

# Influence of hypertension on oral infections and endodontic treatment

João Eduardo **GOMES-FILHO**<sup>1</sup>

Christine Men **MARTINS**<sup>2</sup>

Gustavo **SIVIERI-ARAUJO**<sup>3</sup>

Ludmilla Mota da Silva **SANTOS**<sup>2</sup>

Índia Olinta de Azevedo **QUEIROZ**<sup>3</sup>

Marcelo Tadahiro **WAYAMA**<sup>4</sup>

Guilherme Hiroshi **YAMANARI**<sup>5</sup>

Eloi **DEZAN-JÚNIOR**<sup>1</sup>

Luciano Tavares Angelo **CINTRA**<sup>6</sup>

## ABSTRACT

Hypertension is characterized by peripheral vascular resistance that leads to blood pressure increase and several systemic changes that may negatively influence one's oral health. Thus, the aim of this study was to conduct a literature review on the influence of hypertension over oral conditions and endodontic treatment. Hypertension mainly affects the blood vessels, brain and kidneys. A hypertensive condition can lead to increased levels of parathyroid hormones, abnormal vitamin D metabolism, reduction in the concentration of ionized calcium and decreased calcium absorption. Therefore, hypertension can be closely associated with oral

problems such as periodontal diseases, implant loss, difficulty in bone healing, reduced salivary flow and protein concentration in saliva, increased number of neutrophils and, as a consequence, favoring of inflammatory processes. It has also been suggested that the success rate of endodontic treatment in hypertensive patients is lower than in normotensive ones. The response of hypertensive patients to root canal treatment, intracanal medications and sealers should be further studied in order to provide knowledge on the changes, failures and success of endodontic treatment.

**Keywords:** Hypertension. Endodontics. Endodontic medicine.

**How to cite this article:** Gomes-Filho JE, Martins CM, Sivieri-Araujo G, Santos LMS, Queiroz IOA, Wayama MT, Yamanari GH, Dezan-Júnior E, Cintra LTA. Influence of hypertension on oral infections and endodontic treatment. *Dental Press Endod.* 2014 Jan-Apr;4(1):21-5.  
doi: <http://dx.doi.org/10.14436/2178-3713.V4.N1.021-025.oar>.

<sup>1</sup>Full professor of Endodontics, School of Dentistry — State University of São Paulo/Araçatuba.

<sup>2</sup>Doctorate student of Dental Science, FOA-UNESP.

<sup>3</sup>Postdoc in Endodontics, FOA-UNESP.

<sup>4</sup>Masters student of Endodontics, FOA-UNESP.

<sup>5</sup>MSc in Endodontics, University of Marília (UNIMAR).

<sup>6</sup>Postdoc in Endodontics, State University of Maringá (UEM).

» The authors report no commercial, proprietary or financial interest in the products or companies described in this article.

Submitted: November 10, 2013. Revised and accepted: December 12, 2013.

Contact address: João Eduardo Gomes-Filho  
Faculdade de Odontologia de Araçatuba, UNESP/Araçatuba  
Rua José Bonifácio, 1193 – CEP: 16015-050 – Araçatuba/SP — Brazil  
Email: [joao@foa.unesp.br](mailto:joao@foa.unesp.br)

## Introduction

Hypertension or “high pressure”, as it is popularly known, occurs when blood pressure is equal or higher than 140/90 mmHg for a young adult. Such increase in pressure is due to vascular remodeling that hinders the passage of blood during its journey in the arteries, causing the heart to work harder than it usually does.<sup>1-4</sup> Heart and blood vessels can be simply compared to a system of taps connected to several hoses. If the tips of the hoses are closed, the pressure inside the taps will increase.

