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ORIGINAL ARTICLE/ARTICOLO ORIGINALE

Improved single visit management of old infected iatrogenic root perforations using Biodentine®



Trattamento in singola visita delle « Old infected » perforazioni con Biodentine®

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KEYWORDS

iatrogenic perforation;
Acidic environment;
Bioactivity;
Biodentine;
Single visit.

Abstract

Aim: The aim of this retrospective observational case series study was to evaluate the middle term outcomes on endodontic management of old infected iatrogenic root perforations using Biodentine. The treatments were always concluded in a single visit, without previous medication with calcium hydroxide. Our goal was to facilitate this kind of treatments and to make them more reproducible and manageable even for a general practitioner or a student.

Methodology and methods: Between January 2011 and June 2016, 51 patients with old infected root perforations have been enrolled. All the treatments were performed using Biodentine in a single visit. Infected root perforation repair was performed by supervised dental students (39%) or a qualified endodontist (61%), employing surgical microscope magnification during treatments. After the treatment, the 51 patients were monitored for 18–64 months. We used clinical and radiographic examinations.

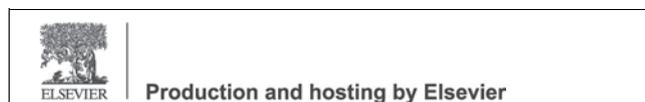
Results: Of 51 examined teeth, 48 (94%) were classified as healed. The time, the size and the location of the perforations did not have a significant effect on the outcome. We proved the ineffectiveness of the null hypothesis. According to this latter, the single visit treatment of old infected perforations with Biodentine was inadequate.

Conclusions: In single visit treatments, Biodentine seems to provide a biocompatible and effective seal in acidic environment, in accidental root perforations, even if the treatment is

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PAROLE CHIAVE

Perforazione iatrogena;
Ambiente acido;
Bioattività;
Biodentine;
Singola visita.

performed by an inexperienced operator and regardless of the location, the size and the time of occurrence of the perforation.

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Riassunto

Obiettivi: Lo scopo di questo studio osservazionale retrospettivo è stato quello di valutare la percentuale di guarigione a medio termine nel trattamento delle “old infected” perforazioni con contaminazione batterica usando biodentine. Il trattamento di tutte le perforazioni è stato fatto in seduta singola, senza medicazione con idrossido di calcio. Altro obiettivo è stato quello di facilitare questo tipo di trattamenti, rendendoli riproducibili e fattibili anche per un dentista generico o uno studente.

Materiali e metodi: Tra Gennaio 2011 e Giugno 2016, abbiamo selezionato 51 pazienti con “old infected” perforazioni. Ogni caso è stato trattato con Biodentine in singola seduta. Il 39% dei casi è stato trattato da studenti della clinica universitaria sotto la supervisione di un tutor senior, mentre il 61% da un endodontista qualificato, usando il microscopio operatorio durante ogni fase del trattamento. Dopo il trattamento, i 51 pazienti sono stati monitorati tra 18 e 64 mesi, con esami radiografici e clinici.

Risultati: Fra i 51 denti esaminati, 48 (94%) sono stati classificati come guariti. Nel nostro studio il tempo, la dimensione e la localizzazione della perforazione non hanno avuto alcun valore prognostico. Abbiamo dunque rigettato l'ipotesi nulla, secondo la quale il trattamento in singola visita delle “old infected” perforazioni con Biodentine fosse inadeguato.

Conclusioni: Il trattamento delle “old infected” perforazioni in ambiente acido in singola visita con Biodentine sembra assicurare un sigillo biocompatibile e tridimensionale della perforazione anche se il trattamento è stato eseguito da operatori senza tanta esperienza (studenti), indipendentemente dalla localizzazione, dimensione e tempo dell'avvenuta perforazione.

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Introduction

Iatrogenic root perforations, resulting from the destruction of the dentine root wall or floor along with the underlying cementum, are defined as mechanical communications defects between the root canal system and the external tooth surface. Such injury of the periodontium leads to localized inflammation and infection, triggering the destruction of periodontal fibers, bone resorption, and the formation of granulomatous tissue. Eventually proliferation of oral mucosa epithelium and development of a periodontal pocket jeopardizes tooth survival. According to Fuss and Trope, the prognosis is particularly poor with larger and older perforations. But above all, the location of the perforation is a key determinant, with particularly bad prognosis for crestal perforations [1].

