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Research Article

Definitive Relief of Severe Dry Socket Pain with Eugenol in Two Minutes

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Abstract

The etiology of dry socket after tooth extraction is still controversial, perhaps due to the lack of interest in researching this pathology, which heals spontaneously in a period of two weeks on average. Various proposed models have unsuccessfully attempted to explain the causal mechanisms of the lack of blood clots inside the dental socket. The main symptom and true protagonist of this pathology, that is, the intense pain perceived by 100% of the patients who have suffered this postoperative complication of extraction, has been underestimated by dental professionals for decades. Treatment orientation should focus on immediate pain relief. Thirty-seven patients were treated with a conservative but intensive treatment of the dental alveolus by washing with 3% hydrogen peroxide. The cavity is immediately filled without compression with gauze soaked in the purest eugenol whose objective is to eliminate pain definitively two minutes after starting the protocol. The simplified treatment protocol with eugenolate gauze allows immediate cessation of pain and eliminates the need for analgesic-anti-inflammatory medication. Eugenol gauze is changed periodically until definitive symptomatic remission in approximately 2 weeks.

Introduction

Dry socket is a frequent complication (1% to 5%) of multifactorial etiology secondary to tooth extraction that can increase up to 38% in mandibular third molar extractions. Although some factors, such as smoking, the use of oral contraceptives, and the presence of fibrinolytic activity in the alveoli after extraction, correlate with a higher incidence of dry socket, it remains difficult to find a definitive mechanism to explain its pathogenesis [1,2]. The degree of incidence of local and systemic factors as triggers for the disease and palliative treatment protocols are still controversial [3-5]. The main symptom and true protagonist of this pathology, that is, the intense pain perceived by 100% of the patients who have suffered this postoperative complication of extraction, has been underestimated by dental professionals for decades. Therefore, the orientation of treatment should focus on immediate pain relief. The placement of a medicated dressing to fill the alveolus with the intention of attenuating painful symptoms is a universally accepted treatment [6-8]. Eugenol has demonstrated various antioxidant, analgesic, antimutagenic, antiplatelet, antiallergic, anti-inflammatory, and anti-inflammatory properties. It has also shown antimicrobial effects against many human pathogens, including a broad group of gram-positive and gram-negative bacteria and fungi, and a number of parasites, including Giardia lamblia, Fasciola gigantica, and Haemonchus contortus [9-13]. Eugenol is a popular antioxidant and monoamine oxidase (MAO) inhibitor, and also exhibits neuroprotective properties [14]. Eugenol is known to scavenge free radicals, inhibit the generation of reactive oxygen species, prevent the production of reactive forms of nitrogen, increase cytoantioxidant potential, and protect microbial DNA and protein function. Additionally, it can help repair oxidative damage, remove damaged molecules, and prevent mutations that could lead to cancer [12,15,16]. The antioxidant potential of eugenol has been attributed to its structure, which allows it to fix phenoxy radicals by receiving donated hydrogen atoms [17]. The anti-inflammatory/antioxidant properties of eugenol, confirmed by various studies in both in vitro and in vivo models, reported a decrease in the expression of several inflammatory mediators (TNF-α, NF-κB, COX-2, IL-1β, IL-4, IL-5, IL-6, iNOS, and NO)and in addition, an increase in antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase) [18,19].

One of the studies addressed the effects of eugenol on the mediators of inflammation derived from arachidonic acid (AA) confirming the inhibitory effect of eugenol on the production of prostaglandins and leukotrienes and the reduction of edema formation in various animal models of inflammation. Furthermore, in human platelets, eugenol inhibited aggregation induced by AA and platelet-activating factor (PAF). Eugenol and sodium eugenol acetate have also been shown to inhibit AA-induced thromboxane B2 and PGE2 formation in a concentration-dependent manner [18]. A structurally similar compound, methyl-eugenol, has been evaluated in models of cerebral ischemia and reported to increase superoxide dismutase and catalase activity, inhibit NO production, decrease proinflammatory cytokines (TNF-α, IL-1β, and IL-1β). -6) and increases anti-inflammatories (IL-10 and TGF-β), indicating a potential role in the treatment of ischemia-related inflammatory diseases [19]. The recruitment of leukocytes to the tissue is of paramount importance in the inflammatory process. In this regard, eugenol was shown to mitigate the rolling, adhesion, and migration of leukocytes to the inflammatory site [20]. In other studies conducted in LPS-treated mice, eugenol reduced neutrophil/macrophage lung infiltration [21] and mitigated the release of inflammatory cytokines (TNF-α, IL-1β, and IL-6) [22] and NF activation. -κB [21]. Furthermore, in a mouse model of ovalbumin-induced allergic asthma, eugenol inhibited eosinophil infiltration into lung tissue and reduced levels of both ovalbumin-specific IgE and IL-4 and IL-5, the key cytokines in the pathologies. thus suppressing the generation of a Th2-type immune response [23].