Hypertension is considered a “silent and democratic” chronic disease. It is silent because patients rarely have evident signs or symptoms, which contributes to late diagnosis and treatment. Moreover, it is democratic because it attacks all kinds of people, regardless of sex, age, social class or physical type.<sup>4</sup>

Hypertension is a chronic disorder of multifactorial etiology.<sup>5</sup> Its incidence has increased in the last few years due to changes not only in the dietary pattern and lifestyle of the general population, but also in the growth of the elderly population as well as an increase in human longevity.<sup>6</sup> For this reason, the Brazilian Society of Hypertension and the World Health Organization understood the importance of waging campaigns to raise public awareness about healthy eating habits and physical exercising.<sup>1,7</sup>

Moreover, hypertension is considered a very common disease, even among different age groups. It attacks 25% of the Brazilian adult population<sup>1,7</sup> (data that corroborates the findings of other countries.<sup>8,9</sup>), 50% of people older than 60 and 5% of children and adolescents,<sup>1</sup> affecting not only blood vessels, but also their heart, brain and kidneys.<sup>3,5,10</sup>

Blood vessels present a very thin and delicate inner layer that can be injured by high pressure. Consequently, blood vessels are narrowed and hardened, and can be blocked or broken over time.<sup>1,3,5</sup>

The blockage of a heart vessel causes angina that can lead to a heart attack. On the other hand, blockage or breakage of brain vessels lead to a stroke. High pressure is currently responsible for 40% of cases of myocardial infarction and 80% of cases of stroke. Therefore, the World Health Organization considers it a deadly disease for 9.4 million people worldwide.<sup>1,3,5</sup>

Changes in kidney filtration as well as renal failure can occur. In fact, researches reveal that 25% of renal failure cases are due to hypertension.<sup>1,11</sup> In addition to

that, hypertension also causes systemic changes such as increase in the levels of parathyroid hormones, abnormal vitamin D metabolism, reduction in the concentration of ionized calcium and decreased absorption of calcium.<sup>12</sup> Therefore, a hypertensive condition may increase the mobilization of calcium from the bones and its consequently excretion by the kidneys. Furthermore, it may lead to a secondary activation of parathyroid hormones of which main function is to increase the level of calcium in one's blood by stimulating the breakdown of osteoclasts, as well as by increasing calcium absorption in the intestines via vitamin D activation and calcium resorption of the kidney; thus resulting in loss of calcium in the body. In addition to that, hypertensive patients present alterations in the activity and differentiation of bone cells mediated by angiotensin II.<sup>13-16</sup>

According to the above, clinical and experimental studies have demonstrated a causal relationship between the presence of hypertension and increased loss of calcium from the bones.<sup>12,17,18</sup> More than that, it can be inferred that hypertension may be closely related to dental problems such as periodontal diseases,<sup>19,20,21</sup> high levels of implant failure due to defects that occur during osseointegration,<sup>22</sup> and also difficulty in bone healing after extraction.<sup>23-25</sup>

Therefore, the aim of this study was to conduct a literature review about the influence of hypertension on oral problems and endodontic treatment.

## Relationship between oral health problems and hypertension

Periodontal problems are closely related to hypertension.<sup>19,20,21</sup> Periodontal infection is a source of pathogenic species and inflammatory mediators that can create a systemic inflammatory burden and increase the risk of developing hypertension and other cardiovascular diseases.<sup>26-32</sup>

Bonato et al<sup>26</sup> observed that after induction of inflammation (periodontitis), there is an additional recruitment of neutrophils due to the increased presence of TNF $\alpha$  and other cytokines involved in the emission of signals to the onset of immune responses.<sup>26</sup>

In other words, the presence of local inflammation, such as apical periodontitis, may be systemically interfering due to the fact that hypertensive patients show an increased amount of cells, proteins and chemical mediators involved in the immune response processes.

## Relationship between hypertension and oral health problems

Hypertension causes high blood pressure that may affect the arterioles along the surface of the alveolar bone, leading to a minor hemorrhage.<sup>20,33,34</sup> Patients with systemic diseases may have decreased resistance to bacterial infection as well decreased tissue repair after endodontic treatment.<sup>35,36</sup> Thus, an inflammatory process characterized by circulation of cytokines and chemical mediators with the presence of a microbiota, may be established.<sup>20,33,34</sup> Within this context, Bonato et al<sup>26</sup> observed that hypertensive rats present a higher number of neutrophils in comparison to normotensive rats. Therefore, hypertensive condition seems to favor the inflammatory process that, in turn, is potentiated.

