Abstract The purpose of this noninferiority trial was to compare postoperative pain relief after one-visit root canal therapy (ORCT) with a pulpotomy performed with a new endodontic calcium-enriched mixture cement (PCEM) in human permanent molars with irreversible pulpitis. A total of 407 selected patients were randomly allocated into the ORCT group (n = 202) or the PCEM group (n = 205). Numerical Rating Scale questionnaires were used to record pain intensity (PI) by the patients during the first 7 days after treatment. While there was no statistically significant difference in the mean PI at baseline between the two study groups (P = 0.45), changes in mean PI were significantly different between them (P < 0.001). In the ORCT group, pain relief was achieved after 36 h [95% confidence interval (CI), 27.00–45.00], compared to 18 h in the PCEM group (95% CI, 15.00–21.00), a significant difference (P < 0.01). Comparison of the mean PI sum recorded over 7 days showed that patients in the ORCT group experienced significantly more pain than those in the PCEM group (P < 0.001); a similar difference was observed for pain in response to percussion tests (P < 0.001). Treatment with PCEM thus had the better pain-reducing effects than ORCT in irreversible pulpitis cases.

Key words CEM cement · NEC · Pain · Pulpitis · Pulpotomy

Introduction

The most common reason for performing endodontic treatment is irreversible pulpitis, which is characterized by prolonged sensitivity to cold or heat. Posterior teeth more often need a root canal treatment (RCT) than their anterior counterparts.1,2 The usual emergency treatment to relieve pain in irreversible pulpitis is removal of caries and inflamed pulp, cleaning of the root canal, and prescription of analgesics, corticosteroids, or antibiotics.3–5 Among the several treatment options, such an emergency pulpotomy or pulpectomy is the most reliable way to obtain pain relief.6 If there are no time restrictions, then RCT is the treatment of choice.7 RCT has an excellent prognosis (success rate ± 95% CI, 82.8 ± 1.19%).8 However, it is expensive, complicated, and time consuming. Unfortunately, in some countries, owing to financial restrictions or the lack of the necessary skills, the only alternative may be extraction of the affected tooth.9 Therefore, an economical, simple, and conservative technique such as pulpotomy should be considered.

Preserving the whole or at least the radicular part of the dental pulp is essential when treating pulp exposures, particularly in carious exposures in young permanent teeth or in the complex root canal systems in primary molars.10,11 Exposures may result from caries, iatrogenic mishaps, or traumatic injury.12 In pedodontics, pulpotomy is a popular treatment with well-documented positive results.10 When the dental pulp of the permanent dentition becomes infected, only the superficial pulp tissue is affected for a considerable period.13 A few case series have suggested that pulpotomy is a viable treatment option for carious pulp exposures with irreversible pulpitis,11,14–16 because of the healing potential of the remaining radicular pulp of mature permanent molars as well as the biocompatibility of pulpotomy agents, especially mineral trioxide aggregate (MTA),11,15,17 but the evidence grade of these reports is low (fourth level).18

Recently, a novel endodontic cement called Calcium-Enriched Mixture (CEM; BioniqueDent, Iran) cement has been developed.19 In vitro studies comparing the sealing ability of CEM and MTA (as the gold standard)20 and in vivo vital pulp therapy performed in animals21 and humans4,15 yielded comparable results, but CEM seems to offer some benefits over MTA. These include a better antibacterial effect,22 improved handling, a shorter setting time, decreased film thickness, and improved flow.19 CEM has the
ability to form hydroxyapatite over material in normal saline solution and it exhibits characteristics similar to the surrounding dentin when used as root-end filling material. Moreover, it costs less.

Clinical trials are a safe and efficient way of collecting new data about new forms of treatment. The trials can be designed using one of three major approaches: superiority, equivalence, and noninferiority. The goal of a superiority clinical trial is to determine if a new treatment is superior to similar established treatments. An equivalence clinical trial is used to show that the efficacy of the new treatment is similar to that of the current treatment used as a control. In contrast, a noninferiority trial is appropriate for evaluating the efficacy of a new therapy versus a reference treatment; it is hypothesized that the new therapy may not be superior to a proven effective treatment, but that it is clinically and statistically not inferior in its effectiveness.

