Toward a Putative Paradigm Shift in Direct Pulp Capping?

KAMEL EARAR[1], MIHAELA GABRIELA LUCA[2]*, ANAMARIA ZAHARESCU[1]*, ANDREI ILIESCU[3], SILVIA MARTU[4], ALEXANDRU-ANDREI ILIESCU[5]

[1]Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, Department of Dentistry, 47 Domneasca Str., 800008, Galati, Romania

[2]University of Medicine and Pharmacy, 38 Gheorghe Marinescu Str., 540072, Targu Mures, Romania

[3]University of Medicine and Pharmacy Carol Davila, 8 Eroii Sanitari Blvd., Bucharest, Romania

[4]Grigore T.Popa University of Medicine and Pharmacy, 16 Universitatii Str., 700115, Iasi, Romania

[5]University of Medicine and Pharmacy of Craiova, Romania, Faculty of Dentistry, Department of Oral Rehabilitation, 2 Petru Rares Str., 200349, Craiova Romania

Conventionally the cases accepted for direct pulp capping are the inadvertently exposed normal pulps and carious exposures in teeth without apical radiolucency. The recent advances in dental materials, namely the bioceramics, allowed successful vital therapy by direct pulp capping even in young permanent teeth with irreversible pulpitis. The choice of pulp capping material is pivotal in pulp vital therapy of carious exposures as tricalcium silicates shift the balance inflammation-healing toward the regeneration of damaged dentin-pulp complex. Anticipating a reliable outcome, the high anti-inflammatory potential and modulating capacity of cytokines and growth factors proved by bioactive endodontic cements in direct pulp capping should be associated with new molecular diagnostic tests and cautious clinical evaluation. However, it seems that a paradigm shift is expected in the decision of direct pulp capping.

Keywords: carious exposure, direct pulp capping, tricalcium silicates, paradigm shift

Commonly the direct pulp capping is defined as a procedure of conservative treatments used to maintain on long-term the vitality of pulpal tissue damaged by an inadvertent pulp chamber exposure during caries removal, tooth preparation or trauma. The operative decision mandatory presumed a previous healthy status of dental pulp without clinical symptoms of irreversible inflammation [1-3].

Many decades the medication of choice aiming to preserve the pulp vitality was a local dressing with calcium hydroxide, which was placed over the unwanted pinpoint aperture of endodontic space [3]. Although before and after clinical use of calcium hydroxide a lot of some other biocompatible dental materials were suggested for the management of exposed pulp it was observed that a successful outcome mainly relies on hampering the bacterial microinfiltration [4].

In the late 1990s it was introduced a promising capping agent, the mineral trioxide aggregate (MTA), which progressively substituted the former calcium hydroxide in clinical practice [1-3]. Pretty soon other materials mainly belonging to bioceramics, also termed bioactive endodontic cements, which similar to MTA release calcium hydroxide during setting came up as tough competitors owing to their superior handling properties and improved ability in pulp healing [5].

Tissue healing direct pulp capping

Histological the main goal of direct pulp capping is to achieve a mineralized barrier able to completely close the former mechanical or traumatic opening of pulp chamber and to support the long-term vitality of damaged tooth [6].

Since 1930 calcium hydroxide was used in endodontic practice almost 70-80 years as dressing of choice due to its antimicrobial high alkalinity and capacity to stimulate the pulp defense by forming tertiary reparatory dentine [1,3]. However, this capping material revealed a lot of shortcomings such as the poor marginal seal against the microleakage, interfacial detachment during subsequent application of final coronal restorative materials, and progressive resorption resulting in a gap that plays the role of a reservoir for subsequently infiltrated biofilms [3,7].

Actually the main disadvantage of calcium hydroxide dressing consists in its inability to generate a homogenous and impermeable barrier of reparative dentin aiming to guarantee a real protection of subjacent pulp tissue against the pathways of bacterial penetration. Its subsequent disintegration worsens the shortcomings. Moreover, even though clinically successful, the direct pulp capping based on calcium hydroxide is histological characterized by additional limited tissue necrosis and mild to moderate inflammatory response [3,7,8].

Nevertheless it has to be highlighted the differences in pulpal effects between pure calcium hydroxide and the hard setting one. The high alkaline *p*H of pure calcium hydroxide when directly placed on pulp wound induces a liquefaction necrosis of most superficial damaged tissue layers and a coagulation necrosis at the border between the remaining vital pulp underneath and upper juxtaposed necrotic layers [7,8].