To prevent or treat periradicular inflammation following root perforation, the standard treatment is sealing the perforation with a bioceramic-based material using orthograde access [2–4]. Success depends mainly on proper cleaning of perforation site and complete tridimensional sealing. Mineral trioxide aggregate (MTA) is the standard material used to seal perforations. The procedure, in case of infection and inflammation, is typically divided in two steps. The first visit involves cleaning and temporarily sealing the

perforation with calcium hydroxide. The second visit (usually ~1 week later) involves placing a definitive MTA seal. Several benefits of MTA include biocompatibility, osteoconductivity, and the promotion of cementum regeneration. Several drawbacks make MTA less suitable for large crestal and/or infected perforations [5–15]. Disadvantages of MTA include its long setting time, compromising the application in large crestal cases. Use of MTA can lead to tooth discoloration. In addition, the local pH variations, acidic in case of an inflammation, can influence material setting [12, 15–19]. Finally, MTA handling requires practice. Particularly challenging is performing complete three-dimensional sealing of deep cavities [20]. Biodentine[®] (Septodont, Saint Maur des Fosses, France) a silicate loaded bioceramic has emerged as an effective cement in several endodontic procedures. Biodentine[®] biocompatibility and osteoconductivity properties are equal to MTA, but thanks to its properties Biodentine is easier to handle. Its chemical qualities also make it more efficient in acidic environment. Collectively, Biodentine[®] might provide clear advantage in the treatment of older perforations [21–24]. To assess this hypothesis clinically, we performed a prospective case series study using reports on outcomes of infected old iatrogenic root perforations referred to our university dental hospital and treated either by supervised dental students, or by a qualified endodontist.

Material and methods

Study design

We performed a retrospective observational study based on documented cases of old infected root perforation (more than 6 months beforehand) treated in the Department of Endodontics at the Strasbourg University Dental Hospital (Pôle de Médecine et Chirurgie Bucco-dentaires, Hôpitaux Universitaires de Strasbourg, Strasbourg, France). Patients were treated by direct sealing with Biodentine[®] in a single visit. The patient enrolment took place from January 2011 to June 2016. Analyses were based on the clinical records and radiographic examination.

Case selection

Cases were selected based on the following criteria:

- Presence of iatrogenic root perforation.
- Signs of infection (either by probing (negative ≤ 4 mm, positive >4 mm), presence of sinus tract, swelling, and bone radiolucency).
- No previous treatment of the perforation.
- Time lapse between perforation injury and its repair was 6 months or more.
- Immunocompetent adults above 18 years of age.
- Complete medical and dental history were available.

Diagnosis of perforation

The correct diagnosis of the presence and localization of an iatrogenic root perforation was made using one or more of the following signs or tools:

- visualization with surgical microscope;
- periodontal probing;
- sudden bleeding;
- radiographic analysis (including fistulography);
- apex locator.

Single step treatment of iatrogenic root perforations

All procedures were done in conformity with current state of the art practices in endodontic. These included effective local anesthesia, appropriate tooth restoration to insure watertight rubber dam installation, and surgical microscopic manipulations for precision (Leika M320).

Procedures began with locating the perforation, then infected dentin was removed with minor enlargements using endodontic ultrasonic tips of different diameters according to the perforation size (Pro-Ultra[®], StartX[®], Dentsply-Sirona). In some cases, when granulation tissue invaded the perforation site, surgical removal was performed using cautery knife (Satelec). Then, keeping the pulp chamber constantly flooded with 6% sodium hypochlorite (Coltene), root canal shaping was performed using either Protaper Universal or Protaper Next (Dentsply-Sirona) instruments. Irrigation helps in perforation disinfection and hemostasis. In case of a large osseous defect and/or when bleeding is still occurring, after sodium hypochlorite irrigation small pieces of resorbable collagen matrix (Pangen, URGO Medical) are used to stop the bleeding. The perforation site was then dried with sterile cotton pellets and/or sterile paper points. In the case of lateral root perforation, the site was always sealed before root canal filling, allowing a 12 min lag time between the two procedures to insure adequate Biodentine[®] setting. In the case of furcal perforations, perforation filling was performed either before or after root canal filling. When performed before root canal filling, a high taper paper point was used to fill root canal to avoid Biodentine[®] contamination. Otherwise the perforation site was protected from endodontic sealer or guttapercha contamination using sterile cotton pellets. Biodentine[®] was mixed according to manufacturers instructions. The material was inserted into the teeth with a spatula then pushed into the perforation using microbrushes (Figs. 1 and 2). In two examples, when the perforation site was very close to the apical foramen, we filled both the perforation and the root canal with Biodentine (Fig. 3).

