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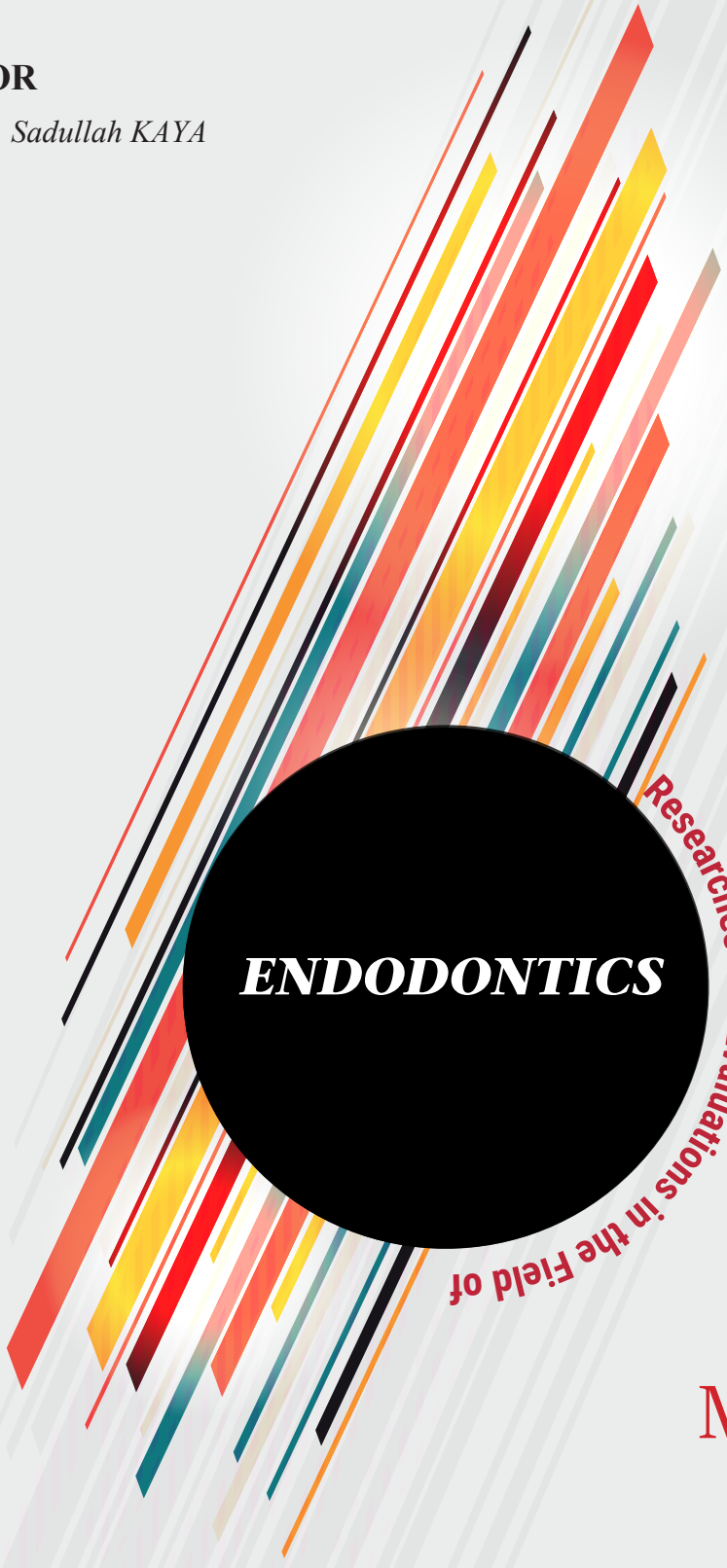
*Prof. Dr. Sadullah KAYA*

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**Adres:** Kızılay Mah. Fevzi Çakmak 1. Sokak Ümit Apt
**No:** 22/A Çankaya/ANKARA Tel: 0312 384 80 40

www.gecekitapligi.com
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# Research And Evaluations In The Field Of Endodontics