The inherent inflammatory reaction is practically mild and the pulpal connective tissue non-infected, so that the tertiary reparatory dentin build up is initiated and the hard tissue bridge finally closes the previous exposed pulp. In case of direct pulp capping using hard setting calcium hydroxide the superficial necrosis of pulp is almost avoided and the healing is improved [7,8].

Without any doubt the MTA promotion as direct capping agent was a veritable acquisition in successful maintenance of pulp vitality [9,10]. Experimentally was proved that in previously healthy pulps MTA direct capping resulted in precocious healing deprived of inflammation and finalized after 3 months with a homogenous hard tissue barrier similar to dentin since resembles hydroxyapatite

*email: gabrielaluca@yahoo.com; anamaria_zaharescu@yahoo.com

In this paper, all authors have an equal contribution as the first author.

[7,8]. In contrast, the hard setting calcium hydroxide Dycal induces a non-homogenous mineralized bridge characterized by numerous tunnel defects overlaying an acute or chronic inflammation of pulp tissue [7].

Novel pulp capping materials

These newcomers are bioactive endodontic cements of various chemical compositions despite the common basic content in calcium silicates. Presently all MTA based cements are considered alkalinizing dental materials releasing bio-interactive ions since subsequent to the hydration mechanism is formed a precipitate of calcium hydroxide and a hydrogel of calcium silicate hydrate. Finally, by chemical reaction with phosphorus ions from surrounding tissue fluids are born crystals of hydroxyapatite [11,12].

Actually bioactive endodontic cements, also routinely termed bioceramics, develop a common beneficial healing effect regardless their use in indirect or direct pulp capping, and other vital treatments such as partial or cervical pulpotomy. These dental materials are differentiated in resorbable, porous and bio-interactive. Additionally the bioceramics are frequently used in endodontic surgery in root perforation repair, apexification, retrograde fillings, and as root canal sealers [5,13,14].

Unlike the basic biocompatibility, to an appropriate clinical use, the bioceramic pulp capping materials demonstrated trouble-free manipulating properties, fast setting and sufficient working time. Other much expected properties are antimicrobial activity, the proper and non-impeded sealing at direct contact with blood, insolubility in tissue fluids, dimensional static and dynamic stability, non-staining quality, and adequate radiopacity [15,16].

The reason of promoting the increasing clinical use of bioactive endodontic cements relies upon their implication in tissue mineralization and strong adhesion to hard tissues of tooth, stimulation of dentinogenesis, cemenogenesis and bone healing [11,13,14,17-20].

Tissue response in inadvertent exposure of dental pulp

Usually in inadvertent opening of pulp chamber an established chronic inflammation is already present owing to the long-term progress of deep caries [1]. The lipoteichoic acid, an important inflammatory byproduct of gram-positive cariogenic bacteria, induce in odontoblasts, the first pulp cells opposing to the advancement front of dentin caries, the expression of some toll-like receptor family (TLR) belonging to pattern recognition receptors (TLR3, TLR5, and TLR9). Gram-negative bacteria stimulate TLR2, another toll-like receptor of odontoblasts [21,22].

A cascade of molecular events is released by excited toll-like receptors and the various proinflammatory cytokines and chemokines subsequently secreted by odontoblasts are involved in local recruitment of chronic inflammatory cells such as lymphocytes, macrophages and plasma cells. Simultaneously a capillary sprouting is associated to the chronic cellular infiltrate, which is increasing in density. Progressively the odontoblasts also participate in specific immune response by elaborating immunoglobulin IgG, IgM, IgA and maintaining the inflammatory response [23-26].

The complement system is also highly involved in pulp defense as its fractions C3a, C4a, and C5a participate in secretion of inflammatory mediators and recruitment of immune cells. C3a is particularly stimulating the proliferation of pulp fibroblasts and dental pulp stem cells (DPSC). It also supports the DPSC mobilization toward the site of tissue damage. C5a demonstrated to be active in DPSC, macrophages and monocytes recruitment, and nerve growth factor release by pulp fibroblasts [27].

The traumatic pulp injury produced during the opening of pulp chamber initially worsens the local tissue lesions related to the previous inflammatory destruction. Nevertheless, the healing aimed by direct pulp capping evolves covering basic biological processes, which are interacting as inflammation, cell proliferation, and tissue remodeling [3,28,29].

Since the primary odontoblasts and a limited pulp tissue are mechanically destroyed, the histological feature is dominated by hemorrhagic foci with extravasated erythrocytes, exudated fibrinogen, necrotic areas, infected dentin chips traumatically inserted, and an acute inflammatory infiltration controlled by neutrophils [3].