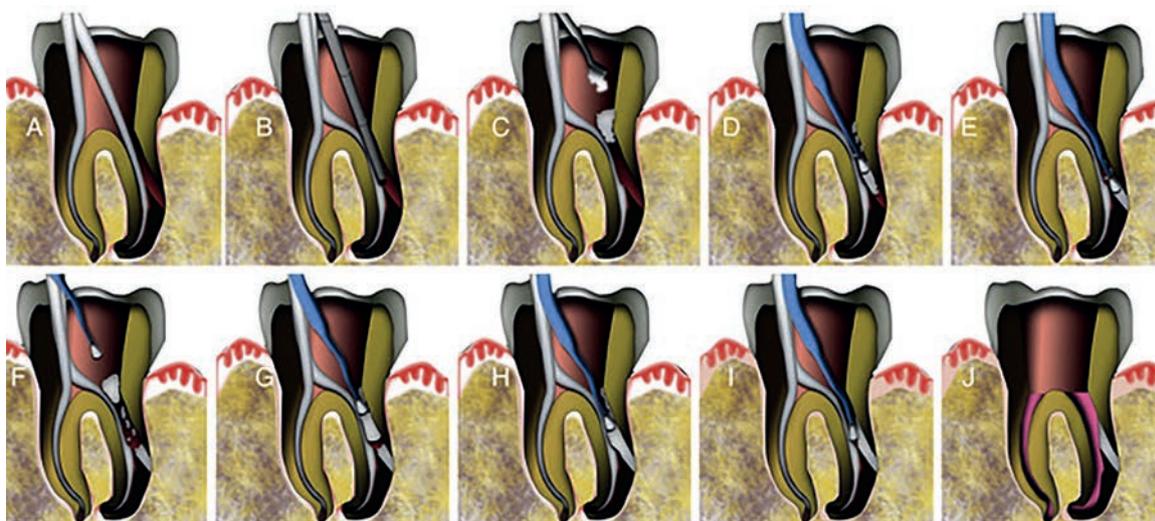


Figure 1 (A–J) Lateral root perforation management procedure.

