



CASE REPORT

Brain injury due to anaphylactic shock as a result of formocresol used during root canal treatment

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Abstract

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Aim Formocresol is still used in many parts of the world despite concerns over its toxicity. A case of a 45-year-old woman who experienced brain injury after an anaphylactic reaction to formocresol is presented.

Summary During routine root canal treatment, the patient experienced nausea and vomiting after formocresol was used as an antibacterial agent in the pulp chamber. The procedure was discontinued and the symptoms resolved. Four days later, the treatment was continued by a different dentist, and the patient developed anaphylactic shock within 10 min of placement of a formocresol-soaked cotton pellet. She received emergency medical treatment and magnetic resonance imaging (MRI) revealed brain injury characterized by swelling of the gyrus in the cerebral watershed territory of the left parietal-occipital lobe. The patient subsequently made a full recovery after supportive treatment.

Key learning points

- A type-I allergic reaction can be induced by formocresol.
- The reasons for the brain injury are thought to be cerebral hypoxia, which was induced by the anaphylactic shock and/or cerebral parenchymal oedema.
- All dentists should be aware of the risks involved in the use of formocresol and avoid using materials containing formocresol and related agents.

Keywords: allergen, anaphylactic shock, formaldehyde, formocresol, root canal treatment.

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Introduction

Many materials used during endodontic treatment contain potential allergens which can induce hypersensitivity reactions (Hensten & Jacobsen 2005). Formocresol has been widely used in dentistry for more than 100 years due to its antibacterial properties (Buckley 1904, Spångberg 1985, Peng *et al.* 2006), despite its uncertain biocompatibility (Lewis 2010). Formocresol and related agents have been traditionally used as disinfectants for root canal treatment, pulpotomy and root canal sealants (Spångberg 1985, Haikel *et al.* 2000, Kunisada *et al.* 2002, Braun *et al.* 2003, Peng *et al.* 2006, Lewis 2010). Formaldehyde (paraformaldehyde and trioxymethylene), a primary component of formocresol, is recognized as an allergen, which can provoke anaphylactic reactions (Haikel *et al.* 2000, Kunisada *et al.* 2002, Braun *et al.* 2003). In addition, the components of formocresol have been reported to be associated with cytotoxicity, carcinogenicity, immune sensitization and mutagenicity (Lewis & Chestner 1981, Ramos *et al.* 2008, Cardoso *et al.* 2010, Lewis 2010).

In China, formocresol is commonly used as an antibacterial agent in root canal treatment. The guidelines for operative dentistry and endodontics as taught to dentistry students in China lists formocresol as the second choice of antibacterial agents for use when performing root canal treatments (Wu & Xiao 2008). Searches of the two main databases of Chinese language scientific literature found that the majority of studies involving disinfection in root canal treatment used formocresol. A search of the China National Knowledge Infrastructure (CNKI) database for clinical research reports involving root canal procedures published from 2009 to 2012 resulted in 141 reports, and 89 used formocresol as the antibacterial agent. A similar search of the WANFANG database resulted in 199 reports, and 138 used formocresol as the antibacterial agent. Although there is no information regarding the prevalence of formocresol use in China, the results of the database searches clearly reveal that formocresol is widely used.

This report presents an unusual case of anaphylactic shock due to an allergic reaction to formocresol used during root canal treatment.

Case report

A 45-year-old woman with a history of allergy to ceftriaxone was treated at a private dental clinic in Hangzhou, China. Her chief complaint was severe pain in the left mandible. The pain started spontaneously, and she experienced extreme tooth sensitivity to hot and cold. The pain was more severe at night. She had received several previous endodontic treatments in other teeth without complication. Due to deep caries and instantaneous extreme pain in response to thermal stimulus, tooth 36 (permanent left mandibular first molar) was diagnosed with acute irreversible pulpitis and root canal treatment was scheduled. Under left mandibular block anaesthesia with lignocaine, the pulp chamber was opened and biomechanical preparation was carried out on tooth 36. A formocresol-soaked cotton pellet was placed in the pulp chamber for antiseptic purposes. Approximately 30 s later, the patient complained of dizziness, dyspnoea and nausea. She vomited before the temporary filling materials could be placed and the cotton pellet was spat out.

The patient was sent to the emergency department of a nearby hospital where she was treated with epinephrine, corticosteroids and oxygen. She recovered without incident. Four days later, with nothing in the pulp chamber of tooth 36, the patient came to the Dental Department of the primary hospital to complete the root canal treatment. The dentist considered tension, tooth pain and allergic reaction to

lignocaine as possible causes of her intense reaction. No local anaesthetic was used, and after biomechanical preparation, a formocresol-soaked cotton pellet was placed in the pulp chamber with zinc phosphate cement. Ten minutes after application of formocresol, the patient began showing signs of hypersensitivity, that is, dizziness, shortness of breath and nausea. The dentist immediately removed the formocresol-soaked cotton. The patient was treated with oxygen and was transported to the emergency department within the same hospital. In the emergency department (30 min after formocresol removal), the patient's systolic blood pressure dropped to 60 mm Hg and she lost consciousness. She was treated with epinephrine, corticosteroids and an intravenous infusion of 5% dextrose. She regained consciousness after 23 min. After regaining consciousness, she began complaining of a headache which increased in severity over time. Her blood pressure returned to normal 4 h from the time she lost consciousness.