The anti-inflammatory and antioxidant effects of eugenol in association with cinnamaldehyde have been reported in peripheral blood mononuclear cells (PBMC) collected from patients with rheumatoid arthritis [24]. In recent years, the inflammatory response has also been related to the appearance of mitochondrial dysfunction. In particular, mitochondrial DNA, but also cardiolipin and N-formyl peptides are released as a result of cell stress/damage and have been reported to induce systemic inflammation [25]. In the presence of severe inflammation, mitochondrial dysfunction was reported to be associated with cell death due to necrosis; conversely, in the setting of moderate inflammation, the intrinsic mitochondrial-dependent form of apoptotic death will prevail. Interestingly, eugenol has been reported to induce early (less than 1 h exposure) mitochondrial collapse and vacuolation, followed by non-apoptotic cell death in normal human oral cells. Thus, unlike the classic pro-apoptotic effect in cancer cells, eugenol might activate pyroptosis (inflammatory cell necrosis) or paraptosis

(associated with mitochondria enlargement and cytoplasmic vacuolation) as cell death pathways in cancer cells. normal [26]. Eugenol is a versatile molecule that has become a promising phytochemical in the armamentarium of complementary therapies through the modulation of chronic inflammation, oxidative stress, and mitochondrial dysfunction, the main pathogenic mechanisms of noncommunicable diseases. The current understanding of the signaling pathways responsible for the interaction of eugenol with cellular metabolism is far from clear. Further studies aimed at characterizing its effects on bioenergetics and mitochondrial metabolism in both normal and malignant cell lines are fully warranted [27]. In the present work, the properties of eugenol as an anesthetic, analgesic, anti-inflammatory and antibacterial agent were used as an alternative for the treatment of pain in dry socket until epithelialization and initial healing of the alveolus is completed in approximately two weeks. Subsequently, the socket continues the process of healing, regeneration and bone remodeling for 3 months.

Material and Methods

37 healthy patients (24 women and 13 men) without pre-existing pathologies, with a mean age of 38.3 years, were diagnosed in our dental clinic with dry socket and intense pain at the sites of recent dental extractions (3 to 7 days). The extractions causing dry socket were classified according to their complexity into three groups: 1) impacted lower third molars, 2) complex extractions that required odontosection or ostectomy, and 3) simple extractions. To record the magnitude of pain, the Verbal Numerical Scale (VNS) was used, in which the patient expresses his perception of pain from 0 ("no pain") to 10 ("worst pain imaginable") [28]. In all patients a simplified surgical protocol was performed as a palliative treatment of pain. In the first intervention, the alveolar cavity was irrigated under pressure to remove food debris with 10 volumes of hydrogen peroxide (H202) diluted 50% in distilled water with a 5ml syringe and trocar needle. Curettage of the alveolar walls was never performed. Afterwards, the post-extraction surgical bed was washed with physiological solution to eliminate the remaining hydrogen peroxide. Subsequently, sterile gauze was cut to a size of approximately 80% of the volume of the alveolus to be filled. The gauze was introduced into the cavity to assess its correct volume and excess gauze was trimmed if it existed. The gauze trimmed and adapted to the size of the alveolus was immersed in Eugenol Farmadental ® (4-Allyl-2-methoxyphenol) - C10H12O2 - (MW: 164.2) [29]. The eugenolated gauze was introduced with a cotton forceps without excessive pressure into the dental socket, carefully without touching the surrounding soft tissues. At this moment the timing was started until the patient gave notice of the definitive cessation of pain "no pain". The patient was then allowed to rinse his mouth with water to remove excess eugenol if any. The eugenolated gauze was changed every 24 hours for 3 days and then renewed every 48 hours for the time necessary for the initial epithelialization of the alveolus, which varied between 7 and 14 days. The patients did not receive any complementary medication and from the beginning of the protocol the analgesics/anti-inflammatories were suspended in the patients who had been previously medicated.

Results

All patients experienced cessation of severe pain within 2 minutes of the application of the eugenolate gauze and did not require analgesic/anti-inflammatory/antibiotic medication during the entire course of treatment regardless of the degree of complexity of the previous surgery. The average time for acknowledgment of "no pain" reported was 84 seconds (Table 1).