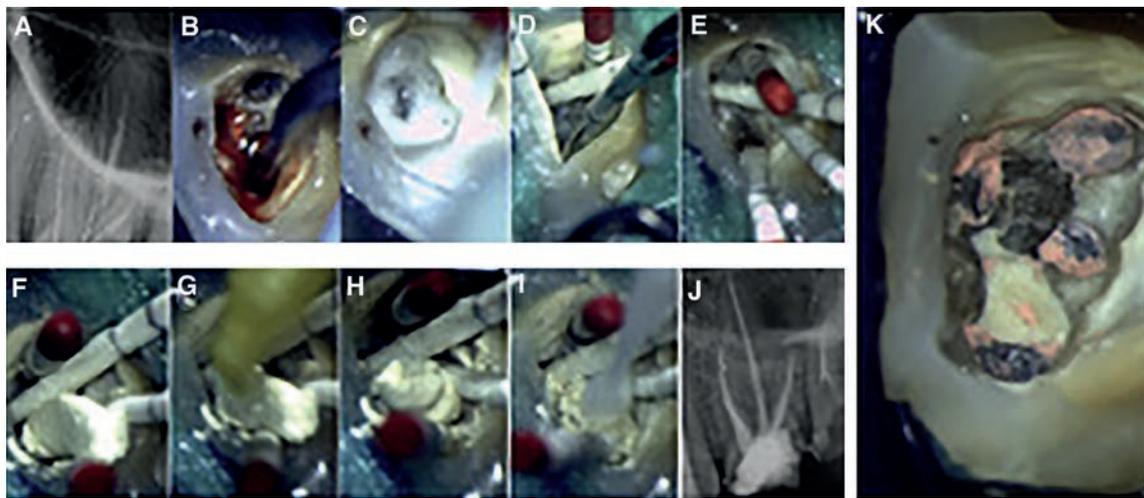


Figure 2 (A) K file highlights perforation in palatal root. (B) Infected dentin removing by a Start X3. (C) Disinfection and hemostasis of the perforation. (D–I) Lateral root perforation management procedure. (J) Post-operative radiograph: root canals filled after 12 min. (K) Pulp floor at the end of procedure.

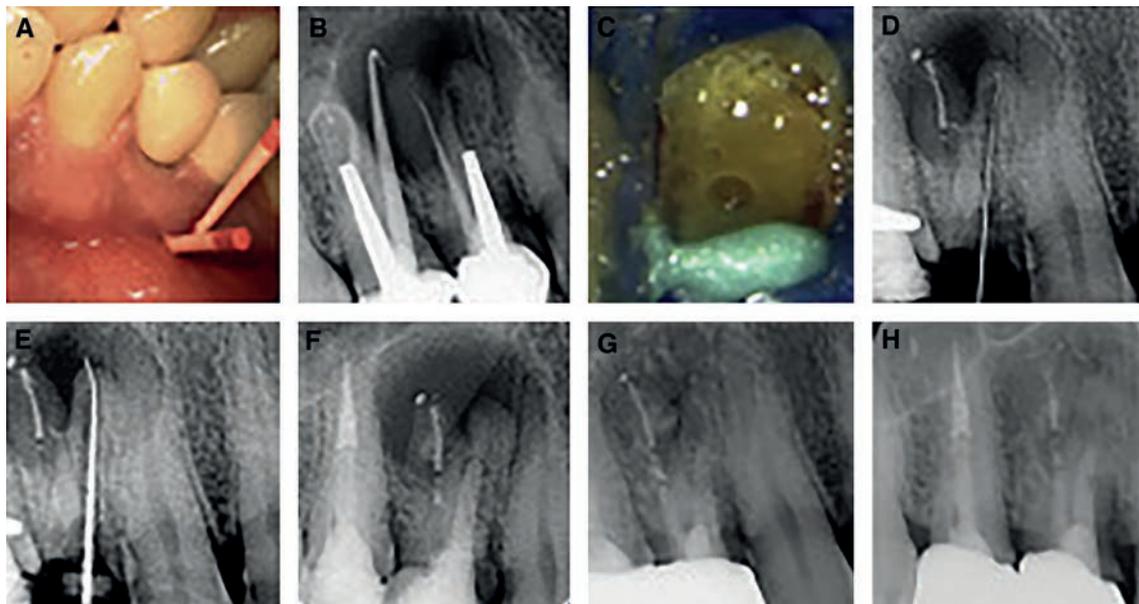


Figure 3 (A) Fistulas. (B) Fistulography. (C) Leaking of pus after crown and post removal. (D–E) Ledge management using manual files. (F) Filling of the perforation and root canal by biodentine. (G) 18 months radiographic follow-up. (H) 48 months radiographic follow-up.

Perforation repair management of 20 perforations was performed by supervised dental students under the direction of a qualified endodontist and 31 were performed exclusively by an expert endodontist (DM).

Preoperative and intraoperative data recording

1. Age;
2. Sex;
3. Tooth type (anterior, premolars, molars);
4. Tooth location (maxilla, mandible)
5. Number of roots;
6. Tooth mobility (Miller);
7. Swelling;
8. Fistula;
9. Presence of post cast or fiber post;
10. Periapical radiolucency;
11. Furcation involvement;
12. Perforation localization (at the crestal level, apical to the crestal level);
13. Time between occurrence and repair (old: from 6m to 12m, very old perforation: >12 mm);
14. Pathological probing: assessed on gingival level by using a dichotomous score (negative for probing <4 mm, positive for probing >4 mm);
15. Step when the perforation occurred (during endodontic treatment; during prosthodontics treatment);

Table 1 Outcome distribution across preoperative variables.