Despite the additional aggravated inflammation the pulp capping agents are called to start the regenerative process of dentin-pulp complex relying on still surviving dental pulp stem cells located in various pulp niches and to promote their multiplication, migration to the site of injury and differentiation in odontoblast-like cells (secondary odontoblasts) [3,28,29].

Involvement of tricalcium silicate in pulp healing

Nowadays obviously the most indicated dental material in direct pulp capping is MTA [5]. As milestone of bioactive endodontic cements, MTA induce a mineralized barrier of impermeable reactionary dentin similar to hydroxyapatite. Though releasing calcium ions supporting the tertiary dentinogenesis, MTA also has an excellent marginal adaptation, which in addition to its high alkaline pH (12,5), hydrophilicity and promotion of active diffusion in dentinal tubules of hydroxyl ions impedes the survival of residual bacteria [3,18].

The *in vitro* formation of either hydroxyapatite or carbonat apatite at the surface of MTA and similar cements coming in contact with phosphate-containing liquids is a strong argument proving their bioactivity [9]. The bioactive endodontic cements used in pulp capping stimulate tissue mineralization and biomaterial-dentine interface formation due to their direct adhesion at the tooth calcified tissues [14].

The amount of new generated apatite crystals is directly related to the exposure time in phosphate containing fluids of aforementioned MTA hydration products, calcium hydroxide and calcium silicate hydrate [11,12].

Pulp healing in direct pulp capping supposes the resolution of inflammation and induction of calcified bridge. It was proved that, based on calcium and silicone ions release, the soluble components of tricalcium silicate cements prompt various bioactive molecules such as anti-inflammatory cytokines and growth factors to orchestrating the dentin-pulp complex regeneration [30].

It seems that lipoxins LXA4 and LXB4 are promptly inactivating pro-inflammatory mediators such as prostaglandins and leukotrienes, and cytokines TNF-α and IL-6, as well. Among the anti-inflammatory cytokines has to be highlighted the pivotal role of IL-10, which suppresses the potent pro-inflammatory cytokines TNF-α, IL-1β, Il-6, IL-8, IL-12, and IFN-γ. The inflammatory proteolyses of pulp tissue induced after injury by MMP-1 and MMP-9 is down-regulated owing to cytokine IL-4 [26].

A recent comparative study of calcium hydroxide and tricalcium silicate cements proved the efficiency of pulp capping materials since they decreased the expression of pro-inflammatory cytokines IL-1β and Il-6 in addition to up-regulation of dentin matrix protein-1 (DMP1) and dentin sialophosphoprotein (DSPP), which are well-known

markers demonstrating the odontoblast-like cells differentiation [31].

As direct pulp capping materials, the bioactive endodontic cements also activate the complement, which is involved in both pulp inflammation and regeneration. This mechanism relies upon their surface modification after exposing to tissue fluids, which activates Hageman Factor XII and on carboxylic, OH or NH_3 groups from own chemical structure [27].

Compared clinically and histological to calcium hydroxide that previously was used as conventional capping agent, MTA-based cements exhibit an improved pulp healing by reducing inflammation outcomes and contributing to a thicker and complete mineralized bridge formation [28].

Extending the direct pulp capping in endodontic pathology

Many decades the direct pulp capping was recommended to preserving the vitality of tooth pulp exposed mechanically or traumatic, which was free of signs and symptoms of irreversible inflammation [3].

Several factors were considered for the successful outcome: size of pulpal exposure, pulp contamination, presence of dentinal chips, control of bleeding and plasma exudates, extruded pulpal tissue, pulp capping agent, and embolization of capping materials [33].

Even still controversial in common practice the direct pulp capping was extended from previously clinical healthy dental pulps to carious exposed pulps with obvious clinical signs and symptoms of irreversible inflammation [34,35].

One of these studies, performed on 44 teeth with carious exposed pulps and clinical symptoms of irreversible pulpitis (spontaneous lingering pain, evoked thermal sensitivity, positive response at percussion) by using a fast setting calcium hydroxide cement (Dycal) as direct capping material, recorded a success rate of 81.8%. A higher success was observed in cases under 40 years than in patients over 40's, and in molars compared to the other types of teeth. However, the differences were not significant. Neither the clinical vitality tests (electric and thermal, at cold and hot stimuli) nor axial percussion of tooth indicated statistically significant differences [34].

