Assessment of palliative approach in the pain management in endodontic emergencies during Covid-19 outbreak: Retrospective cohort study

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Abstract
Aim: During the coronavirus disease, a palliative approach was recommended for the management of endodontic emergencies. This retrospective cohort study was conducted to investigate the effectiveness of dexamethasone or ibuprofen-acetaminophen combination for pain management in endodontic emergencies.

Material and Methods: One hundred and eight records of patients who presented to the emergency department with dental pain were evaluated retrospectively. Since interventional procedures were not performed during the pandemic period, specific analgesics/antibiotics for the management of pain were preferred. A follow-up protocol with a questionnaire was developed to observe the effectiveness of palliative treatment and make changes if necessary. All participants received a questionnaire to rate the pain levels 6, 12, 18, 24, 48, and 72 hours after taking the drug. All data were collected from the patient file and assessed. After inclusion and exclusion criteria, 32 patients were included (n = 19, ibuprofen + acetaminophen; n = 13, dexamethasone). Data were analyzed using the chi-square test (P = 0.05).

Results: In both groups, a significant decrease in pain was experienced immediately after medication and at 6, 12, and 18 hours, with no significant difference (P > .05). However, dexamethasone (Group II) resulted in lower pain levels than ibuprofen-acetaminophen (Group I) at 24 and 48 hours (P < .05)

Discussion: Both dexamethasone and ibuprofen-acetaminophen can be good palliative choices in endodontic emergencies in pandemic conditions. However, at 24 and 48 hours, dexamethasone resulted in lower pain levels.

Keywords
Acetaminophen, Dexamethasone, Endodontic Emergency, Ibuprofen, Pain

DOI: 10.4328/ACAM.20816   Received: 2021-08-14   Accepted: 2021-10-01   Published Online: 2021-10-13

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Annals of Clinical and Analytical Medicine
Introduction
The coronavirus disease 2019 (COVID-19) spreading from Wuhan is originated from coronavirus 2 (SARS-CoV-2), which causes serious acute respiratory syndrome, and has been identified as an international public health emergency by the World Health Organization (WHO) [1]. The most frequent routes of contamination of SARS-CoV-2 include direct contact and direct transmission through oral, nasal and eye mucous membranes [2]. Hence, the pathogens can be generated and transferred during oral examinations and become a real challenge for dental practitioners, and patients [3]. Recently, the American Dental Association (ADA) published a statement that includes the management of emergency dental care against the risk of contamination (available at: https://www.ada.org). They reported that cases regardless of potentially life-threatening, ongoing tissue bleeding, widespread soft-tissue infection with edema and cellulite, and intraoral or extraoral swelling can be treated with elective or palliative procedures [4]. Moreover, the British Endodontic Society suggested using specific analgesics/antibiotics for the management of typical symptoms of endodontic infection according to pain levels (available at: https://britishendodonticsociety.org.uk). Therefore, clinicians have tended to palliative therapy during the pandemic period. Dexamethasone is a corticosteroid drug that has been used to manage pain in endodontic routine proven by experimental and clinical studies [5]. It decreases symptoms of inflammation and the release of inflammatory mediators [6]. Ibuprofen is a safe and successful non-steroidal anti-inflammatory drug (NSAID) that overcomes mild to moderate odontogenic pain and inflammation [7]. The combination of ibuprofen and acetaminophen, defined as crossfire or multimodal analgesia, has been reported to provide greater pain relief without increasing adverse drug reactions [8]. However, there is no study that compares the effect of dexamethasone or ibuprofen-acetaminophen combination on pain levels for endodontic emergency management. Therefore, the aim of this study was to evaluate the success of dexamethasone or ibuprofen-acetaminophen combination in an endodontic emergency in a pandemic period. The initial hypothesis was established that there is no significant difference in pain management between the two groups of medicaments.

Material and Methods
This retrospective cohort study was carried out by evaluating a total of 108 patients aged 18–65 years who applied to the emergency department of the Faculty of Dentistry due to toothache between June and September 2020 during the COVID quarantine period. The study was approved by the Ondokuz Mayis University Clinical Research Ethics Committee (No: OMÜ KAEK 2020/601).

