Patient and Clinical Characteristics Associated with Primary Healing of Iatrogenic Perforations after Root Canal Treatment: Results of a Long-term Italian Study

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Abstract

Introduction: There are few data on the long-term efficacy of mineral trioxide aggregate (MTA) in treating root canal perforations. We investigated the extent of primary healing after perforation repair with MTA and non-healing as a result of repair. We also investigated patient/clinical characteristics affecting treatment outcomes and long-term prognosis. **Methods:** This was a prospective cohort study that enrolled consecutive patients with a single dental perforation treated with MTA (January 1999–June 2009). Patients were followed up until December 2012 for a maximum of 13 years after treatment, with analyses carried out at 8 years. **Results:** Of the 110 patients (median age, 36 years; 54.5% male) eligible for inclusion, 101 were judged to have started to heal at the first (n = 98, 89%) or second (n = 3, 3%) annual post-treatment checkup, and 9 (8%, 4 women and 5 men, aged between 18 and 65 years) did not show any sign of healing. Patients >50 years had a higher percentage of non-healing perforations compared with those ≤50 years (12% versus 7%). The percentages of perforations at post-treatment analysis that failed to heal were 13% (intermediate/middle), 4% (coronal), and 0% (apical). The percentages of non-healing perforations according to size were 16% for >3 mm, 6% for 2–3 mm, and 0% for smaller perforations. Characteristics associated with probability of progressing after initial healing were gender, positive probing, size, and site of perforation. **Conclusions:** Our results show that having obtained primary healing with MTA, the likelihood of progressing is very low. They provide good evidence of the combined effectiveness of experienced operators and use of state-of-the-art materials. *(J Endod 2016;42:211–215)*

Key Words

Iatrogenic, MTA, perforation, root canal treatment, tooth survival

At present, root canal treatment is one of the most commonly performed dental interventions, with 15 million procedures carried out in the United States alone every year (1). After successful treatment, most teeth can remain as functional units within the dental arch. However, as the number of root canal interventions has increased exponentially in recent years, so have the nature and number of complications. Root canal deviations, fractures of endodontic instruments, and root canal perforations are now among the most common complications observed in modern dentistry (2). Although up-to-date reliable data are not available, conservative estimates suggest that perforations occur in around 20% of endodontically treated teeth (3, 4). Furthermore, perforations were detected in up to 12% of patients during nonsurgical retreatment of prior endodontic interventions (5). Root perforations are defined as the communication between the periodontal apparatus of the tooth and the root canal system. Although some of them are pathologic, the majority are caused by iatrogenic events. Regardless of the etiology, a perforation is an invasion into the supporting structures that causes inflammation and loss of attachment. These in turn compromise the health of the periradicular tissues and ultimately the prognosis of the tooth. Left untreated, perforations result in the loss of integrity of the root and further destruction of the adjacent periodontal tissues. Root canal perforations can occur before, during, or after an intervention. Clauder and Shin (6) reported that a high percentage (53%) occurs as a result of prosthodontic treatment, with 47% taking place during routine endodontic treatment.

Effective management of root canal perforations depends on many factors, including early diagnosis, size, shape, location, and nature of the perforation, chosen treatment, materials used for the obturation, host response, and importantly, the experience of the practitioner (7, 8). Fuss and Trope (9) concluded that location is probably the overriding factor affecting prognosis, with crestal root perforations being the most susceptible to epithelial migration and rapid pocket formation and thus having the lowest success rate of repair. Successful treatment depends on accurate diagnosis and visualization of perforations as well as the use of biocompatible materials effective in sealing the perforation and preventing bacterial penetration.

Mineral trioxide aggregate (MTA), a calcium silicate–based biocompatible nonabsorbable material, was developed in the early 1990s. Before then, the choice of effective, well-tolerated sealant materials was limited. *In vitro* and *in vivo* studies have shown that MTA promotes tissue regeneration without causing inflammation and has good biocompatibility and nontoxic sealing properties (10–17). Several case series and retrospective clinical studies have reported healing rates of more than 80% by using MTA (18, 19). However, there are few well-designed prospective studies

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determining its long-term safety and efficacy in the management of root canal perforations, and there is an urgent unmet medical need for evidence-based data.

The primary objectives of this study were to investigate the likelihood of primary healing after perforation repair with MTA and the probability of progression of the inflammatory process after initial healing. We also determined patient/clinical characteristics affecting treatment outcomes and long-term prognosis.

