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Relationship Between Osteoporosis and Periodontal Diseases After RadiationTherapy

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ABSTRACT

Purpose: This study was carried out to discuss the association between Osteoporosis & periodontal diseases after Radiation therapy in animal clinically and histologically. **Material and methods:** A total of Sixty-three (63), female adult Albino rats were used. Animals were divided into 7 groups of 9 rats each, in group 1: the rats were used as control. In group 2, the rats received radiation only. In group 3, osteoporosis was induced. In group 4, periodontitis was induced for this group. In group 5, the rats received radiation and osteoporosis was induced for this group. While, in group 6, the rats received radiation and periodontitis was induced for this group. Finally, group7 rats received radiation in addition to osteoporosis and periodontitis induction. **Results:** Group 7 showed the lowest bone density at different intervals of the study. Osteoporosis and radiation group revealed more inflammatory and focal fibrous osteodystrophy than other groups. **Conclusion:** Radiation therapy potentiates the detrimental effect of osteoporosis on periodontium. Group 7 showed the lowest bone density mean value in all the study parameters.

KEYWORDS

Radiation, Osteoporosis, Periodontitis, Rat model

INTRODUCTION

Osteoporosis is a progressive systematic skeletal disorder characterized by low bone mineral density (BMD), deterioration of microarchitecture of bone tissue, and susceptibility to fracture caused by bone resorption [(1)]. The main mechanism in osteoporosis is an imbalance between bone resorption and bone formation. In normal bone, matrix remodeling of bone is constant; up to 10% of all bone

- A paper extracted from Doctor's thesis titled "relationship between osteoporosis and periodontal diseases after radiation therapy".

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mass may be undergoing remodeling at any point in time [2].

Glucocorticoids are important therapeutic agents that have been used for their strong anti-inflammatory and immunosuppressive properties for over 50 years [3]. Glucocorticoid-induced osteoporosis (GIO) is the most prevalent form of secondary osteoporosis. A lot of side effects can occur with glucocorticoid therapy, with osteoporotic fractures being the most devastating, as it affects 30-50% of patients [4].

On the other hand, Periodontitis is a multifactorial disease with microbial dental plaque as the initiator of periodontal disease [5]. Although the different forms of periodontitis are all caused by bacterial infection, a variety of local and systemic factors are associated with the risk of periodontal disease or the severity of the disease [6].

The similar clinical sign of osteoporosis and periodontitis is bone resorption in nature. These 2 diseases have similar risk factors. Osteoporosis is the most common skeletal disorder in elderly population. Both are characterized by the imbalance between bone resorption and bone formation due to the deucedly activated osteoclast, and the impaired bone quality causes the compromised bone strength then increases the risk of fracture [7].

With the increase in population, the survival rate of cancer patients continues to increase, with a greater number of people receiving cancer therapeutics. The range of cancer therapeutic options has presented the dentist with a new and challenging risk of oral complications [8].

Bones were affected by radiation, causing severe changes of the bone regeneration capacity on injury. Also, there was a disorder in the balance between the osteoblastic and osteoclastic activities, leading to destruction in bone process with lower number of osteocytes and osteoblasts after tissue irradiation. [9].

MATERIALS AND METHODS

Sixty-three (63), adult female Albino rats of average age of 6 months and average weight (230-250 gm) provided by the National Centre for Radiation Research and Technology (NCRRT), Cairo, Egypt. The animals were divided into 7 groups of 9 rats each, in group 1, the rats were used as control, while, in group 2, the rats received radiation only. In group 3, the rats for this group were injected by Depo-Medrol subcutaneous in a dose of 7 mg/kg once a week for 8 weeks. In group 4, the rats for this group were anesthetized by injection of ketamin (25mg/kg0) and ligature (3-0 silk suture) were placed around the cervix of mandibular incisors. In group 5, the rats received radiation and injected by Depo-Medrol subcutaneous in a dose of 7 mg/kg once a week for 8 weeks. In group 6, the rats anesthetized by injection of ketamin (25mg/kg0) and ligature (3-0 silk suture) were placed around the cervix of mandibular incisors and after 10 days they received radiation, and the last group were injected by Depo-Medrol subcutaneous in a dose of 7 mg/kg once a week for 8 weeks, in the 6th week they were anesthetized by injection of ketamin (25mg/kg0) and ligature (3-0 silk suture) were placed around the cervix of mandibular incisors then after 10 days they received radiation.

Osteoporosis was induced by injecting the rats with Depo-medrol (methyl prednisolone) subcutaneously in a dose of 7mg/kg. This protocol was specially undertaken to establish corticosteroid induced osteoporosis as advocated by previous studies [10].

In order to induce periodontitis, Body weight was determined for each rat, a total of 27 rats in groups (IV, VI, and VII) were anesthetized by injection of ketamine (25mg/kg), and ligatures (3-0silk suture) were placed around the cervix of the mandibular incisors, Experimental periodontitis was established after 7 to 12 days according to a previous study [11].

In the present study, DEXA was used, also called

dual-energy x-ray absorptiometry, a small dose of ionizing radiation was used to induce pictures of the inside of the body to measure bone loss. It is considered the most accurate method for diagnosing osteoporosis.

Irradiation of rats in group II, V, VI, VII was made at the National Centre for Radiation Research and Technology (NCRRT), Cairo, Egypt using 137 Cesium Gamma Cell 6 gray once.

At 3, 6 and 9 days after rats received radiation three rats per group were euthanized for each experimental period. To achieve this, the rats were anesthetized, and cardiac perfusion was performed using 4% formalin. The mandible was removed, followed by removal of any excess of soft tissue, and the bone was fixed in 10% formaldehyde solution.

Hematoxyin& eosin stain was used to study the histopathological changes in bone. Sections were deparaffinized in xylene, hydrated in descending grades of ethanol, incubated with Hanishematoxylin for 3 minutes, washed under running water and incubated with eosin for one minute. Sections were then dehydrated in ascending grades of ethanol, cleaned in xylene and mounted with cover slips using per mount.

Histological analysis of the area of the lower incisors was made to calculate osteoblast and osteoclast density, inflammatory infiltration and other signs of periodontal disease.

RESULTS

It was found that Group 4 recorded higher bone density mean value (0.19 ± 0.02), while Group 7 recorded the lowest bone density mean value (0.07 – 0.12) among all groups.

Descriptive statistics of bone density results between group 4 and group 6 and group 7 after 3, 6 and 9 days is summarized in table (1) and figure (1).

It was found that Group 4 recorded higher bone density mean value (0.19 ± 0.02), while Group 7 recorded the lowest bone density mean value (0.07 – 0.12).

There was highly statistically significant difference between the three studied groups regarding bone density at 3& 6 and 9 days. The table shows that there was statistically significant difference between group 4 and 7 and between group 4 and 6 group regarding bone density at 3& 6 and 9 days.

Table (1) *Comparison between group 4, group 6 and group 7 regarding bone density at 3& 6 and 9 days after radiation therapy*

		Group 4	Group 6	Group 7	Test value*	P-value	P1	P2	P3
3rd day	Mean ± SD	0.19 ± 0.02	0.16 ± 0.01	0.10 ± 0.02	58.304	0.000	0.001	0.000	0.000
	Range	0.17 – 0.21	0.15 – 0.16	0.08 – 0.12					
6th day	Mean ± SD	0.19 ± 0.01	0.15 ± 0.01	0.10 ± 0.02	48.132	0.000	0.001	0.000	0.000
	Range	0.17 – 0.20	0.14 – 0.16	0.07 – 0.12					
9th day	Mean ± SD	0.18 ± 0.01	0.15 ± 0.01	0.10 ± 0.02	42.831	0.000	0.001	0.000	0.000
	Range	0.16 – 0.20	0.14 – 0.15	0.07 – 0.12					

**: One Way ANOVA* *P1: P group VS PR group*

P2: P group VS OPR group *P3: PR group VS OPR group*

Descriptive statistics of bone density results between group 3 and group 5 and group 7 after 3, 6 and 9 days is summarized in table (2) and figure (2).

It was found that Group 3 recorded higher bone density mean value (0.18±0.01), while Group 7 recorded the lowest bone density mean value (0.07–0.12).

There was highly statistically significant difference between group 3vs group 5 and between group 3vs group 7 regarding bone density at 3& 6 and 9 days. And there was a non significant difference between group 5 and group 7 in the 3 groups.

Osteoporosis, periodontitis, and radiation group (VII):

The histological findings in this group were more severe than other groups. The osteoporosis was aggressive than osteoporosis group only, periodontitis was more apparent than periodontitis group only, and the radiation dose may help to convert the lesions to be more aggressive and sever and focal fibrous osteodystrophy can be shown (fig 3).

Table (2) *Comparison between group 3, group 5 and group 7 regarding bone density at 3& 6 and 9 days after radiation therapy*

		Group 3	Group 5	Group 7	Test value*	P-value	P1	P2	P3
3rd day	Mean ± SD	0.18 ± 0.01	0.12 ± 0.02	0.10 ± 0.02	38.789	0.000	0.000	0.000	0.162
	Range	0.16 – 0.19	0.09 – 0.14	0.08 – 0.12					
6th day	Mean ± SD	0.18 ± 0.01	0.12 ± 0.02	0.10 ± 0.02	26.236	0.000	0.000	0.000	0.129
	Range	0.16 – 0.18	0.08 – 0.15	0.07 – 0.12					
9th day	Mean ± SD	0.17 ± 0.01	0.12 ± 0.01	0.10 ± 0.02	30.867	0.000	0.000	0.000	0.066
	Range	0.15 – 0.17	0.1 – 0.13	0.07 – 0.12					