The patients in non-COVID status by taking the detailed history and body temperature between 970F-990F were seen in the clinic. Detailed medical and dental histories of previously registered patients were evaluated. Records included age, gender, chronic diseases and medications, date of diagnosis, apical periodontitis symptoms, pulp and periapical diagnoses, radiographic images, and a VAS scale (0-17 cm).
symptoms (cough, dyspnoea, fever); pregnancy and systemic disease (diabetic, bronchial asthma) or allergic reactions; sensitivity or adverse drug reactions; patients who have taken any analgesics or anti-inflammatory medicament within the last 3 days; patients taking steroids, for instance, because of autoimmune diseases; necrotic pulp, periapical index score 4-5 proposed by Ørstavik et al. [11]; serious periodontal infection or periodontal pocket deeper than 4 mm; the presence of large intraradicular posts; swelling or acute/chronic abscess; active orthodontic appliances; cracked teeth.

After inclusion and exclusion criteria, 32 patient records were evaluated for the study. Consort Flow diagram was shown in Figure 1.

**Pain levels on the Heft–Parker VAS diagram (0–170 mm)**

<table>
<thead>
<tr>
<th></th>
<th>Ibuprofen + Acetaminophen</th>
<th>Dexamethasone</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-medication</td>
<td>100.15 ± 10.37</td>
<td>103.76 ± 13.90</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Immediately post-medication</td>
<td>83.15 ± 34.68</td>
<td>88.07 ± 33.71</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>6 Hours</td>
<td>83.57 ± 34.39</td>
<td>75.92 ± 31.56</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>12 Hours</td>
<td>75.52 ± 28.61</td>
<td>60.00 ± 32.91</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>18 Hours</td>
<td>61.84 ± 33.64</td>
<td>50.92 ± 26.18</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>24 Hours</td>
<td>55.57 ± 32.10</td>
<td>35.30 ± 37.34</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>48 Hours</td>
<td>54.63 ± 36.49</td>
<td>30.76 ± 42.37</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>72 Hours</td>
<td>41.31 ± 33.08</td>
<td>29.23 ± 43.58</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

**Discussion**

In the pandemic stage of the COVID-19, pain management has become challenging for dentists due to the inability to use most of the diagnostic tools and the lack of active clinical interventions to relieve pain [2]. According to a new study conducted in Turkey, it was reported that the number of patients and interventional procedures in dental clinics decreased by approximately 90% [10]. Another study from Italy reported that, on average, only three patients per month were treated daily in clinics due to the pandemic period [11]. The British Endodontic Society published a document recommending pharmacological treatment method with analgesic and antibiotic prescription for alleviating non-life-threatening endodontic pain and inflammation (available at: https://britishendodonticsociety.org.uk).

NSAIDs inhibit cyclooxygenase (COX) enzymes (COX-1) and (COX-2), which play a key role in the development of inflammation and pain [12]. Acetaminophen is a powerful analgesic, although it has poor anti-inflammatory action. Unlike NSAIDs, it is not a potent prostaglandin (PG) inhibitor, but its clinical efficacy is similar to that of selective COX-2 inhibitors [8]. Dexamethasone is a corticosteroid drug that exhibits perfect anti-inflammatory activity by interrupting synthesis and/or release of inflammatory mediators [13,14]. Systematic reviews showed that the ibuprofen-acetaminophen combination has a perfect analgesic effect on pain of endodontic origin and they can be given alternately or together to prolong the effect without overdose [15]. However, data on the success of palliative treatment in endodontic emergencies during the pandemic are limited. Thus, this study aimed to research the success of dexamethasone or ibuprofen-acetaminophen combination in endodontic emergencies during the pandemic stage.

In the present study, 13 of 32 patients were prescribed dexamethasone 4 mg (2 × 1) for 1 day, while 19 patients were prescribed ibuprofen 600 mg + acetaminophen 500 mg (2 × 1) for 3 days. It has been reported in the literature that a single dose of dexamethasone (4 mg) is effective in relieving pain in the short term without side effects [16]. Therefore, analgesic
intake was limited to the minimum number of days during which the analgesic effect was achieved in order to minimize the risk of liver damage.