Though non-significant, the pin-point exposure (0.5 mm) had a lower favorable outcome (84.2%) than the exposures with diameter between 0.5-1 mm (86.7%). The lowest success rate (77.8%) was seen in exposure sizes between 1-2 mm. The study promotes the opinion that the degree of bleeding as clinical marker of inflammatory status might be a putative index of success prognosis in direct pulp capping since [34]. However, while applying a direct capping shall be considered more relevant the levels in inflamed pulp of biological markers IgG, IgM, IgA, prostaglandins, substance P, elastase and other matrix metalloproteinases, hopefully chairside collected in the future [35,36].

During last decade the key dental materials used in direct pulp capping are un-doubtfully the bioactive endodontic cements such as MTA or Biodentine, which are increasingly replacing the old-timer calcium hydroxide since they proved to be both efficient suppressors of prostaglandins and pro-inflammatory cytokines, and up-regulators of odontoblast-like cells differentiation or growth factors involved in pulp regeneration [37-39].

Relying on the improvement that bioactive endodontic cements brought in healing ability of pulp injuries, despite the conventional advice of performing the direct pulp capping only in mechanical or traumatic exposure, the vital therapy by this procedure was also successfully extended either in clinical cases of carious exposure having the size of pulp chamber opening up to 2.5 mm or in cases associated with reversible pulpitis, irreversible pulpitis, and even early periapical radiolucency [36,38-40].

Recently was reported a successful outcome as high as 94.5% of direct pulp capping using ProRoot MTA and Biodentine in cariously exposed pulp with both types of pulpitis, reversible and irreversible, and imagistic apical involvement [37].

The teeth with periapical radiolucency obviously are a challenge [37,39]. However, the radiological image is not mandatory corresponding to pulp necrosis since the neurogenic inflammation supported by neuropeptides may mimic the apical demineralization associated to an infected root canal. Undergoing a direct pulp capping with MTA in cariously exposed pulps such teeth healed successfully in 76% of cases proving that if reversible damaged the vital pulp may recover after the removal of microbial stimuli [37].

Moreover the pulp capping was performed in young permanent teeth with wide-open apices, rich vascularization and cellularity. Accordingly, unlike the vital pulpotomy resulting in partial removal of the pathological pulp tissue, the healing confirmed after a follow-up period of 6-54 months in direct pulp capping can be explained only by immune defense response [39-42].

Further clinical studies should confirm this very attractive therapeutic approach of carious exposures in young permanent teeth, which it seems to promote a new paradigm in vital pulp therapy.

Conclusions

The choice of pulp capping material is pivotal in pulp vital therapy of carious exposures. Tricalcium silicates shift the balance inflammation-healing toward the regeneration of damaged dentin-pulp complex. The high anti-inflammatory potential and modulating capacity of cytokines and growth factors proved by bioactive endodontic cements in direct pulp capping of young permanent teeth, associated to new molecular diagnostic tests, open the opportunity of increased success rates to conservatively approaching the carious exposures even in cases diagnosed as irreversible pulpitis.

References

1. FOUAD A.F., LEVIN L., Pulpal reactions to caries and dental procedures. In: Hargreaves K.M., Cohen S. (eds). Cohen's pathways of the pulp, 10th ed. Mosby, St.Louis, 2011, 504-528.
2. TORABINEJAD M., CHIVIAN N., Clinical applications of mineral trioxide aggregate. J Endod; 1999;25:197-205.
3. BOGEN G., CHANDLER N.P., Vital pulp therapy. In: Ingle JI, Bakland L.K., Baumgartner J.C. (eds). Ingle's endodontics 6, 6th ed. BC Decker, Hamilton, 2008, 1310-1329.
4. COX C.F., KEALL C.L., KEAL H.J., OSTRO E., BERGENHOLTZ G., Biocompatibility of surface-sealed dental materials against exposed pulp. J Prosthet Dent; 1987;57:1-8.
5. PARIROKH M., TORABINEJAD M., DUMMER P.M.H., Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview – part I: vital pulp therapy. Int Endod J; 2018;51:177-205.
6. ***AAE (American Association of Endodontists), Glossary of endodontic terms. 9th ed. Chicago, 2016.
7. NAIR P.N.R., DUNCAN H.F., PITT FORD T.R., LUDER H.U., Histological, ultrastructural and quantitative investigations on the response of healthy human pulps to experimental capping with mineral trioxide aggregate: a randomized controlled trial. Int Endod J; 2008;41:128-150.
8. SIGURDSSON A., TROPE M., CHIVIAN N., The role of endodontics after dental traumatic injuries. In: Hargreaves K,M,, Cohen S. (eds). Cohen's pathways of the pulp, 10th ed. Mosby, St.Louis, 2011, 620-654.

9. SARKAR N.K., CAICEDO R., RITWIK P., MOISEYEVA R., KAWASHIMA I., Physicochemical basis of the biologic properties of mineral trioxide aggregate. J Endod; 2005;31:97-100.
10. BERZINS D.W., Chemical properties of MTA. In: Torabinejad M. (ed). Mineral trioxide aggregate. Properties and clinical applications. Wiley Blackwell, Oxford, 2014, 17-35.
11. ONCEL TORUN Z., TORUN D., DEMIRKAYA K., YAVUZ S.T., ELCI M.P., SARPER M., AVCU F., Effects of iRoot BP and white mineral trioxide aggregate on cell viability and the expression of genes associated with mineralization. Int Endod J; 2015;48:986-993.
12. SHOKOUHINEJAD N., NEKOOFAR M.H., RAZMI H., SAJADI S., DAVIES T.E., SAGHIRI M.A., GORJESTANI H., DUMMER P.M.H., Bioactivity of EndoSequence Root Repair Material and Bioaggregate. Int Endod J; 2012;45:1127-1134.
13. PARIROKH M., TORABINEJAD M., Calcium silicate-based cements. In: Torabinejad M. (ed). Mineral trioxide aggregate. Properties and clinical applications. Wiley Blackwell, Oxford, 2014, 281-332.
14. MODARESZADEH M.R., DI FIORE P.M., TIPTON D.A., SALAMAT N., Cytotoxicity and alkaline phosphatase activity evaluation of EndoSequence root repair material. J Endod; 2012;38:1101-1105.
15. GARTNER A.H., DORN S.O., Advances in endodontic surgery. Dental Clinics North Am; 1992;36:357-378.
16. DAMAS B.A., WHEATER M.A., BRINGAS J.S., HOEN M.M., Cytotoxicity comparison of mineral trioxide aggregates and EndoSequence bioceramic root repair materials. J Endod; 2011;37:372-375.
17. PARIROKH M., TORABINEJAD M., Mineral trioxide aggregate: a comprehensive literature review - Part I: chemical, physical, and antibacterial properties. J Endod; 2010;36:16-27.
18. LOVATO K.F., SEDGLEY C.M., Antibacterial activity of EndoSequence root repair material and ProRoot MTA against clinical isolates of Enterococcus faecalis. J Endod; 2011;37:1542-1546.
19. ZHANG J., ZHU L., PENG B., Effect of BioAggregate on osteoclast differentiation and inflammatory bone resorption *in vivo*. Int Endod J; 2015;48:1077-1085.
20. MA J., SHEN Y., STOJICIC S., HAAPASALO M., Biocompatibility of two novel root repair materials. J Endod; 2011;37:793-798.
21. ROCAS I.N., LIMA K.C., ASSUNCAO I.V., GOMES P.N., BRACKS I.V., SIQUEIRA J.F., Advanced caries microbiota in teeth with irreversible pulpitis. J Endod; 2015;41:1450-1455.
22. HAHN C.L., LIEWEHR F.R., Relationship between caries bacteria, host responses, and clinical signs and symptoms of pulpitis. J Endod; 2007;33:213-219.
23. BRUNO K.F., SILVA J.A., SILVA T.A., BATISTA A.C., Alencar A.H.G., Estrela C., Characterization of inflammatory cell infiltrate in human dental pulpitis. Int Endod J; 2010;43:1013-1021.
24. CARROUEL F., STAQUET M.J., KELLER J.F., BAUDOUIN C., MSIKA P., BLEICHER F., ALLIOT-LICHT B., FARGES J.C., Lipopolysaccharide-binding protein inhibits toll-like receptor 2 activation by lipoteichoic acid in human odontoblast-like cells. J Endod; 2013;39:1008-1014.
25. CHANG J., ZHANG C., TANI-ISHII N., SHI S., WANG C.Y., NF-kappaB activation in human dental pulp stem cells by TNF and LPS. J Dent Res; 2005;84:994-998.
26. FOUAD A.F., HUANG G.T.J., Inflammation and immunological responses. In: Ingle JI, Bakland L.K., Baumgartner J.G. (eds). Ingle's endodontics 6. 6th ed. BC Decker Inc, Hamilton, 2008, 343-375.
27. GIRAUD T., RUFAS P., CHMILEWSKY F., ROMBOUTS C., DEJOU J., JEANNEAU C., ABOUT I., Complement activation by pulp capping materials plays a significant role in both inflammatory and pulp stem cells' recruitment. J Endod; 2017;43:1104-1110.