Methods

Study Design

This was a prospective cohort study with enrollment from January 1999 to June 2009 at the Unit of Endodontics, DMCO San Paolo, Department of Dentistry, University of Milan, Italy. Follow-up was closed on December 2012. The study was carried out in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki 1964 as currently amended. The protocol was approved by the local ethics committee, and all patients gave written informed consent to participate in the study.

Patients

Male and female patients with a single dental perforation were eligible for enrollment. The recruitment was consecutive starting from January 1999 until June 2009. A detailed medical and dental history was obtained from each patient. Exclusion criteria were the following:

1. Age < 18 years
2. Women of child-bearing age not using adequate contraception, pregnant women, and those lactating
3. Compromised immune status
4. Incomplete pretreatment or intra-treatment records
5. Unwillingness to participate in the study

Diagnosis of Perforations

Perforations were diagnosed by clinical (visualization, periodontal probing, bleeding spots on paper points) and radiographic examinations. Blood on the side of a paper point was recorded as a strip perforation. Detailed records of presence/location/intensity of pain and episodes of swelling/inflammation or abscess were recorded together with details of prior treatment of the affected tooth. Location and extent/size of each perforation were determined and recorded on enrollment and at regular intervals, thereafter using a calibrated periodontal probe. In the few cases where it was not clearly visible, size was estimated on the basis of the length of the root canal.

Treatment of Perforations

Before sealing the perforation, the area was debrided, cleaned, disinfected, and dried. If there was bleeding from the site of the perforation, the area was pre-prepared with an antimicrobial agent such as calcium hydroxide ($Ca(OH)_2$) powder. MTA (ProRoot MTA; Dentsply Maillefer, Baillagues, Switzerland; gray and white versions) powder was mixed with distilled water at a ratio of 3:1 as recommended (15, 20, 21). An MTA gun (Dentsply Maillefer) was used to insert the material into the perforation, and a smooth humid cotton pellet was gently pressed over the material to allow setting. After 48–72 hours when the MTA was completely set, the final filling was performed. All clinical maneuvers were performed by using magnification, either loupes (×5.5) or surgical microscope (×8 or higher) by an expert operator. After the procedure, patients underwent an x-ray to ensure that the perforation was adequately sealed.

Preoperative and Intraoperative Measurements

The following data were recorded:

1. Age and gender
2. Location of the tooth (anterior, premolar, or molar)
3. Perforation site/location:
   - *Coronal*: The upper one third of the root canal
   - *Intermediate/middle*: Middle one third of the root canal
   - *Apical*: Lower one third of root canal
4. Perforation size (≤1 mm, 2–3 mm, >3 mm)
5. Probing: Assessed on a gingival level by using a dichotomous score:
   - Negative probing for probing depth <4 mm
   - Positive probing for probing depth ≥4 mm
   - No distinction made whether 1 or more aspects of the tooth exceeded the 4-mm cutoff
6. Findings of x-rays taken at 3 key time points:
   - Preoperative (before perforation repair)
   - After repair
   - At follow-up (up to a maximum of 13 years)
7. Demographic, clinical, and radiologic data recorded on enrollment and at annual reviews

Outcome Measures

Perforations were classified as healed when there was/were none of the following:

1. Clinical signs/symptoms: pain, inflammation, bleeding, no sinus tract
2. Loss of function
3. Periradicular periodontitis
4. Radiolucency near perforation site
5. Evidence of ongoing root resorption

Perforations were judged not to have healed if any of the above was observed/recorded within the second annual follow-up.

Statistical Analysis

The percentages of teeth healing and not showing signs of healing within each stratum (eg, male) of the patient (eg, gender) or perforation characteristics were calculated.

Teeth determined to have healed, according to predefined criteria, at the second annual follow-up ($n = 101$) were stratified for gender, age (≤50 years versus >50 years), location, probing result, and site and size of the perforation. Patients were followed up to assess progressing inflammation after initial healing, and discrete hazard and survival functions were calculated to describe progression over time (22). Person-time (combining the number of persons and their time contribution) was computed from primary healing (either first or second annual follow-up date). Follow-up was curtailed at 8 years because only 24% of patients had a longer follow-up. Median length of follow-up was determined by using the reverse Kaplan-Meier method (23). A discrete time hazard model that uses the complementary log-log link was used to examine the role of patient and clinical characteristics associated with progressing during follow-up (22). Exploratory analysis by using life tables was carried out initially and then followed by univariate analysis for all predictors: age (≤50 and >50 years), tooth location (anterior + premolar versus molar), perforation location (coronal versus apical + intermediate), size (≤3 mm versus >3 mm), and probing. Categorization was done on the basis of previous studies and clinical considerations (4).

In addition, exploratory graphical analyses were performed to verify the proportional hazard assumption together with the presence