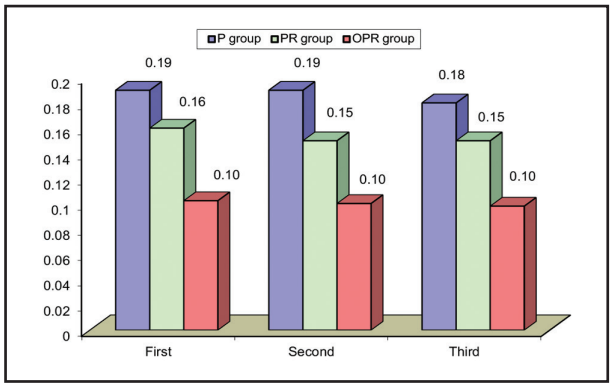

Fig. (1) Comparison between group 4, group 6 and group 7 regarding bone density at 3& 6 and 9 days after radiation therapy.

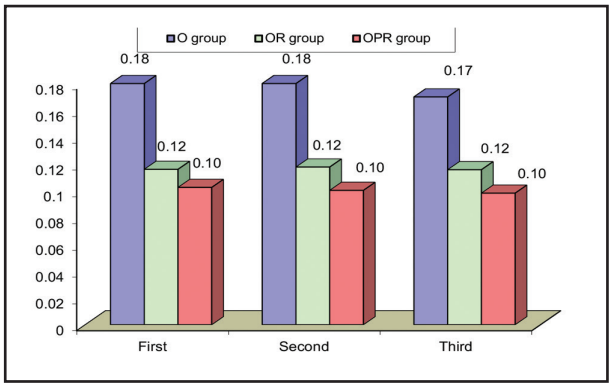

Fig. (2) Comparison between group 3, group 5 and group 7 regarding bone density at 3& 6 and 9 days after radiation therapy.

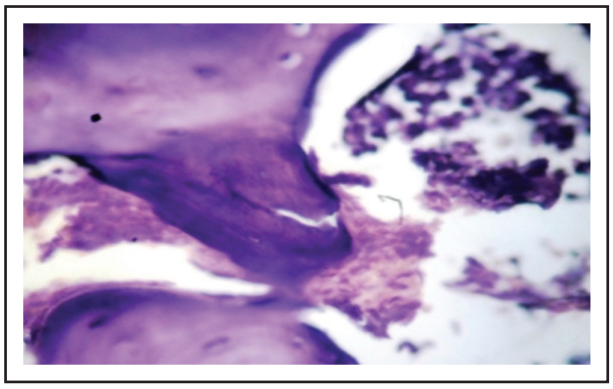

Fig. (3) Mandible of rat of (group 7) 9 days after radiation therapy showing Focal fibrous osteodystrophy (H&E x 400)

DISCUSSION

The relationship between osteoporosis and periodontitis was valued gradually, but till now the association between osteoporosis and periodontitis remains a controversial issue, this correlation and potential mechanisms linking of these 2 bone-loss diseases are still uncertain**.** Thus, this study was carried out to discuss the effect of radiation therapy on osteoporosis and periodontal diseases in animal clinically and histologically.

In the present study, a new means of ligature placement was attempted that comprised tying the ligature around the contact point between the lower incisors. This method successfully retained the ligature in place, thereby preventing direct ligature-gingiva contact and resulting mechanical stimulation. This method impairs the self-clearing function and that captured food residues caused inflammation and induced experimental periodontitis [(12)].

On the contrary, in another study, ligatures were displaced apically into the gingival sulci to ensure a subgingival position [(13)]. Also in other studies, placement of a loose cotton ligature between the right maxillary first and second molars for nine weeks. However, in their model, the loose ligature might have pushed the gingiva while the ligature was settling during the experimental period, which, in addition to food impaction, might have caused periodontitis directly [(14)].

Histologically, there was some thickening of the trabeculae after exposure in some areas forming osteophyte but osteoblasts remain after high-dose exposure. There was an early and transient increase in volumetric bone mineral density and mineral apposition rate was noted within the first week after exposure in rodent models. These observations suggest an early and dispersed enhancement of bone formation after exposure, but the mechanisms are completely unknown.

The results revealed that there was statistically significant high difference found between control group and osteoporosis, periodontitis and radiation groups at 3&6 and 9 days regarding bone density with the highest difference in group VII (osteoporosis, radiation and periodontitis group).

A previous study showed that direct and indirect effects after high-dose Radiation treatment on periodontium resulted in increased risk of attachment loss and bone loss, and an increased risk for development of osteoradionecrosis [(15)].These results were parallel to bone changes in the present study.

CONCLUSION

In conclusion, There is a direct association between osteoporosis and periodontal breakdown in a diseased-induced rodent model, And radiation therapy considered as a potent risk factor of periodontitis, as it exaggerates the response of periodontal tissue to the local factors, Also it potentiates the detrimental effect of osteoporosis on periodontal tissues.

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