Variable	Variable	Variable	Variable	Variable
Age				1
Until to 50	28 (93%)	2 (7%)	30 (59%)	
>50	20 (95%)	1 (5%)	21 (41%)	
Gender				1
Female	27 (93%)	2 (7%)	29 (57%)	
Male	21 (95%)	1 (5%)	22 (43%)	
Tooth type				0,59
Anteriors + premolars	22 (92%)	2 (8%)	24 (47%)	
Molars	26 (96%)	1 (4%)	27 (53%)	
Tooth location				0,28
Maxilla	32 (97%)	1 (3%)	33 (65%)	
Mandible	16 (89%)	2 (11%)	18 (35%)	
Number of roots				0,25
Single root	15 (88%)	2 (12%)	17 (33%)	
Multirooted	33 (97%)	1 (3%)	34 (67%)	
Tooth mobility (Miller)				1
Yes (class I, II, III)	13 (93%)	1 (7%)	14 (27%)	
No (class 0)	35 (96%)	2 (4%)	37 (73%)	
Sinus tract				1
Yes	25 (93%)	2 (7%)	27 (53%)	
No	23 (96%)	1 (7%)	24 (47%)	
Swelling				1
Yes	16 (94%)	1 (6%)	17 (33%)	
No	32 (94%)	2 (6%)	34 (67%)	
Presence of post (cast or fiber)				0,59
Yes	22 (92%)	2 (8%)	24 (47%)	
No	26 (96%)	1 (4%)	27 (53%)	
Periapical radiolucency				0,28
Yes	16 (89%)	2 (11%)	18 (35%)	
No	32 (97%)	1 (3%)	33 (65%)	
Furcation involvement				0,52
Yes	10 (91%)	1 (9%)	11 (22%)	
No	38 (95%)	2 (5%)	40 (78%)	
Localisation of perforation				1
Crestal	23 (96%)	1 (4%)	24 (47%)	
Apical to crestal bone	25 (93%)	2 (7%)	27 (53%)	
Time between occurrence and repair				1
From 6 m to 12 m	17 (94%)	1 (6%)	18 (35%)	
>12 mm	31 (94%)	2 (6%)	33 (65%)	
Pathological probing				0,28
Yes (>4 mm)	16 (89%)	2 (11%)	18 (35%)	
No (≤4 mm)	32 (97%)	1 (3%)	33 (65%)	
Occurrence of perforation				1
During endodontic treatment	19 (95%)	1 (5%)	20 (39%)	
During prosthodontic treatment	29 (93%)	2 (7%)	31 (61%)	
Size of perforation				1
≤1 mm	9 (100%)	0 (0%)	9 (18%)	
1–3 mm	29 (93%)	2 (7%)	31 (61%)	
>3 mm	10 (91%)	1 (9%)	11 (21%)	

Table 2 Outcome distribution across intra-operative and post-operative variables.

Variable	Healing N (%)	Non-healing N (%)	Total N (%)	P value
Bleeding leaking				1
Yes	20 (95%)	1 (5%)	21 (41%)	
No	28 (93%)	2 (7%)	30 (59%)	
Pus leaking				0.57
Yes	20 (91%)	2 (9%)	22 (43%)	
No	28 (96%)	1 (4%)	29 (57%)	
Root filling				1
Continuous wave	21 (95%)	1 (5%)	22 (43%)	
Carrier based filling	25 (93%)	2 (7%)	27 (53%)	
Bio dentine filling	2 (100%)	0 (0%)	2 (4%)	
Practitioner				1
Qualified endodontist	29 (93%)	2 (7%)	31 (61%)	
Supervised undergraduate student	19 (95%)	1 (5%)	20 (39%)	
Type of restoration after repair perforation				0.60
Crown + access cavity sealed with composite	25 (96%)	1 (4%)	26 (51%)	
Crown + access cavity sealed with composite ant fiber post	23 (92%)	2 (8%)	25 (49%)	

16. Perforation size (<1 mm, 1–3 mm, >3 mm);
17. Bleeding after the final irrigation (from perforation site);
18. Pus leaking (from perforation site);
19. Root filling technique;
20. Practitioner (expert, supervised undergraduate).