**March 2025**

Editor:
Prof. Dr. Sadullah KAYA

# İÇİNDEKİLER

# BÖLÜM 1

## POSTOPERATIVE PAIN IN ENDODONTIC TREATMENT

*Feyzanur ERGÜNER*[1]

*Selen İNCE YUSUFOĞLU*[2]

1 Department of Endodontics, Faculty of Dentistry, Ankara Yıldırım Beyazıt University, Ankara, Turkey

ORCID: 0009-0007-6224-259X

2 Department of Endodontics, Faculty of Dentistry, Ankara Yıldırım Beyazıt University, Ankara, Turkey

ORCID: 0000-0002-7826-6023

## Pain

Pain has been attempted to be understood, defined, and described since ancient times. In Merskey's article, which compiles the historical development of the modern definition of pain, it is noted that in ancient times, Homer described pain as arrows sent by the gods (Merskey, 1980). This understanding that pain originates from an external source has persisted for centuries. Aristotle, perhaps the first person to define the five physical senses, distinguished pain from these senses, defining it as "the passion of the soul" and referred to pain as an intensification of these five senses (Aristotle, 1931). Over time, Plato, who developed Aristotle's ideas, stated that pain and pleasure come from the heart and liver. It is believed that these approaches by Aristotle and Plato laid the foundation for the understanding that pain is not only a physically localized discomfort but also an emotional experience (Okeson, 2014). From ancient times to the present, many different disciplines, from philosophy to neurological sciences, from psychology to social sciences, have contributed to science in explaining, understanding, diagnosing, and treating pain (Price et al., 2002). Today, as a result of all this scientific accumulation, it is known that pain is subjective. Moreover, the multidimensional nature of pain, which can be summarized as biopsychosocial, is widely accepted without dispute (Gatchel et al., 2007).

## The Neurophysiology of Pain

The nociceptive system is a specialized neural route that processes noxious sensations from the peripheral receptors to the cerebral brain. Peripherally, harmful stimuli activate specific receptors (nociceptors) of thin myelinated A delta fibers and unmyelinated C fibers that terminate in the dorsal horn of the spinal cord (Schnitzler & Ploner, 2000). Nociceptors, activated as a result of tissue injury in any part of the body, transmit this harmful stimulus to the central nervous system. These neural structures integrate the harmful stimulus and lead to physiological, biochemical, and psychological responses. The entirety of these electrochemical events is referred to as nociception. As a result of the impulses transmitted to the central nervous system, afferent fibers originating from the trigeminal ganglion release various neuropeptides. The generated signals are transmitted to the thalamus. The impulses transmitted from the thalamus reach the cerebral cortex, and the patient perceives the stimulus as pain at the cortical level. The patient's perception of pain occurs at this level (Aydin, 2002).

**Pain Receptor**

The perception of pain and the body's response to pain as a whole is called nociception, and the nerve endings specialized for perception are called nociceptors. Substances functioning as neuromediators released in the body stimulate the nociceptors through strong mechanical and thermal stimuli. Neuromediators have various chemical derivatives such as amino acid structures (GABA, glycine, glutamic acid, aspartic acid), amine structures (dopamine, norepinephrine, adrenaline, serotonin, acetylcholine, histamine), and peptide structures (substance P, endogenous opioid peptides, somatostatin, vasoactive intestinal peptide - VIP). Activated nociceptors transmit harmful impulses to the central nervous system through A delta and C fibers (Serdar ERDİNE, 2007).

**Stages of Pain Stimulation**

A stimulus that causes pain reaches the higher centers in four stages.

