ScienceDirect

Archives of Oral Biology

Volume 65, May 2016, Pages 59-65

Histopathological features of bisphosphonates related osteonecrosis of the jaw in rats with and without vitamin d supplementation

Saim Yanık [a], Mutan Hamdi Aras [a], Suna Erkılıç [b], Zehra Bozdağ [b], Tuncer Demir [c], Sedat Çetiner [d]

Show more

https://doi.org/10.1016/j.archoralbio.2015.10.010

Get rights and content

Highlights

- Vitamin D affects histopathological parameters, such as the numbers of osteoblasts and osteoclasts, as well as histological and macroscopic osteonecrosis, especially in the group administered vitamin D after tooth extraction
- Vitamin D diminished the suppressive effects of BPs.

Abstract

Objective

Aim of this study was to investigate the effect of vitamin-D3 on the osteonecrosis of bone that was induced after tooth extraction was conducted on rats that were given zoledronic acid (Z.A).

Material and methods

Animals were divided into four groups. Two of the experimental groups were divided into two subgroups, third study group was not divided into subgroups, and control group was divided into three subgroups. Z.A was administered twice per week over the course of 7 weeks, dexamethasone was administered twice a week during the 5th-6th-7th weeks to all groups. Dental extraction was performed by drilling around the tooth at 7th week. In study-group-1; vitamin-D was administered twice per week during the 5th-6th-7th weeks. In study-group 2; vitamin-D was administered twice per week during the 8th-9th-10th weeks. In study-group-3; vitamin-D was administered twice per week during the 15th-16th-17th weeks. The animals were sacrificed at 10th-15th-17th weeks, and histologic samples were taken.

Results

Postoperative-15-group had a lower osteoblast number, which was statistically significant as compared to preoperative-15 and control-15-group. Control-10-group showed significantly lower osteoclast number in comparison to preoperative-10 and postoperative-10-group. Osteoclast number was significantly higher in the osteonecrosis-17-group as compared to control-17-group. Preoperative-10-group showed significantly higher inflammation in comparison to control-10-group. Postoperative-15-group had a lower histologic osteonecrosis, which was statistically significant as compared to the control-15-group. Macroscopic osteonecrosis was significantly higher in the control-17-group in comparison to the osteonecrosis-17-group.

Conclusions

We concluded that there are some proofs for the treatment of BRONJ with systemic using of vitamin-D.

Introduction

Vitamin D plays important roles in calcium and phosphorus homeostasis and is indispensable for the normal development and maintenance of the skeleton (Jameson, 2004). Moreover, vitamin D regulates many genes involved in cell differentiation and cell proliferation through its active form, 1,25-dihydroxy vitamin D_3, and the nuclear vitamin D receptor (Jones, 2012). Beyond these important effects, vitamin D contributes to the prevention of various cancers, such as colon cancer, breast cancer, ovarian cancer, and

prostate cancer, autoimmune diseases, such as multiple sclerosis and diabetes, allergic diseases, and cardiovascular and infectious diseases (Zhang & Naughton, 2010).

Bisphosphonates (BPs) are non-metabolizable endogenous analogs of pyrophosphate that inhibit osteoclast function and bone resorption mediated by osteoclasts. BPs are used in the routine treatment of malignancies characterized by bone metastasis, such as breast, prostate, and lung cancers, as well as systemic health problems, such as multiple myeloma, osteoporosis, osteopenia, Paget's disease, and osteogenesis imperfecta, due to their inhibitory effects on osteoclast activity and antiangiogenic properties (Ruggiero et al., 2009). One of the significant adverse effects of these drugs is BP-related osteonecrosis of the jaw (BRONJ), a rare condition that can develop as a result of inhibition of the blood supply to the jawbones temporarily or permanently. The incidence of osteonecrosis has been reported to range between 1% and 12% in individuals with intravenous BP administration and 0.07/10000 patients receiving oral BPs (Ruggiero et al., 2009).

Some studies indicated that vitamin D insufficiency was related to BRONJ (Hokugo et al., 2010; Silvina, Macarena, Silvia, & Susana, 2006). Hokugo et al. (2010) developed a vitamin D-deficient rat model and tested combinations of risk factors for BRONJ. They suggested that the group with intravenous zoledronic acid and vitamin D deficiency showed a higher rate of BRONJ. Silvina et al. (2006) indicated that a vitamin D insufficiency plus BP therapy group showed significantly lower values of bone mass and bone volume.