The relationship between oral chronic inflammatory processes of infectious origin, for example, apical periodontitis and periodontal disease, and systemic health is a very interesting aspect that should be covered. In a retrospective study, Segura-Egea et al<sup>37</sup> found that there is a higher prevalence of chronic apical periodontitis in hypertensive patients than in normotensive patients.<sup>37</sup> In 2011, the authors reported that the association between higher blood pressure and smoking habits further increased this prevalence.<sup>38</sup>

Hypertension can also be associated with a high susceptibility to the development of pathologies that impair oral health, which can decrease salivary flow and protein concentration of saliva. Elias et al<sup>39</sup> found that salivary flow and average concentration of proteins in saliva were reduced, but with no changes in salivary amylase activity in hypertensive cases. Additionally, the authors also observed, by means of microhardness analysis, that teeth of hypertensive rats have lower enamel and dentin resistance.<sup>39</sup> Furthermore, Inoue et al<sup>40</sup> suggested that the mechanism of mineralization in hypertensive rats is abnormal, given that their trabecular bone presented a lower mineral state in both young and adult rats.

Moreover, hypertension can cause negative histometric and molecular changes in the alveolar bone, even in the absence of an inflammatory process. According to Bastos et al,<sup>24</sup> there is an increased expression of RANKL protein and a higher ratio of RANKL/OPG proteins that, when combined with other factors, decrease bone density. RANKL protein is closely related to the activation of osteoclasts responsible for the

reabsorption process, whereas OPG protein is an osteoclastogenesis inhibitory factor. These data suggest that a hypertensive condition may directly affect the alveolar bone. Zhang et al<sup>41</sup> also found that bone mineral density is lower in hypertensive rats in comparison to normotensive rats, thus confirming increased bone loss in the presence of high blood pressure.

Corroborating and further investigating these results, Bastos et al<sup>25</sup> conducted a study in hypertensive rats and observed that not only the bone density of pre-existing bone is affected by hypertension, but also the newly formed tissue of the spinal region. In that study, the trabecular bone area of normotensive 150-day old rats was considerably larger than in hypertensive rats. Moreover, 8 days after bone defect was carried out, bone formation in hypertension rats was significantly lower.

It has been suggested that hypertension may contribute to difficult in retention of endodontically treated teeth. Mindiola et al<sup>42</sup> observed that 7.8% of endodontically treated teeth of hypertensive patients were not satisfactory. Additionally, further aggregation of diabetes to this systemic condition increased that rate. Altogether, these data justify the hypothesis that systemic diseases, such as diabetes mellitus, coronary artery disease and hypertension, increase the risk of tooth extraction after endodontic treatment or retreatment.<sup>43</sup>

## Relationship between hypertension and Endodontics

According to the aforementioned information, hypertension promotes systemic changes that are directly related to the oral condition, healing and bone formation, mineralization processes and the process of speeding up an infection. Furthermore, these changes may be responsible for endodontic treatment failure in those patients.

Periodontal disease and chronic apical periodontitis share a common microbiota composed of anaerobic gram negative bacteria, in addition to being similar inflammatory processes.<sup>44,45</sup> Therefore, in this context, a possible association can be established between hypertension and endodontic treatment.

Endodontic treatment aims to restore the normality of lost apical and periapical tissues<sup>46,47</sup> by means of not only deeply cleaning and disinfecting the root canal system so as to control pathogenic microorganisms,

but also through complete three-dimensional sealing of the root canal with filling materials that present adequate physical and biological properties for tissue repair, by means of inducing mineralization.<sup>48-50</sup>

Some materials used in endodontic treatment function as anti-inflammatory and antibacterial drugs, as well as inducers of osteogenesis and cementogenesis.<sup>48-52</sup> Calcium hydroxide is widely used during endodontic treatment, given that it eliminates bacteria and their toxins, has an anti-inflammatory action, neutralizes acid products and activates alkaline phosphatase. All these functions are associated with tissue and bone repair processes. In addition to calcium hydroxide, MTA also induces osteogenesis and cementogenesis.<sup>48,52-57</sup>

Hence, the response of hypertensive patients to endodontic treatment, intracanal medications and sealers should be further studied in order to provide knowledge on the changes, failures and success of endodontic treatment.

## Conclusion

Based on the results of this study it is reasonable to conclude that hypertension influences patients' overall oral health and seems to be related to success in endodontic treatment. The response of hypertensive patients to root canal treatment, intracanal medications and sealers should be further studied, in order to provide knowledge on the changes, failures and success of endodontic treatment.