Outcome measures

Treatment outcome was assessed on the basis of clinical picture and radiographic analysis. A binary classification was used: “healed” or “not healed”. Perforation was classified as healed when there were not any of the following findings: pain or discomfort, presence of a sinus tract infection or swelling, positive probing and radiolucency. Perforation was classified as not healed when at least one of these findings was observed. Follow-up examinations were performed every 6 months after treatment, for up to 24 months. After this period annual exams were performed.

Statistical analysis

The Fisher exact test was performed to investigate the effect of potential preoperative, intraoperative and postoperative outcome predictors as shown in [Tables 1 and 2](#). Data was processed using SigmaPlot (Version 11.2; Systat Software, INC., San Jose, CA). Data was considered significant at $p \leq 0.05$.

Results

51 patients with an old infected root perforation resulting from endodontic or prosthodontic treatments were eligible and included in this study. Patients were treated from January 2011 to June 2016, either by supervised dental students (20 patients), or exclusively by a qualified endodontist (31 patients). Our patient panel shows broad variations in localization and type of tooth involved, as well as the location of the perforation. 24 perforations were in the crestal area and

27 were apical to the crestal area. Perforations in maxillary teeth were observed almost twice as often (65%) as in mandibular teeth (35%). Multi-root teeth were perforated twice as often (67%) as single root teeth (33%). 61% of perforations occurred during prosthodontic treatment (post-space preparation), the remaining 39% were induced during routine endodontic treatment.

The patient follow-up rate at 18 months was 100%. 46 patients were assessed having complete healing at 18 months following the initial treatment, and 48 completely healed at 24 months. We thus obtained a success rate of 94%.

As perforations characteristics can influence treatment prognosis, we evaluate the potential influence of preoperative ([Table 1](#)), intraoperative, and postoperative variables ([Table 2](#)).

The healing rate of perforations associated to sinus tract was lower than perforations without sinus tract (93% versus 96%, $p = 1$). The healing rate of large perforations (>3 mm) was lower than that of small ones (≤ 1 mm) (91% versus 100%, $p = 1$). The healing rate of perforations with leaking pus was lower than for perforations without leaking pus (91% versus 96%, $p = 0.57$). However, none of the differences observed were statistically significant.

Discussion

Iatrogenic root perforations are commonly occurring problems affecting 12–20% of primary endodontic treatments [2]. Perforation management represents a major challenge, even for experienced endodontists [1,2]. There is thus an urgent need to find a more suitable procedure to make treatment easier, more reproducible, and manageable even for general dentists and for student. In the present study, we investigated the healing rate of accidental old infected perforations after treatment with Biodentine[®] in a single visit using a simplified handling protocol. Moreover, unlike previous studies, we included in our study only old infected perforations. These sorts of lesions have the lowest reported

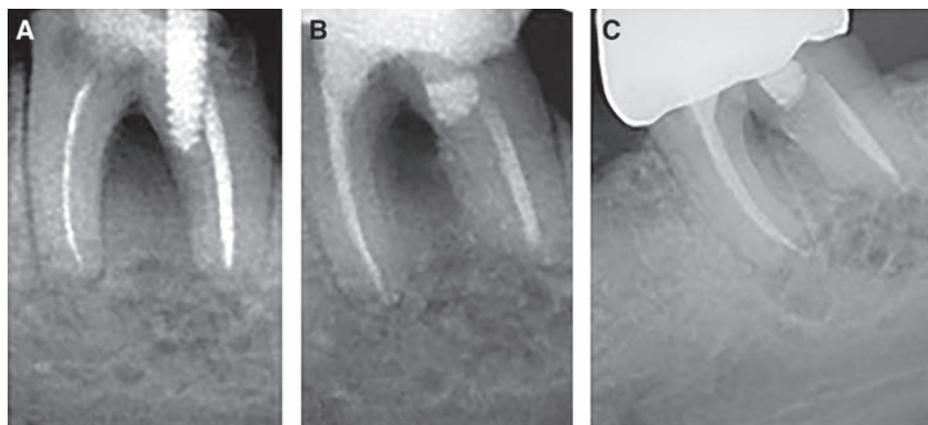


Figure 4 (A) Pre-operative radiograph. (B) 48 months radiographic follow-up. (C) 48 months radiographic follow-up.