The main goal of the present study was to develop a BRONJ model and investigate the effects of vitamin D_3 given before and after tooth extraction and after the development of osteonecrosis in BRONJ induced by tooth extraction. In this study, histopathological parameters, including osteoblasts, osteoclasts, macroscopic osteonecrosis, histological osteonecrosis, and inflammation, were assessed. To our knowledge, this is the first experimental study to investigate the effects of vitamin D treatment on BRONJ and histopathological parameters in rats given intravenous zoledronic acid.

Section snippets

Animals

The Inonu University Animal Ethics Committee approved the present study. A total of 80 adult male albino Wistar rats, aged 90 days, with a body weight of 325±25g, were housed at room temperature (24°C±2°C), 55%±10% humidity, and a 12/12-h light/dark cycle. The animals had free access to drinking water and a standard rodent diet. …

Experimental design and surgical procedures

After 1 week of acclimatization, the animals were divided into four groups (a control group and three study groups). Two of the experimental groups were divided into two …

Osteoblasts

The postoperative-15 group had a lower osteoblast number, which was statistically significant compared with the preoperative-15 (p=0.001) and control-15 (p=0.002) groups (Table 2 and Supplementary Table 5). However, the differences in osteoblast number were not statistically significant in all groups sacrificed on the 10th or 17th weeks (Table 1 and Supplementary Tables 4 and 6). …

Osteoclasts

The control-10 group had a significantly lower osteoclast number than the preoperative-10 (p=0.010) and …

Discussion

BPs are used in patients with several pathological conditions, including multiple myeloma, bone metastasis hypercalcemia, Paget's disease, and osteoporosis, but their use contributes to the risk of BRONJ (Russell et al., 2007). Since 2003, there has been an increase in number of case reports regarding BRONJ induced by BPs, especially with intravenous administration. BRONJ is described as the presence of exposed bone in the jaws that does not heal and persists for more than 8 weeks in patients …

Funding

None. …

Competing interests

The authors declare no competing interests relevant to this work. …

Ethical approval

The Inonu University Animal Ethics Committee approved the present study.

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see:

http://www.textcheck.com/certificate/DNvGlM ↗. …

Recommended articles

References (27)

A. Bedogni *et al.*
Bisphosphonate-associated jawbone osteonecrosis: a correlation between imaging techniques and histopathology
Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology (2008)

Y.A. Cho *et al.*
Histopathological features of bisphosphonate-associated osteonecrosis: findings in patients treated with partial mandibulectomies
Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology (2012)

M.A. Khokher *et al.*
Diphosphonates inhibit human osteoblast secretion and proliferation
Metabolism (1989)

P.P. Major *et al.*
Zoledronic acid in the treatment of hypercalcemia of malignancy: results of the international clinical development program
Seminars in Oncology (2001)

C. Pautke *et al.*
Bisphosphonate related osteonecrosis of the jaw: a minipig large animal model
Bone (2012)

K. Thompson *et al.*
Cytosolic entry of bisphosphonate drugs requires acidification of vesicles after fluid-phase endocytosis
Molecular Pharmacology (2006)

H. Tsurushima *et al.*
Bacterial promotion of bisphosphonate-induced osteonecrosis in Wistar rats
International Journal of Oral and Maxillofacial Surgery (2013)

F. von Knoch *et al.*
Effects of bisphosphonates on proliferation and osteoblast differentiation of human bone marrow stromal cells
Biomaterials (2005)

J.I. Aguirre *et al.*
Effects of alendronate on bone healing after tooth extraction in rats
Oral Diseases (2010)

M. Biasotto *et al.*
A novel animal model to study non-spontaneous bisphosphonates osteonecrosis of jaw
Journal of Oral Pathology & Medicine (2010)

View more references

Cited by (16)

Preclinical models of medication-related osteonecrosis of the jaw (MRONJ)
2021, Bone

Show abstract

Benefits of Natural Antioxidants on Oral Health ↗
2023, Antioxidants

Bisphosphonate-related osteonecrosis induced change in alveolar bone architecture in rats with participation of Wnt signaling ↗
2021, Clinical Oral Investigations

Synthetic calcium phosphate ceramics as a potential treatment for bisphosphonate-related osteonecrosis of the jaw ↗
2019, Materials

Chapter 6: Vitamins and oral health ↗

2019, Monographs in Oral Science

Pathogenesis of medication-related osteonecrosis of the jaw: a comparative study of in vivo and in vitro trials ↗

2018, Journal of International Medical Research

View all citing articles on Scopus ↗

View full text