## References

1. World Health Organization. A global brief on hypertension: silent killer, global public health crisis. Geneva: World Health Organization; 2013.
2. Johnson RJ, Feig DI, Nakagawa T, Sanchez-Lozada LG, Rodriguez-Iturbe B. Pathogenesis of essential hypertension: historical paradigms and modern insights. *J Hypertens*. 2008;26(3):381-91.
3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42(6):1206-52.
4. Lessa I. Epidemiologia da hipertensão arterial sistêmica e da insuficiência cardíaca no Brasil. *Rev Bras Hipertens*. 2001;8(4):383-92.
5. Carretero OA, Oparil S. Essential hypertension: part I - definition and etiology. *Circulation*. 2000;101:329-35.
6. Passos VMA, Assis TD, Barreto SM. Hipertensão arterial no Brasil: estimativa de prevalência a partir de estudos de base populacional. *Epidemiol Serv Saúde*. 2006;15(1):35-45.
7. Sociedade Brasileira de Hipertensão. Hipertensão: silenciosa, doença atinge um em cada três brasileiros. Sociedade Brasileira de Hipertensão, 2013 [Acesso 2013 Nov 18]. Disponível em: <http://www.sbh.org.br/geral/sbh-na-midia.asp?id=416>.
8. Nguyen QC, Tabor JW, Entzel PP, Lau Y, Suchidran C, Hussey JM, et al. Discordance in national estimates of hypertension among young adults. *Epidemiology*. 2011;22(4):532-41.
9. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365(9455):217-23.
10. Pierdomenico SD, Di Nicola M, Esposito AL, Di Mascio R, Ballone E, Lapenna D, et al. Prognostic value of different indices of blood pressure variability in hypertensive patients. *Am J Hypertens*. 2009;22(8):842-7.
11. World Health Organization Guidelines Subcommittee. 1999 World Health Organization-International Society of Hypertension guidelines for the management of hypertension. *J Hypertens*. 1999;17:151-83.
12. Izawa Y, Sagara K, Kadota T, Makita T. Bone disorders in spontaneously hypertensive rat. *Calcif Tissue Int*. 1985;37(6):605-7.
13. Nakagami H, Morishita R. Hormones and osteoporosis update. Effect of angiotensin II on bone metabolism. *Clin Calcium*. 2009;19(7):997-1002.
14. Oshima T, Young EW. Systemic and cellular calcium metabolism and hypertension. *Semin Nephrol*. 1995;15(6):496-503.
15. Young EW, McCarron DA, Morris CD. Calcium regulating hormones in essential hypertension. Importance of gender. *Am J Hypertens*. 1990;3(8 Pt 2):161S-6S.
16. McCarron DA, Pingree PA, Rubin RJ, Gaucher SM, Molitch M, Krutik S. Enhanced parathyroid function in essential hypertension: a homeostatic response to a urinary calcium leak. *Hypertension*. 1980;2(2):162-8.
17. Tsuda K, Nishio I, Masuyama Y. Bone mineral density in women with essential hypertension. *Am J Hypertens*. 2001;14(7 Pt 1):704-7.
18. Cappuccio FP, Meilahn E, Zmuda JM, Cauley JA. High blood pressure and bone-mineral loss in elderly white women: a prospective study. *Study of Osteoporotic Fractures*. *Lancet*. 1999;354(9183):971-5.

