

Caffeine Intake Decreases Osteoclastogenesis in Alveolar Bone Post Extraction

Christian Khoswanto^{1*}

1. Department of Oral Biology Faculty of Dentistry, Airlangga University, Surabaya, Indonesia.

Abstract

Coffee is one of the most common dietary beverages in the world, it is the main natural source of caffeine in the diet.

Clinical research suggests that drinking coffee, which contains Caffeine, along with antioxidants and other active components, are all found in coffee. Some research findings that Coffee has been shown to reduce the risk of pathological conditions, and because of that, these positive physiologic impacts coffee appear to be roughly related to serum levels of cytokines biomarkers, coffee might indeed presumably influence its preventative effects by reducing inflammation. In vitro investigations have also indicated that caffeine has direct or indirect negative effects on osteoblasts. Wounds due to tooth extraction require fast healing so that complications do not occur after tooth extraction. Osteoclasts are an indicator to determine whether the healing of a tooth extraction wound is healing well or not. All of the studies were conducted on adult male Wistar rats n = 20, 250-280 g at the start of the study.

There was a reduction in the number of osteoclasts in the wound area after tooth extraction after caffeine administration.

Experimental article (J Int Dent Med Res 2023; 16(2): 624-627)

Keywords: Caffeine, osteoclastogenesis, alveolar bone.

Received date: 14 January 2023

Accept date: 05 February 2023

Introduction

Caffeine is a biologically main ingredient found in a variety of foods, drinks, nutritional supplements, and prescription medications. Coffee is one of the most common dietary beverages in the world, it is the main natural source of caffeine in the diet. Clinical research suggests that drinking coffee, which contains Caffeine, along with antioxidants and other active components, are all found in coffee, may aid in the protection of the human brain and reduce the chance of acquiring neurodegenerative illnesses. Furthermore, some research findings that coffee has been shown to reduce the risk of pathological conditions, and because of that, these positive physiologic impacts of coffee considered to be mutually exclusive to serum levels of cytokines biomarkers, coffee might indeed presumably influence its preventative

effects by reducing inflammation.^{1,2}

Other research, on the other hand, have identified coffee consumption as a potential contributor for bad health. Coffee use is not typically regarded to be a component of a balanced lifestyle especially when drank in excess because it includes caffeine, a stimulant. Caffeine abuse can result in insomnia, anxiousness, anxiety, impatience, an upset stomach, a racing heart, or even stiff muscles. Caffeine can also produce dehydration and a shift in fluid balance due to its diuretic properties.^{3,4}

Choi et al. discovered that caffeine increases osteoclastogenesis, implying that caffeine may have a role in osteoclastogenesis-related disorders such as osteoporosis.⁵ In vitro investigations have also indicated that caffeine has direct or indirect negative effects on osteoblasts. Wounds due to tooth extraction require fast healing so that complications do not occur after tooth extraction. Osteoclasts are an indicator to determine whether the healing of a tooth extraction wound is healing well or not. The purpose of this study is to determine the effect of caffeine on the number of osteoclasts after tooth extraction.

*Corresponding author:

Christian Khoswanto,
Department of Oral Biology Faculty of Dentistry,
Jln. Mayjend. Prof. Dr. Moestopo No. 47, 60132,
Surabaya Indonesia.
E-mail : christiankhoswanto@hotmail.com

Materials and methods

All of the studies were conducted on adult male Wistar rats (n = 20; 80 days old, 250-280 g at the start of the study). The animals were maintained in a climate-controlled environment (28 ± 2°C) and During the trial, the animals were kept on a 12 h circadian rhythm with ad libitum availability to food and drink, and the animals were kept in cages (60 x 25 x 25 cm). All of the protocols were carried out in strict accordance with Airlangga University's Animal Care and Use Committee

In a 24-hour period, the rats in the experimental group were given continuous access to a caffeine 0.2 mg/mL solution. The animals in the control group (n = 10) were given no caffeine during the study, while the animals in the experimental group (n = 10) had constant access to caffeine for seven days.