1. Transduction: This is the stage where the stimulus is converted into electrical activity at the sensory nerve endings. It is the process of transforming a painful stimulus into another form of energy. Nociceptors are activated when the stimulus exceeds a certain threshold value.
2. Transmission: This is the propagation of impulses along the sensory nervous system. Pain perceived by nociceptors is transmitted to higher centers through myelinated A-delta fibers and unmyelinated C fibers.
3. Modulation: This is the modification of nociceptive transmission by neural factors. It is primarily an event that occurs at the spinal cord level. The painful stimulus undergoes changes in the spinal cord and is transmitted to higher centers.
4. Perception: This is the final stage where the stimulus is perceived, resulting from the interaction with the individual's psychology and subjective emotional experiences. After the spinal cord, it is transmitted to higher centers through various pathways and is perceived there (Aydin, 2002).

It can be challenging to objectively determine and standardize the amount of pain by having individuals form groups (Attar et al., 2008). The use of scales when evaluating a patient's pain helps to transform the pain intensity and quality reported by the patient using numbers or words into as objective a measure as possible, eliminating different interpretations.

In clinical studies, numerical and verbal assessment scales or behavioral observations are traditionally used (Attar et al., 2008).

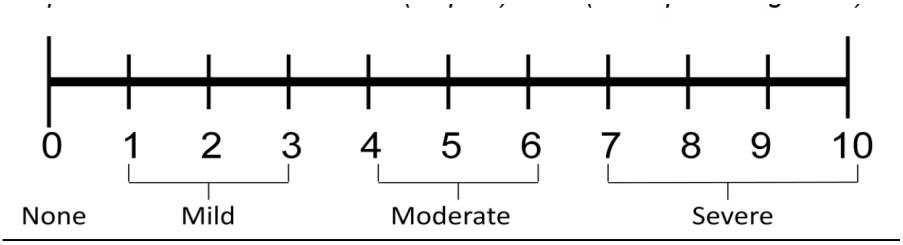
The following image presents the numerical, verbal, visual, and mixed classifications of these unidimensional scales used in pain intensity measurement (Yeşilyurt & Faydalı, 2020).

It is important to ensure active participation of patients in pain assessment. Especially in unidimensional pain assessment scales, where the patient evaluates and marks their own pain, it is expected that the patient understands the scale, interprets it, and, as a result, makes a decision and provides an assessment (Tan & Özyurt, 2006).

**Numerical Scales**

Numerical Rating Scale (NRS)

The patient is asked to provide three pain ratings corresponding to the current, best, and worst pain experienced in the past 24 hours. The average of these three ratings is used to represent the patient's pain level over the last 24 hours.




Because of their efficiency and convenience of use, numerical scales are among the most widely used unidimensional pain intensity scales (Tandon et al., 2016). Numerical scales include versions with 4, 5, 6, 11, 21, and 101 items. In actuality, patients are asked to select the number that most accurately represents the level of pain they are experiencing. Zero represents no pain, while the highest number represents the worst pain imaginable (Van Dijk et al., 2012). Numerical scales are easy to manage and score, and they are frequently preferred in practice because they help simplify the definition of pain intensity, as well as scoring and documentation (Hawker et al., 2011).

**Verbal Scales**

Verbal Descriptor Scale (VDS)

The patient's choice of the best term to describe their pain situation serves as the basis for the simple descriptive scale. The range of pain severity is minor to excruciating. (Eti-Aslan Fatma, 2002). Verbal scales are generally 4 or 5-item scales, where the patient is asked to choose the word that best describes their pain (Edelen & Saliba, 2010). The second type of pain scale classifies pain into four stages: no pain (0), mild pain (1), moderate pain (2), and severe pain (3) (Attar et al., 2008).

The patient selects the category that matches their condition. The advantages of the verbal descriptor scale include its ease of application and simple classification. It is valid and reliable. It has a high success rate in reflecting the multidimensional nature of pain. Additionally, more consistent results have been obtained in the elderly population. Its disadvantage is that it depends on the number of words available in the list for describing pain intensity, and there may be difficulties in making a selection or recalling the word that describes the pain intensity on the scale. It is also noted in the literature that patients tend to choose words from the middle of the scale rather than the extreme words (Eti-Aslan Fatma, 2002). While there is a wide range of responses in the Visual Analog Scale (VAS), there are similarities between the categories in each categorical scoring (Attar et al., 2008). This also complicates the patient's choice (Eti-Aslan Fatma, 2002).

**Visual Scales**

Facial Pain Scale (FPS) Facial Expression Scale (Wong-Baker Faces Scale – FS)

It is a simple instrument that is ideal for people who are illiterate because it doesn't require reading or writing. In various types of the scale, 6, 7, 9, or 11 facial expressions are used. The Facial Pain Scale (FPS) is a horizontal scale with 7 painful facial expressions that describe the intensity of pain (Dogan et al., 2010).

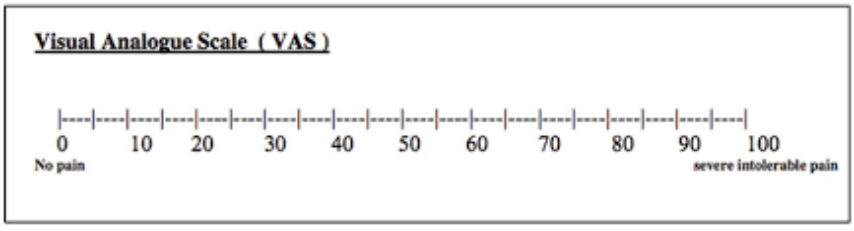
The 'no pain' expression is typically shown with a smiling face, while the 'most pain' expression is shown with a crying face (Yeşilyurt & Faydalı, 2020).


This scale is suitable for use in children, as well as in cases where the VAS cannot be used, such as communication and mental capacity limitations. A facial expression that closely matches the patient's is identified, and pain is scored accordingly (Dogan et al., 2010).

**Visual Comparison Scale (VCS)**

Visual Analog Scale (VAS)

The standard Visual Comparison Scale (VCS) is a semi-dimensional, ordered scale consisting of a 100 mm line, widely accepted. The scientifically accepted standard length of this scale aims to provide an easy and quantitative assessment (Ahearn, 1997). A 10 cm long horizontal or vertical line with the words "No Pain" at the beginning and "Unbearable Pain" at the end is commonly used to represent VCS. This line can be a simple straight line or divided into equal intervals. Additionally, when used for pain assessment, it may have pain descriptor labels placed along the line. The VCS has been a successful assessment tool in many studies to determine treatment effects (Yeşilyurt & Faydalı, 2020). In this assessment, pain average scores ranging from 0 to 10 are provided. Accordingly, '0' indicates no pain, while an average VCS score of 1-4 indicates mild pain, 5-6 indicates moderate pain, and 7-10 indicates severe pain (Ayan et al., 2013).




Coll et al. evaluated publications aimed at healthcare professionals regarding the subjective measurement of pain and its alignment with objectivity, and determined that the Visual Analog Scale (VAS) is suitable for measuring pain intensity after surgery. Based on the criteria they established, it was found that the VAS is methodologically sound, simple, meaningful, easy to apply, and does not disturb the person responding (Marie

et al., 2004). It has been shown that the VAS is highly reproducible and unaffected by gender differences (Attar et al., 2008).

**Analog Colored Continuous Scale (ACCS)**

Analog Chromatic Continuous Scale (ACCS)

It is a scale similar to the VAS. On one side of the scale, there is a 100 mm ruler, and on the other side, there are stripes that gradually change in color from light pink to dark red. The evaluation can be made using a scale with color differences corresponding to the endpoints of no pain and unbearable pain. (Green color = No pain, Red color = The most intense pain imaginable). Although the results of the ACCS and VAS show similarities, situations such as blindness or the fading or changing of the printed colors on the strip create a disadvantage for the ACCS (M.E. Güzeldemir, 1995). When comparing the results of the ARDÖ with VAS, similarities have been found (Altan et al., 2019).

**Oucher-Photographic Pain Scale**

The Oucher scale was developed to help children relate more easily to images. The Oucher scale includes two vertical pain scales: a numerical rating scale from 0-10 for older children, and colored faces depicting different expressions of pain for younger children (with photos of faces showing increasing levels of pain severity). The child is asked to rate their pain from 0, representing 'no pain,' to 10, representing 'the worst pain you could have.' The scale depicts a real child (Huguet et al., 2010; Yeşilyurt & Faydalı, 2020).

**Endodontic Pain**

Odontogenic pain is a significant reason for patients to visit the dentist (Law et al., 2014). In a postal survey conducted by Locker and Grushka in Toronto, 39.7% of the 594 participants reported having dental, facial, and oral pain in the four weeks prior to the survey (Locker & Grushka, 1987). More importantly, the same study examined how this pain affected patients' quality of life behaviorally and found that 58% of patients with pain were behaviorally affected, and 70.3% were psychologically affected (Locker & Grushka, 1987). Lipton and others conducted a survey in the United States regarding the prevalence and frequency of dental pain and found that 12.2% of the adult American population had experienced dental pain at least once in the past six months (Lipton et al., 1993). This rate is the highest among all orofacial pains (Lipton et al., 1993). On the other hand, pain can be a contributing factor to the initiation of dental fear and anxiety

(Maggirias & Locker, 2002), or it may be culturally and socially accepted that endodontic treatment is a painful procedure, which can be a significant reason for patients to avoid dental treatment (Rosenberg, 2014). All these studies, when considered from the patient's perspective, show that pain can be both a reason for visiting the dentist on one hand and a reason for avoiding dental treatment on the other. Pain holds different significance for each stage of endodontic treatment (Rosenberg, 2014).

## Postoperative Pain in Endodontics

The primary objective of endodontic treatment is to remove bacteria, bacterial irritants, and vital, infected, or necrotic tissues from the root canal system. The canal is then shaped in accordance with its anatomy and hermetically filled to create an environment that promotes the healing of periradicular tissues (Christopher & Emmanuel, 2010; Siqueira, 2001). Postoperative pain is an unwanted but commonly encountered condition after endodontic treatments (Gondim et al., 2010). Postoperative pain is a frequent complication after root canal treatment (Nekoofar et al., 2015; Shahi et al., 2013). It can be caused by many factors (Genet et al., 1987).

Common factors influencing the occurrence of pain after root canal treatment include missed canals, number of sessions, preoperative factors, preoperative complications, periapical index (PAI) score, size of radiolucency, quality of coronal restoration, factors during the procedure, intracanal medication use, the tooth's location in the arch, insufficient instrumentation, age, gender, periapical pathology, apical debris extrusion, hyperocclusion, and irrigation extrusion (Nekoofar et al., 2015). This pain can be bothersome for both practitioners and patients and may begin several hours or days after the treatment (Sathorn et al., 2008).

## Factors Affecting Postoperative Pain

### 1. Age

There is no consensus on the effect of age on postoperative pain in the results of studies examining this topic. In many studies, the impact of patient age on the occurrence of postoperative pain has been reported as insignificant (Balaban et al., 1984; Morse et al., 1990; Walton & Fouad, 1992).

Some studies suggest that younger patients encounter more pain compared to older patients, while others suggest that older patients experience more pain than younger patients (Ali et al., 2012; Watkins et al., 2002).

In a study by Ali et al. (2012), it was reported that postoperative pain observed in patients aged 41-65 years was greater than the pain observed in patients aged 15-40 years (Ali et al., 2012).

Watkins et al. argued that the likelihood of postoperative pain occurring is more common in younger patients (Watkins et al., 2002). In their 2010 study, El Mubarak et al. reported that postoperative pain was more common in younger patients aged 18-33 years compared to older patients (El Mubarak et al., 2010). On the other hand, Arias et al. suggested in their study that the likelihood of postoperative pain increases with age (Arias et al., 2013).

**2. Gender**

Many researchers argue that there is no relationship between gender and the frequency, intensity, or triggering of postoperative pain in their studies (A et al., 2024; Arias et al., 2013; Georgopoulou, 1986; Wójcik et al., 2019).

There are studies showing that younger patients experience more pain compared to older patients, as well as studies suggesting that older patients experience more pain than younger patients (Ali et al., 2012; Watkins et al., 2002). In a study by Ali et al., it was reported that postoperative pain observed in patients aged 41-65 years was greater than the pain observed in patients aged 15-40 years (Ali et al., 2012).

Fox et al. reported that the incidence of postoperative pain was higher in female patients (Fox et al., 1970). Comparin et al. found in their studies that the incidence of postoperative pain was higher in male patients compared to female patients (Comparin et al., 2017).

**3. Patient's general health status**

Fouad and Burleson, in their study investigating the effects of Type I and Type II diabetes on endodontic treatment, stated that in patients using insulin, the risk of symptomatic periradicular diseases and acute flare-ups was higher compared to individuals without systemic diseases (Fouad and Burleson, 2003). In this study, Anagha et al. evaluated the prevalence of postoperative discomfort following single and two-session endodontic treatment in people with managed Type 2 diabetes and those without the disease. They found no statistically significant difference (Anagha et al., 2022).

Hargreaves and Costello demonstrated that the application of glucocorticoids reduced bradykinin levels and postoperative pain (Hargreaves &

Costello, 1990). Alajlan et al. reported that the use of systemic corticosteroids decreased the incidence of postoperative pain (Alajlan et al., 2024).

Anxiety stimulates the patient's nociceptors, leading to genomic changes, which negatively affect the healing process of the resulting injury. Therefore, rehabilitating the patient may be beneficial in reducing postoperative pain. In endodontics, analgesics are administered prophylactically to lower the pain threshold before treatment and to reduce pain after treatment. Non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and opioids are used for this purpose in endodontic treatment (Schwartz & Fransman, 2005). In our country, opioids, which are not commonly prescribed by dentists, can be combined with paracetamol and some NSAIDs in endodontic treatment due to their lack of anti-inflammatory properties (Yamauchi et al., 2006). However, in Torabinejad et al.'s study on postoperative pain, a placebo was used, and when the values provided by patients were scored, there was no difference between the groups, and they observed that the placebo reduced pain as much as the analgesic (Torabinejad et al., 2002).

**4. Presence of Pain Before Endodontic Treatment**

Many studies have reported that patients with preoperative pain have a higher incidence of postoperative pain (Jain, 2024; Mattscheck et al., 2001; Siqueira et al., 2002). Therefore, when planning postoperative pain management strategies, preoperative pain must be taken into consideration (Risso, 2009).

In their studies, Genet et al. reported that postoperative pain was more frequent within the first 24 hours in patients with preoperative pain (Genet et al., 1987).

**5. Tooth Type**

Overall, it has been determined that mandibular teeth experience more postoperative pain than maxillary teeth (Ali et al., 2012; ElMubarak et al., 2010; Shibu, 2015). According to some reports, the mandible's dense trabecular structure causes decreased blood flow and a delayed infection healing pattern (Ali et al., 2012).

**6. Medication Use**

When the literature is reviewed, it shows that the preoperative administration of medications may have an effect in suppressing or reducing postoperative pain. The use of nonsteroidal anti-inflammatory drugs

(NSAIDs) before endodontic treatment can suppress postoperative pain. This effect can be explained by the inhibition of prostaglandin synthesis through the blockade of Cox pathways by NSAIDs (Menke et al., 2000).

Another important topic is intracanal medicament application. Antibacterial intracanal medicaments have been recommended to eliminate surviving microorganisms after chemomechanical preparation. In dentistry, various intracanal medicaments with a wide range of uses are employed to reduce residual bacterial load after root canal instrumentation, as well as to effectively manage postoperative inflammation and pain. However, there is no consensus regarding the effect of intracanal medicament application on postoperative pain (Hegde et al., 2023).

**7. Number of Sessions**

In studies evaluating the effect of completing retreatment in one session versus multiple sessions on postoperative pain, there has been no consensus in the literature. Hepşenoğlu et al. stated that the incidence of postoperative pain was lower in one-session retreatment procedures without intracanal medicament use compared to multiple-session non-surgical retreatments (Erdem Hepşenoğlu et al., 2018). However, there are also studies in the literature that argue there is no difference in postoperative pain between one-session and multiple-session treatments (DiRenzo et al., 2002; Rao et al., 2014).

DiRenzo et al. examined the effect of one-session and two-session root canal treatments on postoperative pain (DiRenzo et al., 2002). Patients with vital and non-vital permanent molars were divided into two groups. For the teeth to be treated in two sessions, after the enlargement procedure, a temporary restoration was placed with a cotton pellet, and the treatments were completed 7-14 days later. The pain levels of the patients treated in one session and the patients treated in two sessions were rated using the Visual Analog Scale (VAS) at 6, 12, 24, and 48 hours after the first session. As a result, no statistically significant difference was found in postoperative pain between the two groups. El Mubarak et al.'s study showed similar results to this research (El Mubarak et al., 2010).

In multiple-session treatments, various intracanal medicaments (such as calcium hydroxide, Ledermix, chlorhexidine, and antibiotics) are used to reduce the amount of residual bacteria after root canal instrumentation, as well as to effectively manage postoperative inflammation and pain, which have a wide range of applications (Georgopoulou, 1986). This allows for the reassessment of tissue response. On the other hand, the increased risk of flare-ups during intermediate sessions, increased patient stress, and

patient reluctance due to the greater number of sessions are disadvantages (Schwendicke & Göstemeyer, 2017).

In single-session root canal treatments, both the dentist and the patient save time, and the absence of the need for repeated anesthetic or rubber dam application reduces the patient's dental anxiety. Additionally, there is no risk of microleakage associated with temporary restorations. However, total elimination of microorganisms may not be achieved (Schwendicke & Göstemeyer, 2017).

### 8. Instrumentation and Obturation Technique

The dentist is particularly concerned about postoperative pain following instrumentation because over-instrumentation may increase the risk of irrigation and filling material extrusion, which raises the risk of pain following treatment. Compared to the step-back approach, the step-down or crown-down technique has a reduced incidence of postoperative pain. This might be because, as several studies have shown, there is a greater chance of moving material past the apical foramen. The step-down approach significantly lowers the danger of extrusion producing periapical inflammation by removing a large amount of tissue remnants and germs prior to beginning apical instrumentation (Shibu, 2015).

The importance of using a technique that reduces postoperative complications is increasingly recognized today. All instrumentation techniques cause some degree of debris extrusion, but the amount of extruded debris may vary depending on the preparation technique and file design. Studies comparing different mechanical systems have reported variability in debris extrusion (Kherlakian et al., 2016).

The gutta-percha filling techniques used in root canal obturation are among the factors affecting postoperative pain. Nair et al. reported that the warm gutta-percha filling technique causes more postoperative pain compared to the cold lateral compaction technique (NAIR et al., 1993). In an in vivo study, Alaçam investigated four different root canal filling techniques in terms of postoperative pain and found no significant difference between the groups (Alaçam, 2006).

Root canal filling techniques play a role in the occurrence of postoperative pain. Luis O et al. found that the Thermafil technique caused more postoperative pain compared to cold lateral compaction and Backfill-Thermafil techniques in their study comparing three different obturation techniques (Alonso-Ezpeleta et al., 2012). Nino-Barrera et al. reported that there was no significant difference in postoperative pain between two

different obturation techniques, Calamus® and Guttacore®, applied to anterior and molar teeth (Nino-Barrera et al., 2018).