healing rate [1]. Our results show Biodentine is highly effective as repair material in a single visit, with a success rate of 94% (among a patient sample of 51 patients). This could show that the procedure is equal or superior to the standard two-step procedure, involving a first treatment with calcium hydroxide and a subsequent perforation sealing using MTA. Indeed Mente et al. using MTA in their study of 26 teeth, reported a success rate of 90% with old perforation and 86% for those at the crestal level, they thus obtained a total success rate of 86% [3]. Aside Gorni et al. record 96% of success rate for coronal perforation and 87% for intermediate ones, they thus obtained a total success rate of 92% [2].

Our high success rate might be explain because by two factors: first the effectiveness of Biodentine[®] and second, the simplification of the handling procedure. Concerning its effectiveness as perforation repair material, Biodentine[®] has the shortest setting time, good handling properties, and setting capability within an acidic environment [16,21–24]. A simplified procedure makes the outcomes more reproducible. The MTA-gun is not required to place the Biodentine[®] bioceramic material into the tooth, a simple spatula is sufficient. To pack Biodentine[®] into the bottom of the perforation, we use microbrushes instead of paper points, plastic carriers, and/or metal pluggers. Our failure rate was low, with only 3 out of 51 teeth scored as unhealed. Of these three failures, one tooth was extracted because of a fracture (detected in the 18th month follow-up visit). The others showed residual radiolucency at the perforation site, with no other clinical sign that could explain delayed healing (Fig. 4) [25].

In our study, size of the perforation, location and time, does not appear to influence treatment prognosis. It is in accordance with the study of Gorni et al. and Mente et al. [2–4]. It disagrees the historical description by Fuss and Trope's. However, to answer further this question our study should be extended to include more cases.

There was no difference, in terms of efficacy, if the management of perforations repair was directly performed by supervised dental students or by a qualified endodontist. That further confirms the robustness of the procedure. Unlike Gorni et al. [2]. Our study concluded that the perforation

repair is reproducible, provided they use strict isolation and disinfection protocols and sufficient magnification.

Conclusion

The results of this study are encouraging nevertheless it is only a retrospective observational case series study with a low sample size.

The high success rate achieved supports that Biodentine[®] is an effective and well-tolerated agent in repairing old infected perforations in one step procedure.

In our study, time, size and location of the perforation does not appear to influence treatment prognosis. Moreover the success rate was comparable between supervised dental students and a qualified endodontist thanks to the superior handling properties simplifying Biodentine[®] application. This retrospective case series study proves that the management of old infected perforations using Biodentine[®] is a reproducible treatment even if performed by an inexperienced operator provided they use strict isolation and disinfection protocols and sufficient magnification.

Clinical relevance

The management of old infected iatrogenic root perforations using Biodentine might be considered an alternative treatment, since it usually requires a easier procedure and tends to be a more affordable option.

Conflict of interest

The authors deny any conflicts of interest.

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References

- Fuss Z, Trope M. Root perforations: classification and treatment choices based on prognostic factors. *Endod Dent Traumatol* 1996;12:255–64.
- Gorni FG, Andreano A, Ambrogi F, Brambilla E, Gagliani M. Patient and clinical characteristics associated with primary healing of iatrogenic perforations after root canal treatment: results of a long-term Italian study. *J Endod* 2016;42:211–5.
- Mente J, Hage N, Pfeifferle T, Koch MJ, Geletneký B, Dreyhaupt J, et al. Treatment outcome of mineral trioxide aggregate: repair of root perforations. *J Endod* 2010;36:208–13.
- Mente J, Leo M, Panagidis D, Saure D, Pfeifferle T. Treatment outcome of mineral trioxide aggregate: repair of root perforations-long-term results. *J Endod* 2014;40:790–6.
- Camilleri J, Montesin FE, Papaioannou S, McDonald F, Pitt Ford TR. Biocompatibility of two commercial forms of mineral trioxide aggregate. *Int Endod J* 2004;37:699–704.
- Haglund R, He J, Jarvis J, Safavi KE, Spångberg LS, Zhu Q. Effects of root-end filling materials on fibroblasts and macrophages in vitro. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:739–45.
- Keiser K, Johnson CC, Tipton DA. Cytotoxicity of mineral trioxide aggregate using human periodontal ligament fibroblasts. *J Endod* 2000;26:288–91.
- Krupp C, Bargholz C, Brüsehaber M, Hülsmann M. Treatment outcome after repair of root perforations with mineral trioxide aggregate: a retrospective evaluation of 90 teeth. *J Endod* 2013;39:1364–8.
- Nosrat A, Nekoofar MH, Bolhari B, Dummer PMH. Unintentional extrusion of mineral trioxide aggregate: a report of three cases. *Int Endod J* 2012;45:1165–76.
- Parirokh M, Torabinejad M. Mineral trioxide aggregate: a comprehensive literature review – part I: chemical, physical, and antibacterial properties. *J Endod* 2010;36:16–27.
- Parirokh M, Torabinejad M. Mineral trioxide aggregate: a comprehensive literature review – part III: clinical applications, drawbacks, and mechanism of action. *J Endod* 2010;36:400–13.
- Roy CO, Jeansonne BG, Gerrets TF. Effect of an acid environment on leakage of root-end filling materials. *J Endod* 2001;27:7–8.
- Torabinejad M, Parirokh M. Mineral trioxide aggregate: a comprehensive literature review – part II: leakage and biocompatibility investigations. *J Endod* 2010;36:190–202.
- Torabinejad M, Hong CU, Lee SJ, Monsef M, Pitt Ford TR. Investigation of mineral trioxide aggregate for root-end filling in dogs. *J Endod* 1995;21:603–8.
- Watts JD, Holt DM, Beeson TJ, Kirkpatrick TC, Rutledge RE. Effects of pH and mixing agents on the temporal setting of tooth-colored and gray mineral trioxide aggregate. *J Endod* 2007;33:970–3.
- Elnaghy AM. Influence of acidic environment on properties of biodentine and white mineral trioxide aggregate: a comparative study. *J Endod* 2014;40:953–7.
- Lee Y-L, Lee B-S, Lin F-H, Yun Lin A, Lan W-H, Lin C-P. Effects of physiological environments on the hydration behavior of mineral trioxide aggregate. *Biomaterials* 2004;25:787–93.
- Namazikhah MS, Nekoofar MH, Sheykhrezae MS, Salariyeh S, Hayes SJ, Bryant ST, et al. The effect of pH on surface hardness and microstructure of mineral trioxide aggregate. *Int Endod J* 2008;41:108–16.
- Saghiri MA, Shokouhinejad N, Lotfi M, Aminsobhani M, Saghiri AM. Push-out bond strength of mineral trioxide aggregate in the presence of alkaline pH. *J Endod* 2010;36:1856–9.
- Giovarruscio M, Uccioli U, Malentacca A, Koller G, Foschi F, Mannocci F. A technique for placement of apical MTA plugs using modified Thermafil carriers for the filling of canals with wide apices. *Int Endod J* 2013;46:88–97.
- Aggarwal V, Singla M, Miglani S, Kohli S. Comparative evaluation of push-out bond strength of ProRoot MTA, Biodentine, and MTA Plus in furcation perforation repair. *J Conserv Dent* 2013;16:462–5.
- Akçay H, Arslan H, Akçay M, Mese M, Sahin NN. Evaluation of the bond strength of root-end placed mineral trioxide aggregate and Biodentine in the absence/presence of blood contamination. *Eur J Dent* 2016;10:370–5.
- Han L, Okiji T. Uptake of calcium and silicon released from calcium silicate-based endodontic materials into root canal dentine. *Int Endod J* 2011;44:1081–7.
- Vallés M, Roig M, Duran-Sindreu F, Martínez S, Mercadé M. Color stability of teeth restored with biodentine: a 6-month in vitro study. *J Endod* 2015;41:1157–60.
- Leprince JG, Zeitlin BD, Tolar M, Peters OA. Interactions between immune system and mesenchymal stem cells in dental pulp and periapical tissues. *Int Endod J* 2012;45:689–701.