Alveolar bone samples were taken in the incisive area, Fixation is a technique that employs chemicals to preserve the tissue's original structure while also protecting it from deterioration by persistently protein cross-linking. This step was completed with Neutral Buffered Formalin. The fixing stage is crucial to the rest of the histopathology stain procedure because it solidifies the sample and facilitates sectioning by retaining the tissue's molecular structure. The dehydration of a sample is accomplished by adding ethanol. It takes the moisture out of the sample and dries the tissue, even more in preparation for light microscopy. Following the application of ethanol and the tissue dehydration is accomplished, the ethanol is removed with xylene. The process of embedding a sample in a synthetic resin or paraffin wax to aid in the extraction of cellular components is known as embedding. Using a microtome to attach the material and cut it into parts is known as sectioning. A thickness of 4-5 micrometers is ideal for staining and mounted for examination on a microscope slide. The next step was to stain for HE. All samples were examined under a light microscope magnified 400 times once all histology specimens were completed.

Results

Figure 1 shows the state of alveolar bone 7 days in the control group after tooth extraction. Several osteoclasts were found in the area where

the tooth was extracted, especially in the apical third. Figure 2 shows osteoclasts in the treatment group, caffeine administration, a reduction number of osteoclasts found in the tooth extraction wound. Both groups are shown in the boxplot image (Figure 3). Statistical calculations using T-test showed a significant variance of osteoclasts between both the intervention group and the control group (P<0.001). In the treatment group, significantly reduced osteoclasts were found on day 7 (Table 1).

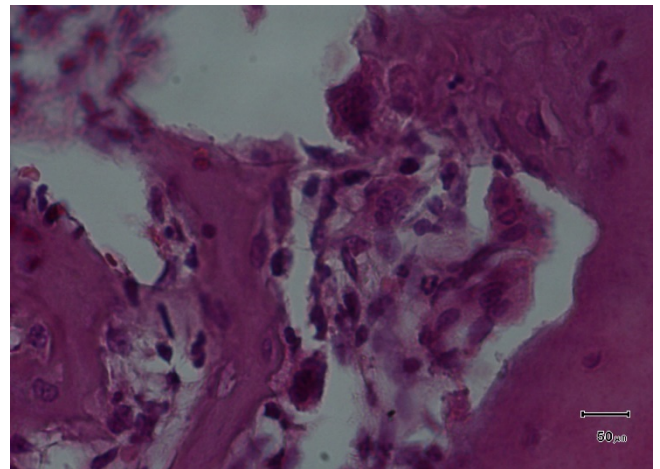


Figure 1. Shows the osteoclast in the control group (400x magnified).

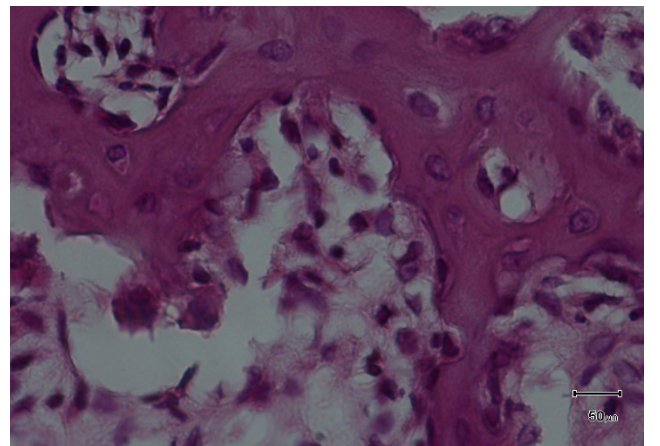


Figure 2. The treatment group's osteoclasts are visible in the apical third (400x magnified).

Group	X±SD Day 7
Caffein	2.20 ^a ±1.13
K	4.40 ^b ±1.17

Table 1 shows the mean Osteoclast cells in the treatment and control groups.