In both groups, a significant reduction in pain was observed immediately after the medication. At 6, 12, and 18 hours, the pain gradually decreased with no significance in both groups. However, at 24 and 48 hours, dexamethasone resulted in lower pain levels than the ibuprofen-acetaminophen combination. Consistent with this result, it was reported that dexamethasone showed greater pain reduction compared to a single dose of NSAIDs at 6, 12, 24, 48 and 72 hours [17]. In another study, Pochapski et al [16], reported that although dexamethasone resulted in greater pain reduction than acetaminophen at 4 and 12 hours, no significant difference was detected at 24 and 48 hours. On the contrary, in a meta-analysis, NSAIDs were found to be more effective at 6 hours, whereas corticosteroids were found to be more effective at 12 and 24 hours [18]. Differences between the results may be due to different kinematics of the medicaments, patient’s genotype and polymorphism, age, emotional status, anxiety, periapical anatomy, pulpal status or pulp vitality [19]. During the chronic pulp and periapical inflammation process, nociceptor terminals may sprout, and thus the peripheral anatomy of the pain system may change [20]. Therefore, the patient’s individual response to pain and the systemic effect of oral drugs may not be the same.

With oral administration, absorption through the gastrointestinal mucosa is delayed and well-defined peaks (Cmax) values are reduced by 41% and 50% for ibuprofen and paracetamol respectively [21]. Ibuprofen starts to react rapidly between 0.5-1 hours after oral consumption, reaches a plasma half-life between 2-4 hours, and is absorbed approximately between 4 and 6 hours [22]. Similarly, the plasma half-life of dexamethasone is almost 1.5-4 hours, but the period of action is 36–54 hours [16]. From a clinical point, this may explain the lack of significant difference between the two groups at the time immediately post medication.

Another factor affecting drug activity is the genetic polymorphism of the cytochrome P450 enzyme. When patients with CYP-2CB and CYP-2C9 polymorphisms have a reduced ability to clear ibuprofen, cumulative strain produces an increased magnitude of analgesia, but this can also increase side effects [19]. On the other hand, the analgesic and anti-inflammatory efficacy of NSAIDs is much more selective, in contrast to the multiple anti-inflammatory effects of glucocorticoids [14]. This might be one of the reasons for the higher efficacy of dexamethasone than ibuprofen.

A limitation of the current study was the difficulty of reflecting the subjective experience of pain on a quantitative scale.

Although the VAS is practical, it requires training to administer, and especially elderly patients with physical impairment may have difficulty understanding and therefore completing the scale [23]. In the present study, age-related problems in scoring are thought to be minimal, by including the relatively young and middle-aged group and excluding the over-65 age group. Another limitation was that dose scaling based on body mass index was not considered at the prescribing stage. In the present study, standard drug doses were administered to each patient. However, for an accurate assessment of the effectiveness of oral drugs, it is more appropriate to consider the optimum or minimum effective dose and work on a mg/kg basis [24]. However, in oral administration of systemic drugs, patient compliance is required to maintain optimum blood levels.

Third, the sample size was not sufficient to allow multivariate analysis. The decrease in the number of patients admitted to the hospital with the risk of COVID-19 transmission during the pandemic period has resulted in a small sample size.

**Conclusion**

Within the limitations of this retrospective cohort study, the use of dexamethasone or ibuprofen-acetaminophen combination can be a good palliative choice for pain management in patients with endodontic emergencies in pandemic conditions. In both groups, a gradual reduction in pain was detected immediately after medication. However, at 24 and 48 hours after medication, dexamethasone resulted in lower pain levels than the ibuprofen-acetaminophen combination.

**Scientific Responsibility Statement**

The authors declare that they are responsible for the article’s scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

**Animal and human rights statement**

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

**Funding: None**

**Conflict of interest**

The authors declare that they have no conflicts of interest.

**References**


How to cite this article: