors' declaration:

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to the current study, have been given permission for re-publication attached to the manuscript. Authors sign on ethical consideration's approval-Ethical Clearance: The project was approved by the local ethical committee in (College of Dentistry, University of Baghdad) according to the code number (488) on (19/ 01/ 2022).

Author Contributions:

Study conception & design: (Ahlam Taha Mohammed). Literature search: (Shams Waleed Khalid). Data acquisition: (Shams Waleed Khalid). Data analysis & interpretation: (Shams Waleed Khalid). Manuscript preparation: (Shams Waleed Khalid). Manuscript editing & review: (Shams Waleed Khalid).

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How to Cite this Article

Effect of Salivary Melatonin on Ionizing Radiation Worker and its Effect on Periodontal Disease. *JFacMedBagdad* :66 (1). Available from: <https://ijjmc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/2183>

تأثير الميلاتونين اللعابي على العاملين في مجال الإشعاع وتأثيرها على صحة ماحول الاسنان

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الخلاصة

المقدمة:- يعد استخدام الإشعاعات المؤينة، مثل العلاج الإشعاعي والتصوير الطبي، أمراً شائعاً في الطب الحديث. ومع ذلك، يمكن أن يكون لها آثار سلبية على الجسم، مثل خلل في الإجهاد التأكسدي، مما قد يؤدي إلى أمراض اللثة أو اللثة. يتعرض فنيو الأشعة بشكل خاص لخطر الإصابة بهذا بسبب زيادة مستويات أنواع الأكسجين التفاعلية. قد يساعد العلاج بمضادات الأكسدة، مثل الميلاتونين، في تقليل الإجهاد التأكسدي وحماية الأنسجة.

هدف الدراسة: هدفت هذه الدراسة إلى تقييم تأثير الإشعاع على أمراض اللثة بين العاملين في مجال الإشعاع، وكذلك تقييم مستويات الميلاتونين في أجسامهم.

الطريقة:- تكونت مجموعة الدراسة من 40 رجلاً عملوا بالإشعاعات المؤينة لمدة 5 سنوات أو أكثر، بينما تكونت المجموعة الضابطة من 40 رجلاً عملوا كمرضى أو عمال مختبر. تم جمع عينات من اللعاب غير المحفزة من جميع المواد لقياس مستويات الميلاتونين اللعابي. تم بعد ذلك تقييم كلتا المجموعتين بحثاً عن مؤشر البلاك والنزيف عند الفحص وعمق الجيب اللثوي وفقدان الارتباط السريري.

النتائج:- أظهرت نتائج الدراسة أن مجموعة الدراسة كان لديها مؤشر البلاك أعلى (0.484 ± 1.41) مقارنة بالمجموعة الضابطة (1.14 ± 0.524) ($p = 0.013$)، ومتوسط عمق جيب اللثوي أعلى (1.463 ± 4.40) مقارنة بالمجموعة الضابطة (2.328 ± 2.82) ($P = 0.0002$)، ومتوسط أعلى لفقدان الارتباطات السريرية (1.461 ± 2.67) مقارنة بالمجموعة الضابطة (1.919 ± 1.59) ($P = 0.004$). ومع ذلك، لم يكن هناك اختلاف كبير في متوسط نزيف اللثة بين المجموعتين. بالإضافة إلى ذلك، كان لدى مجموعة الدراسة انخفاض متوسط مستوى الميلاتونين اللعابي (13.849 ± 34.19) مقارنة بالمجموعة الضابطة (16.783 ± 42.43) ($P = 0.013$).

الاستنتاج:- تشير هذه الدراسة إلى أن التعرض للإشعاع قد يزيد من خطر الإصابة بأمراض اللثة. تشير النتائج أيضاً إلى أن كلا من الإشعاع والتهاب اللثة يمكن أن يؤثر على علامات الميلاتونين اللعابي، والتي قد تكون مفيدة في تحديد التهاب اللثة. تشير هذه الدراسة إلى أن التعرض للإشعاع قد يزيد من خطر الإصابة بأمراض اللثة. تشير النتائج أيضاً إلى أن كلا من الإشعاع والتهاب اللثة يمكن أن يؤثر على علامات الميلاتونين اللعابي، والتي قد تكون مفيدة في تحديد التهاب اللثة.

الكلمات المفتاحية:- أمراض اللثة، الإشعاع، الميلاتونين، أنواع الأوكسجين التفاعلية، مضادات الأكسدة.