Note that the varied superscripts revealed a significant difference (0.05).

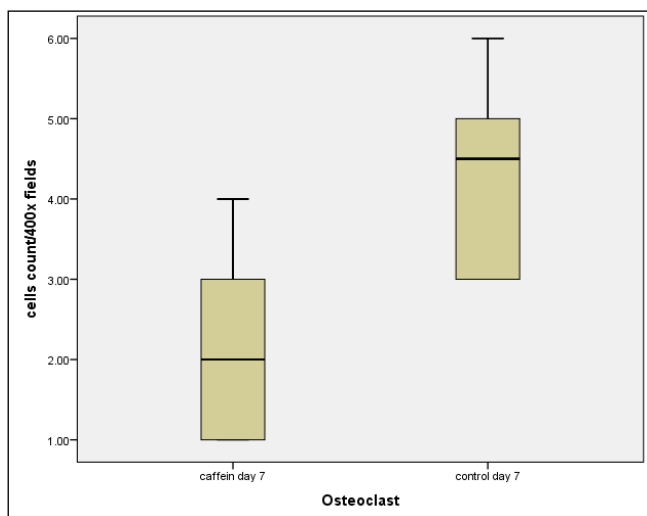


Figure 3. Data showing the number of Osteoclast per 400 fields in treated for 7 days.

Discussion

Bone sialoprotein, osteoclastin, osteonectin, osteopontin, and proteoglycans make up 5% of alveolar bone, which is a mineralized substance made up of 28% type I collagen and 5% non-collagen. The alveolar bone also contained several growth agents and serum proteins. Alveolar bone is divided into two types: cortical bone and trabecular bone. Inorganic minerals account for about 67 percent of bone, organic matrix for 33 percent, organic components comprising of collagen for 28 percent and non-collagen for 5 percent, as well as osteoblasts, osteoclasts, osteocytes, and water. The hydroxyapatite type of bone mass is the anorganic component. Osteoclasts are enormous cells in comparison to alveolar bone cells, and their size allows them to be easily detected with a light microscope. Clusters of osteoclasts are common. The hemopoietic pathway, which also produces macrophages and monocytes, creates osteoclasts. Circulation or direct migration transport these cells from the bone marrow. Precursor cells for osteoclasts can be identified in the bone marrow and blood circulation. These cells are present on the surface of bone and undergo resorption, resulting in Howship's lacunae, which are depressions. To supply energy for the bone resorption process, osteoclasts in the cytoplasm will be loaded with mitochondrial components. Osteoclasts break down the bone matrix, cling to the surface of the bone, and separate cells from the matrix, reducing the pH from 7 to 4. Acidity dissolves

minerals and damages the cell matrix, allowing proteases to escape.⁶⁻⁹

Caffeine affects in a variety of tissues by interfering with phosphodiesterase activity and thereby potentiating the efficacy of agonists working via the adenylate cyclase-cAMP pathway. direct effects on the cellular receptors that control bone remodeling. Caffeine is a component of pain medications and has anti-inflammatory and vasoconstricting properties. Caffeine's ability to diminish pain feeling Its consequences on adenosine receptors appear to be connected, particularly through central blockage of pain signaling receptors or peripheral Adenosine receptors on sensorimotor afferents are inhibited. The anti-nociceptive and supporting effects of caffeine may be explained by the antagonistic impact of Inhibition of cyclooxygenase action in certain regions, as well as adenosine receptors.¹⁰⁻¹⁴

Caffeine can reduce TNF- and IL-6 production caused by LPS in a dose-dependent manner. Caffeine also inhibits inflammation by regulating NFkB activity, which stimulates the expression of inflammatory genes such as iNOS, COX2, and cytokines. The main component of coffee extract, chlorogenic acid, has a substantial anti-inflammatory impact by reducing the release of the proinflammatory cytokine IL-6. It also reduces TNF-a generation in LPS-stimulated macrophages by lowering COX2 expression due to NFkB signaling pathways that are less activated. The mechanism behind coffee's primary effect on bone health is unidentified. However, its antioxidant and anti-inflammatory capabilities can help explain some of it. Coffee, for example, contains high levels of chlorogenic acids, which have the ability to suppress osteoclastogenesis.^{5,15-17}

Conclusions

There was a reduction in the osteoclast cells in the wound area after caffeine administration.