28. COOPER P.R., TAKAHASHI Y., GRAHAM L.W., SIMON S., IMAZATO S., SMITH A.J., Inflammation-regeneration interplay in the dentine-pulp complex. J Dent; 2010;38:687-697.
29. ROSA W.L.O., PIVA E., SILVA A.F., Disclosing the physiology of pulp tissue for vital pulp therapy. Int Endod J; 2018;51:829-846.
30. GIRAUD T., JEANNEAU C., BERGMANN M., LAURENT P., ABOUT I., Tricalcium silicate capping materials modulate pulp healing and inflammatory activity *in vitro*. J Endod; 2018;44:1686-1691.
31. KIM D.H., JANG J.H., LEE B.N., CHANG H.S., HWANG I.N., OH W.M., KIM S.H., MIN K.S., KOH J.T., HWANG Y.C., Anti-inflammatory and mineralization effects of ProRoot MTA and Endocem MTA in studies of human and rat dental pulps *in vitro* and *in vivo*. J Endod. 2018;44:1534-1541.
32. NOWICKA A., WILK G., LIPSKI M., KOLECKI J., BUCZOWSKA-RADLINSKA J., Tomographic evaluation of reparative dentin formation after direct pulp capping with Ca $(OH)_2$, MTA, Biodentine, and dentin bonding systems in human teeth. J Endod. 2015;41:1234-1240.
33. STANLEY H., Calcium hydroxide and vital pulp therapy. In: Hargreaves K.M., Goodis H.E. (eds). Seltzer and Bender's dental pulp. Quintessence, Chicago, 2002, 309-324.
34. MATSUO T., NAKANISHI T., SHIMIZU H., EBISU S., A clinical study of direct pulp capping applied to carious-exposed pulps. J Endod; 1996;22:551-556.
35. NAKANISHI T., MATSUO T., EBISU S., Quantitative analysis of immunoglobulins and inflammatory factors in human pulpal blood from exposed pulps. J Endod; 1995;21:131-136.
36. LINSUWANONT P., WIMONSUTTHIKUL K., POTHIMOKE U., SANTIWONG B., Treatment outcomes of mineral trioxide aggregate pulpotomy in vital permanent teeth with carious pulp exposure: the retrospective study. J Endod; 2017;43:225-230.
37. MENTE J., GELETNEKY B., OHLE M., KOCH M.J., DING P.G.F., WOLFF D., DREYHAUPT J., MARTIN N., STAEHLE H.J., PFEFFERLE T., Mineral trioxide aggregate or calcium hydroxide direct pulp capping: an analysis of the clinical treatment outcome. J Endod; 2010;36:806-813.
38. GRIGORE, M, TELEMAN, SI, PRISTAVU, A, MATEI, M. Awareness and Knowledge About HPV and HPV Vaccine Among Romanian Women. JOURNAL OF CANCER EDUCATION, 2018, 33, no.1, p.154-159.
39. PARINYAPROM N., NIRUNSITTIRAT A., CHUVEERA P., LAMPANG S.N., SRISUWAN T., SASTRARUJI T., BUA-ON P., SIMPRASERT S., KHOIPANICH I., SUTHARAPHAN T., THEPPIMARN S., UE-SRICHAI N., TANGTRAKOOLJAROEN W., CHOMPU-INWAI P., Outcomes of direct pulp capping by using either ProRoot mineral trioxide aggregate or Biodentine in permanent teeth with carious pulp exposure in 5- to 18-year-old patients: a randomized controlled trial. J Endod; 2018;44:341-348.
40. ASGARY S., FAZLYAB M., SABBAGH S., EGHBAL M.J., Outcomes of different vital pulp therapy techniques on symptomatic permanent teeth: a case series. Iran Endod J; 2014;9:295-300.
41. GRIGORE, M, BLIDARU, I, IORDACHE, F. Intrauterine foreign bodies, other than contraceptive devices and systems, may affect fertility - Report of two very different cases. EUROPEAN JOURNAL OF CONTRACEPTION AND REPRODUCTIVE HEALTH CARE, 2014, 19, no. 2, p. 141-143.
42. AGUILAR P., LINSUWANONT P., Vital pulp therapy in vital permanent teeth with cariously exposed pulp: a systematic review. J Endod; 2011;37:581-587.

Manuscript received: 21.11.2018