Table 1: Times of acknowledgment of "no pain" in relation to the surgical complexity of the precursor tooth extraction of dry socket.

Surgical Complexity	Total Patients	Time Start "No Pain"	Time "No Pain" Average
Impacted lower 3rd molars	16	85 SEG	
ostectomy/odontosection/flap	7	94 SEG	84 SEG
Flapless simple extraction	14	79 SEG	

95% of the patients who received our simplified surgical protocol as initial treatment completed the initial healing in 2 weeks. The alveolar cavity was left without gauze protection after approximately 15 days; however, in alveolitis of lower third molars with previous complex surgeries (43% of patients), the patient was instructed to swish and pressure irrigation with a syringe or oral irrigator to remove accumulated food debris for one more week.

5% of the patients who had previously been treated iatrogenically with fillings of different cements (Figure 1a) had delayed healing (20 to 40 days) because the cements prevent neovascularization and intraalveolar epithelization, favoring superficial necrosis of the tissue. After extracting the cement, the alveolar walls appeared extremely white with remnants of cement penetrated that could not be removed (Figure 1b). The volume of the gauze exchanged generally decreased in the second week of treatment. No postoperative complications were recorded in any patient. Only one patient whose socket had been completely filled with cement had to be treated with analgesics for two weeks, and initial healing took 40 days.

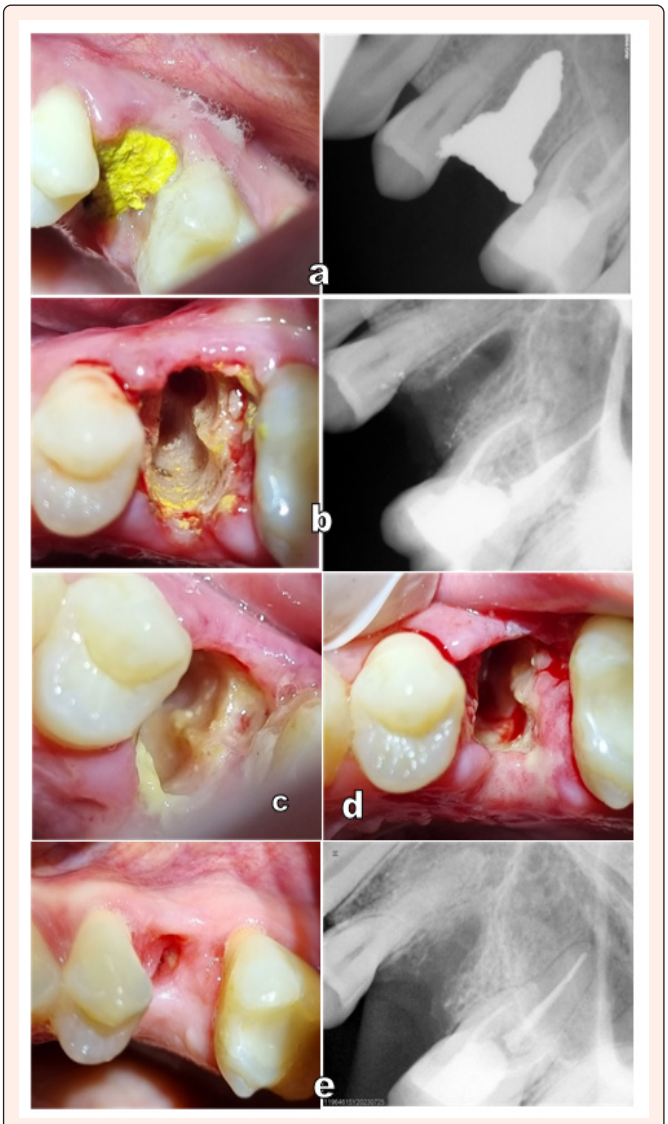

Figure 1: a) Dry socket incorrectly treated with iodoformed cement. b) Loss of perfusion bone wich can be observed immediately after removing the cement, remnants of cement that could not be removed are showed, Rx of socket filled with eugenolated gauze. c) beginnings of epithelial healing at 72 hours d) 7 days e) Clinical vision and Rx at 55 days the bone and soft tissue healing that now allows the insertion of the dental implant.

Conclusion

Dry socket is a frequent complication in extraction surgery, intense pain is present in 100% of patients. The simplified treatment protocol with eugenolate gauze allows for immediate cessation of pain and eliminates the need for additional medication. In

addition, the properties of eugenol favor the evolution of socket healing in two weeks. The improper use of different intra-alveolar cements during treatment prevents normal perfusion into the dry socket, in addition, after the initial setting period, they exacerbate intense pain and delay normal tissue healing.

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