19. Holmlund A, Holm G, Lind L. Severity of periodontal disease and number of remaining teeth are related to the prevalence of myocardial infarction and hypertension in a study based on 4,254 subjects. *J Periodontol*. 2006;77(7):1173-8.
20. Leite CL, Redins CA, Vasquez EC, Meyrelles SS. Experimental-induced periodontitis is exacerbated in spontaneously hypertensive rats. *Clin Exp Hypertens*. 2005;27(6):523-31.
21. Angeli F, Verdecchia P, Pellegrino C, Pellegrino RG, Pellegrino G, Prosciutti L, et al. Association between periodontal disease and left ventricle mass in essential hypertension. *Hypertension*. 2003;41(3):488-92. Epub 2003 Feb 10.
22. Alsaadi G, Quirynen M, Komárek A, van Steenberghe D. Impact of local and systemic factors on the incidence of late oral implant loss. *Clin Oral Implants Res*. 2008;19(7):670-6.
23. Manrique N, Pereira CCS, Garcia LMG, Micaroni S, Carvalho AAF, Perri SHV, et al. Alveolar bone healing process in spontaneously hypertensive rats (SHR), A radiographic densitometry study. *J Appl Oral Sci*. 2012;20(2):222-7.
24. Bastos MF, Brilhante FV, Bezerra JP, Silva CA, Duarte PM. Trabecular bone area and bone healing in spontaneously hypertensive rats. A histometric study. *Braz Oral Res*. 2010;24(2):170-6.
25. Bastos MF, Brilhante FV, Gonçalves TED, Pires AG, Napimoga MH, Marques MR, et al. Hypertension may affect tooth-supporting alveolar bone quality: a study in rats. *J Periodontol*. 2010;81(7):1075-83.
26. Bonato CF, do-Amaral CCF, Belini L, Salzedas LMP, Oliveira SHP. Hypertension favors the inflammatory process in rats with experimentally induced periodontitis. *J Periodontol Res*. 2012;2:1-10.
27. Vidal F, Figueredo CM, Cordovil I, Fischer RG. Periodontal therapy reduces plasma levels of interleukin- 6, C-reactive protein, and fibrinogen in patients with severe periodontitis and refractory arterial hypertension. *J Periodontol*. 2009;80(5):786-91.
28. Golub LM, Payne JB, Reinhardt Ra, Nieman G. Can Systemic diseases co-induce (not just exacerbate) periodontitis? A Hypothetical "two-hit" model. *J Dent Res*. 2006;85(2):102-5.
29. Boos CJ, Lip GY. Elevated high-sensitive C-reactive protein, large arterial stiffness and atherosclerosis: A relationship between inflammation and hypertension? *J Hum Hypertens*. 2005;19(7):511-3.
30. Beck JD, Offenbacher S. Systemic effects of periodontitis: Epidemiology of periodontal disease and cardiovascular disease. *J Periodontol*. 2005;76(Suppl.):2089-100.
31. De Nardin E. The role of inflammatory and immunological mediators in periodontitis and cardiovascular disease. *Ann Periodontol*. 2001;6(1):30-40.
32. Haraszthy VI, Zambon JJ, Trevisan M, Zeid M, Genco RJ. Identification of periodontal pathogens in atheromatous plaques. *J Periodontol*. 2000;71(10):1554-60.
33. Tsioufis C, Kasiakogias A, Thomopoulos C, Stefanadis C. Periodontitis and blood pressure: the concept of dental hypertension. *Atherosclerosis*. 2011;219(1):1-9.
34. Ford PJ, Yamazaki K, Seymour GJ. Cardiovascular and oral disease interactions: what is the evidence? *Prim Dent Care*. 2007;14(2):59-66.
35. Joshupura KJ, Pitiphat W, Hung HC, Willett WC, Colditz GA, Douglass CW. Pulpal inflammation and incidence of coronary heart disease. *J Endod*. 2006;32(2):99-103.
36. Eriksen HM. Epidemiology of apical periodontitis. In: Ørstavik D, Pitt Ford TR, editors. *Essential endodontology: prevention and treatment of apical periodontitis*. Oxford: Blackwell Science; 1998. p. 179-91.
37. Segura-Egea JJ, Jimenez-Moreno E, Calvo-Monroy C, Rios-Santos JV, Velasco-Ortega E, Sánchez-Domínguez B, et al. Hypertension and dental periapical condition. *J Endod*. 2010;36(11):1800-4.
38. Segura-Egea JJ, Castellanos-Cosano L, Velasco-Ortega E, Rios-Santos JV, Llamas-Carreras JM, Machuca G, et al. Relationship between smoking and endodontic variables in hypertensive patients. *J Endod*. 2011;37(6):764-7.
39. Elias GP, Santos OAM, Sasaki KT, Delbem ACB, Antoniali C. Dental mineralization and salivary activity are reduced in offspring of spontaneously hypertensive rats (SHR). *J Appl Oral Sci*. 2006;14(4):253-9.
40. Inoue T, Moriya A, Goto K, Tanaka T, Inazu M. What is the difference of bone growth in SHR and SD rats? *Clin Exp Pharmacol Physiol*. 2007;22(1):242-3.
41. Zhang YF, Wang YXJ, Griffith JF, Kwong WKM, Ma HT, Qin L, Kwok TCY. Proximal femur bone marrow blood perfusion indices are reduced in hypertensive rats: a dynamic contrast-enhanced MRI study. *J Magn Reson Imaging*. 2009;30(5):1139-44.
42. Mindiola MJ, Mickel AK, Sami C, Jones JJ, Lalumandier JA, Nelson SS. Endodontic treatment in an American indian population: a 10-year retrospective study. *J Endod*. 2006;32(9):828-32.
43. Wang CH, Chueh LH, Che SC, Feng YC, Hsiao CK, Chiang CP. Impact of diabetes mellitus, hypertension and coronary artery disease on tooth extraction after nonsurgical endodontic treatment. *J Endod*. 2011;37(1):1-5.
44. Martinho FC, Chiesa WM, Leite FR, Cirelli JA, Gomes BP. Antigenic activity of bacterial endodontic contents from primary root canal infection with periapical lesions against macrophage in the release of interleukin-1beta and tumor necrosis factor alpha. *J Endod*. 2010;36(9):1467-74.
45. Rôças IN, Alves FR, Santos AL, Rosado AS, Siqueira JF Jr. Apical root canal microbiota as determined by reverse-capture checkerboard analysis of cryogenically ground root samples from teeth with apical periodontitis. *J Endod*. 2010;36(10):1617-21.
46. Nakamura H. Success rate of endodontic treatment of teeth with vital and nonvital pulps. A meta-analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2004;97(1):95-9.
47. Holland R, Otoboni Filho JA, de Souza V, Nery MJ, Bernabé PF, Dezan E Jr. A comparison of one versus two appointment endodontic therapy in dogs' teeth with apical periodontitis. *J Endod*. 2003;29(2):121-4.
48. Gomes-Filho JE, Watanabe S, Bernabé PFE, Costa MTM. A mineral trioxide aggregate sealer stimulated mineralization. *J Endod*. 2009;35(2):256-60.
49. Gomes-Filho JE, Bernabé PFE, Nery MJ, Otoboni-Filho JA, Dezan-Junior E, Costa MTM, et al. Reaction of rat connective tissue to a new calcium hydroxide-based sealer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;106(2):e71-6.
50. Valera MC, Anbinder AL, Leonardo MR, Parizoto NA, Kleinke MU. Cimentos endodônticos: análise morfológica imediata e após seis meses utilizando microscopia de força atômica. *Pesquisa Odontol Bras*. 2000;14(3):199-204.
51. Bernades RA, Campelo AA, Junior DS, Pereira LO, Duarte MAH, Moraes IG, Bramante CM. Evaluation of the flow rate of 3 endodontic sealers: Sealer 26, AH Plus, and MTA Obtura. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;109(1):e47-9.
52. Gomes-Filho JE, Watanabe S, Gomes AC, Faria MD, Lodi CS, Penha SH. Evaluation of the effects of endodontic materials on fibroblast viability and cytokine production. *J Endod*. 2009;35(11):1577-9.
53. Estrela C, Estrada-Bernabé PF, de Almeida-Decurcio D, Almeida-Silva J, Estrela CRA, Poli-Figueiredo JA. Microbial leakage of MTA, Portland cement, Sealapex and zinc oxide-eugenol as root-end filling materials. *Med Oral Patol Oral Cir Bucal*. 2011;16(3):e418-24.
54. De-Deus G, Souza MCB, Fidel RAS, Fidel SR, Campos RC, Luna AS. Negligible expression of arsenic in some commercially available brands of portland cement and mineral trioxide aggregate. *J Endod*. 2009;35(6):887-90.
55. Accorinte Mde L, Holland R, Reis A, Bortoluzzi MC, Murata SS, Dezan E Jr, et al. Evaluation of mineral trioxide aggregate and calcium hydroxide cement as pulp-capping agents in human teeth. *J Endod*. 2008;34(1):1-6.
56. Bramante CM, Demarchi ACCO, Moraes IG, Bernadineli N, Garcia RB, Spangberg LSW, et al. Presence of arsenic in different types of MTA and white and gray Portland cement. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;106(6):909-13.
57. Bernabé PF, Gomes-Filho JE, Rocha WC, et al. Histological evaluation of MTA as a root-end filling material. *Int Endod J*. 2007;40(10):758-65.