Due to the patient's persistent and severe headache, magnetic resonance imaging (MRI) performed the next day revealed hyperintensity on T2-weighted imaging and hypointensity on T1-weighted imaging, corresponding to swelling of the gyrus in the cerebral watershed territory of the left parietal-occipital lobe (Fig. 1). Based on her history, symptoms, and MRI findings, the patient was diagnosed with brain injury due to anaphylactic shock caused by formocresol. She was then admitted to the Department of Neurology. Following a series of treatments, including hydration, reduction of intracranial pressure and improvement of cerebral circulation, she demonstrated early recovery. At day 4, the patient had achieved close to complete recovery, but a slight headache persisted. MRI performed on day 5 after anaphylactic shock revealed no obvious abnormalities (Fig. 2). The patient was discharged on day 7 in a stable condition.

The patient was transferred to the Department of Stomatology to complete the root canal treatment. After isolation with a rubber dam, three roots were identified, the working lengths determined, and root canal preparation was carried out with hand files using the step-back technique and sodium hypochlorite irrigation. No local anaesthetic was used. After cleaning and shaping, the canals were dried and calcium hydroxide was used as the antibacterial medicament. One week later, the root canal treatment was successfully completed without the use of formocresol-containing products. Pre- and postoperative radiographs of the tooth are shown in Fig. 3.

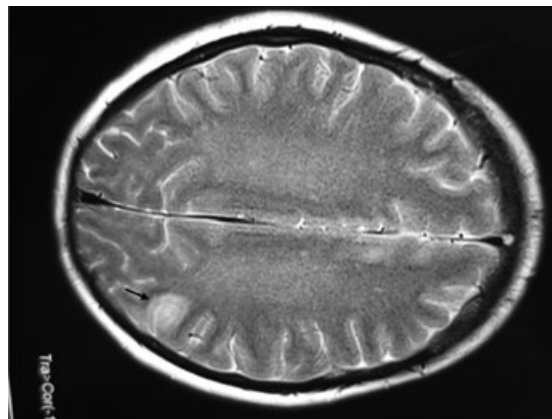


Figure 1 MRI on day 1 revealed hyperintensity on T2-weighted imaging, which corresponded to swelling of the gyrus in the cerebral watershed territory of the left parietal-occipital lobe (arrow).

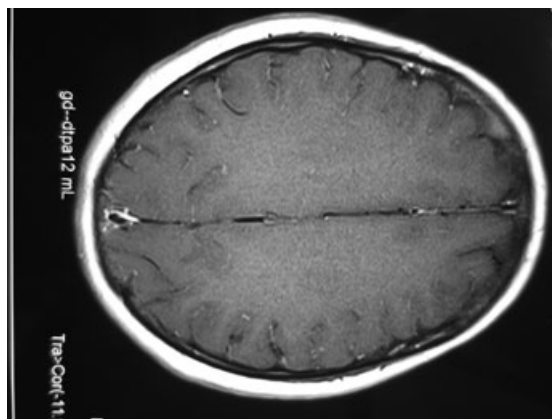


Figure 2 MRI performed on day 5 after anaphylactic shock revealed no obvious abnormalities.

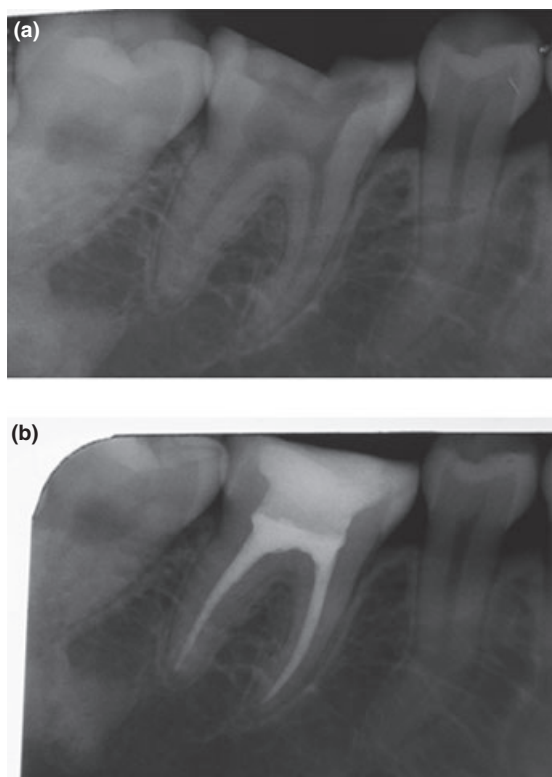


Figure 3 Preoperative (a) and Postoperative (b) radiographs of the affected tooth (36).