Declaration of Interest

The authors report no conflict of interest.

References

1. Lee CH, George O, Kimbrough A. Chronic voluntary caffeine intake in male Wistar rats reveals individual differences in addiction-like behavior. *Pharmacol Biochem Behav.* 2020 ; 191:1-20.

2. Dingle RN, Dreumont-Boudreau SE, Lolordo VM. Caffeine dependence in rats: effects of exposure duration and concentration. *Physiol. Behav.* 2008; 95: 252–7.
3. Heaney RP. Effects of caffeine on bone and the calcium economy. *Food and Chemical Toxicology.* 2002. 40:1263–70.
4. Harris SS, Dawson HB. Caffeine and bone loss in healthy postmenopausal women. *American Journal of Clinical Nutrition.* 1994. 60:573–8.
5. Choi J, Choi SY, Lee SY, et al. Caffeine enhances osteoclast differentiation and maturation through p38 MAP kinase/Mitf and DC-STAMP/CtsK and TRAP pathway. *Cell Signal.* 2013;25:1222–7.
6. Nanci A. *Oral Histology : Development, Structure and Function.* 9th ed. Missouri: Mosby Co; 2018:12-60.
7. Chiego DJ. *Essentials of Oral Histology and Embryology: A Clinical Approach.* 5th ed. Missouri: Elsevier; 2019:67-71.
8. Khoswanto, A High Sucrose Diet Affects Calcium Levels and the Number of Osteoblasts in the Wistar Rat Extraction Socket. *Journal of International Dental and Medical Research.* 2020, 13(1):134-7.
9. Khoswanto C, Quercetin Accelerated Hypoxia Inducible Factor-1 α Expression in Tooth Sockets Wistar Rats. *J Int Dent Med Res* 2022; 15(3): 1043-1045.
10. Shushtari N, Abtahi Froushani SM. Caffeine augments the instruction of anti-inflammatory macrophages by the conditioned medium of mesenchymal stem cells. *Cell J.* 2017; 19(3): 415-24.
11. Su SJ, Chang KL, Su SH, Yeh YT, Shyu HW, Chen KM. Caffeine regulates osteogenic differentiation and mineralization of primary adipose-derived stem cells and a bone marrow stromal cell line. *Int J Food Sci Nutr.* 2013; 64(4): 429-36.
12. Antoniolia L, Hasko G. Caffeine and Bones: If Less Is Good, More May Not Be Better. *Journal Of Caffeine And Adenosine Research.* 2019;9(2): 38-9.
13. Metro D, Cernaro V, Santoro D, et al. Beneficial effects of oral pure caffeine on oxidative stress. *J Clin Transl Endocrinol.* 2017;10:22–7.
14. Paiva CLRS, Beserra BTS, Reis CEG et al. Consumption of coffee or caffeine and serum concentration of inflammatory markers: A systematic review. *Crit. Rev. Food Sci. Nutr.* 2019; 59:652–663.
15. Cornelis MC. The impact of caffeine and coffee on human health. *Nutrients.* 2019;11:416.
16. Tang QY, Kukita T, Ushijima Y, Kukita A et al. Regulation of osteoclastogenesis by Simon extracts composed of caffeic acid and related compounds: successful suppression of bone destruction accompanied with adjuvant-induced arthritis in rats. *Histochem Cell Biol.* 2006;125(3):215–25.
17. Khoswanto C, Hypoxia Inducible Factor 1 α as Key Factor in Wound Healing Post Tooth Extraction: an Overview. *J Int Dent Med Res* 2020; 13(3): 1191-1197