No clinical trials have compared pulpotomy as an alternative permanent treatment to RCT in irreversible pulpitis. Hence, the purpose of this randomized clinical trial was to compare pain alleviation of pulpotomy with CEM (PCEM) and one-visit RCT (ORCT) in human molar teeth. We hypothesized that PCEM would not be inferior to ORCT in efficacy in irreversible pulpitis.

**Materials and methods**

**Study design**

Our project was evaluated and approved by the Iranian Ministry of Health as well as by the Ethics Committee of the Dental Research Center of Shahid Beheshti University MC, Tehran, Iran. It was also sponsored by the Ministry of Health. The trial was conducted in compliance with the ethical principles of the Helsinki Declaration.

The trial was led by academic professors and managed by the Iranian Center for Endodontic Research (ICER). It was a 12-week multicenter, primary care-based, noninferiority trial with a randomized, parallel-grouped, and open-labeled design conducted by 23 general dentists (GDs).

**Hypothesis**

We hypothesized that PCEM would be noninferior to ORCT in efficacy. The primary end point for efficacy is long-term clinical and radiographic success (results to be published in a future report) and the secondary end point is pain relief within 1 week postoperatively (this report). In this study, we formally tested the hypothesis at the secondary end point.

**Criteria for selection of patients**

Subjects were recruited from a pool of patients referred to 23 healthcare centers of five medical universities in four different states of Iran. Subjects were recruited from both sexes. For standardization, we used inclusion criteria similar to those of the trials that established the efficacy of RCT. To be included, subjects were required (1) to have a vital molar tooth (i.e., vitality tests were conducted before anesthesia; in particular, radicular pulp bleeding after coronal pulp amputation was ascertained to be present); (2) to report pain indicating irreversible pulpitis (i.e., a history of spontaneous pain lasting for a few seconds to several hours, exacerbation of pain by hot and cold fluids confirmed with a hot/cold test, and radiating pain); (3) to have opted for extraction for pain relief; (4) to be between 9 and 65 years old; (5) to be prepared to appear for follow-up; and (6) to provide written informed consent.

Subjects who had (1) moderate or severe marginal periodontitis, (2) a nonrestorable tooth, (3) internal or external root resorption, (4) root canal calcification, (5) active systemic disease, (6) physical or mental disability, or were (7) pregnant or nursing were excluded.

Once eligibility was confirmed, the study was thoroughly explained verbally and in writing to the patients by the GDs. The subjects were also informed that they could suspend their cooperation at any time without penalty or loss of benefits. Demographic data, patient numbers, and the teeth to be treated were recorded before treatment.

**Randomization**

Patients were randomly assigned by a computer-based randomization schedule to receive either ORCT or PCEM. The allocation was performed centrally at ICER to ensure that it was conducted in a blind manner. The patients were not aware of their group assignment before participation. Neither the medical universities (healthcare centers) nor the GDs participated in the randomization procedure.

**Sample size**

On the basis of previous studies, a primary event rate of 83% (long-term success rate) was estimated for patients in both treatment groups, with a delta of $-0.02$ and an effect size of 15%. Even a success rate of 68% for PCEM would be considered noninferior to ORCT. To obtain 90% power with a 2-sided $\alpha$ equal to 0.05, approximately 100 patients per group were considered necessary. With a 10% annual drop-out rate, and assuming an average follow-up of 5 years, approximately 400 patients were thus required.

**General dentists**

Thirty GDs attended a training workshop at ICER, which included discussion of the study protocol, hands-on training in standardized RCT, and instructions in the pulpotomy treatment. Twenty-three GDs passed the final exam and qualified for the trial. Each dentist was asked to recruit 18 patients with irreversible pulpitis of a permanent molar.