Discussion

Materials used in endodontic treatments such as anaesthetics, mummifying agents, barrier equipment, surface and root canal disinfectants, sealants, core materials, and apical filling materials all contain potential allergens (Hensten & Jacobsen 2005). Most of these allergens are haptens, which turn into full antigens when combined with host tissue proteins and then induce hypersensitivity (Hensten & Jacobsen 2005). Because

anaphylaxis is primarily a clinical diagnosis, typical systemic manifestations often with a history of exposure to an allergenic agent are diagnostic (Simons 2010).

Formocresol is mainly composed of formaldehyde and cresol, which act as an alkylating agent and a phenolic protein-coagulating compound, respectively (Buckley 1904). Formaldehyde is a low molecular weight chemical which acts as a hapten and may react with tissue proteins on macrophages and Langerhans cells to produce a complete allergen which can induce immunological reactions (Smedley 1996, Braun *et al.* 2003). It can provoke contact dermatitis mediated by a delayed-type allergic reaction (type-IV) (Kunisada *et al.* 2002), and a few cases of immediate-type allergic reaction (type-I) to formaldehyde have been reported (Haïkel *et al.* 2000, Kunisada *et al.* 2002). Braun *et al.* (2003) reported anaphylactic shock in four patients and urticaria in another three patients associated with formaldehyde. The authors also reviewed the literature and found 35 cases of immunoglobulin E-dependent allergic reactions to formaldehyde; Kunisada *et al.* (2002) reported a case of anaphylaxis caused by a type-I reaction to formaldehyde in a dental disinfectant and reviewed 15 previous reports of type-I reactions to formaldehyde used as a root canal disinfectant. The hypersensitivity reactions can occur immediately, appearing within several minutes to 1 h after treatment, or be delayed, appearing 2–24 h after dental treatment (Kunisada *et al.* 2002, Braun *et al.* 2003). Based on the history of events, a type-I allergic reaction was induced by formocresol in the case presented here.

Although hypersensitivity reactions such as necrosis, asthma, rhinitis, nausea, dyspnea, urticaria, pruritus, and even anaphylactic shock are known side-effects of formocresol/formaldehyde (Haïkel *et al.* 2000, Kunisada *et al.* 2002, Braun *et al.* 2003), brain injury has not been reported. However, secondary brain injury due to anaphylactic reactions to other agents has been reported (Speech *et al.* 1998, Schäbitz *et al.* 2001, Arishima *et al.* 2009). The reasons for the brain injury in the case presented here are thought to be cerebral hypoxia caused by hypoperfusion after hypotension as a result of anaphylactic shock and/or cerebral parenchymal oedema caused by local allergic vasculitis secondary to vascular injury as a result of shock.

The safety of formocresol has been questioned for over 30 years (Lewis & Chestner 1981). The components of formocresol, especially formaldehyde, have been reported to be associated with cytotoxicity, carcinogenicity, immune sensitization and mutagenicity (Lewis & Chestner 1981, Ramos *et al.* 2008, Cardoso *et al.* 2010, Lewis 2010). Formocresol has been shown to cause DNA damage in mouse bone marrow (Ramos *et al.* 2008), and formocresol induces apoptosis and necrosis in murine peritoneal macrophages (Cardoso *et al.* 2010). Additionally, while generally accepted as a direct cause of nasopharyngeal cancer, formaldehyde has also been strongly associated with leukaemia (Zhang *et al.* 2009).

Shaping and cleaning may play a more important role than intracanal medicaments in disinfecting root canals during root canal treatment (Kawashima *et al.* 2009). In addition, if multiple treatment visits are required, calcium hydroxide is the recommended intracanal medicament (instead of formocresol) due to its biocompatibility and stability (Kawashima *et al.* 2009). The use of formocresol has now virtually ceased in Europe following the publication of the British Society of Paediatric Dentistry guidelines in 2006 (Rodd *et al.* 2006). In addition, the American Association of Endodontists (AAE) recommends against the use of formocresol and other materials containing paraformaldehyde because they 'have been proven to be both unsafe and ineffective' (American Association of Endodontists 1998). Despite these recommendations, many practitioners are still using formocresol as a root canal disinfectant (Kunisada *et al.* 2002, Verma *et al.* 2009). From this case report, it is clear that the use of formocresol has not been abandoned in some dental clinics and primary hospitals in China,

and some practitioners do not appreciate the contraindications to its use (Milnes 2008).

Conclusion

Formocresol can induce severe anaphylactic reactions. Due to its toxicity, carcinogenicity, and severe adverse reactions, all dentists should be aware of the risks involved in its use and avoid using materials containing formocresol and related agents.

Disclaimer

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