### 9. Pulp Vitality

The evidence in the literature regarding the effect of pulp vitality on postoperative pain incidence is insufficient. It has been reported that endodontic treatment performed on vital pulp teeth is associated with less postoperative pain, while asymptomatic necrotic pulp teeth with periapical lesions are the most likely clinical condition to trigger postoperative pain formation (Martins et al., 2020).

Farzaneh et al. demonstrated in their studies that necrotic pulp teeth can cause more postoperative pain than vital teeth. They attributed this to the fact that damaged periapical tissues can more easily extrude irrigation agents and debris (Farzaneh et al., 2018).

### 10. Irrigation Procedures

Although NaOCl is of great importance in endodontics, its toxicity to the periapical area is a disadvantage of this solution (Zehnder, 2006). NaOCl should be used at a concentration of 0.025% to prevent damage to the periapical area (Heggers et al., 1991). However, in endodontics, it is recommended to use NaOCl at concentrations between 0.5% and 5.25% (Zehnder, 2006). When NaOCl is extruded into the periapical area, the hypochlorous acid in its composition reacts with tissue proteins (Estrela et al., 2002). As soon as the reaction occurs, NaOCl's effect diminishes quickly due to its neutralization. Upon contact with tissue proteins, NaOCl causes the proteins to break down into nitrogen, formaldehyde, and acetaldehyde (Mehdipour et al., 2007). The proteins break down due to the disruption of peptide bonds (Estrela et al., 2002). The metabolic byproducts released as a result of this reaction increase tissue inflammation (Estrela et al., 2002). Inflammation, in turn, leads to pain and swelling. The greater the concentration and volume of NaOCl extruded into the periapical area, the more severe the symptoms (pain, swelling, hematoma, burning, necrosis, abscess) will be (Mehdipour et al., 2007).To prevent the extrusion of toxic solutions into the periapical area, certain techniques have been developed. Closed-ended needles are designed for controlled canal irrigation in endodontics. Irrigation with these needles is considered safe as the solution is directed toward the canal walls rather than the apical area (Gu et al., 2009). Systems working on the principle of negative pressure (e.g., EndoVac) prevent the solution from leaving the apical area and help avoid potential complications (Gondim et al., 2010; Gu et al., 2009). Inflamma-

tion that occurs in the apical area after root canal treatment will also affect postoperative pain (Seltzer, 1986).

Demenech et al. evaluated the postoperative pain of 180 patients who underwent single-session endodontic treatment with irrigation using 2.5%, 5.25%, 8.25% Sodium Hypochlorite (NaOCl) or 2% Chlorhexidine (CHX) solutions and concluded that there was no significant difference between the groups (Demenech et al., 2021).

Although conventional irrigation is a well-known method, it often fails to affect the canal sufficiently, reach lateral and accessory canals, and adequately eliminate microorganisms. As a result, sonic, ultrasonic, and laser systems have been introduced in recent years (Erkan et al., 2022). According to Chalub et al.'s research, using ultrasonic irrigation instead of traditional irrigation led to less postoperative pain (Chalub et al., 2022).

### 11. Occlusal Reduction

Rosenberg et al. reported that teeth with reduced occlusal load produce less postoperative pain (Rosenberg et al., 1998). Occlusal reduction is effective not only in reducing postoperative pain but also in decreasing preoperative pain, percussion sensitivity, and abscess discomfort (Rosenberg, 2014). In postoperative pain, the continuation of occlusal stimuli following apical trauma leads to the sensitization of nociceptors and the development of mechanical allodynia (increased sensitivity to biting and percussion) (Ow3atz et al., 2007).

## Conclusıon

Root canal treatment alleviates patients' symptoms and improves their quality of life. Preoperative pain, which is observed at 54%, decreases to 40% after 24 hours of treatment and to 11% after one week. After two weeks, patients' pain has significantly reduced (Pak & White, 2011). However, postoperative pain is an inevitable condition. In the literature, postoperative pain ranges from 3% to 58% (Sathorn et al., 2008). Twelve percent of patients report having excruciating pain 24 to 48 hours following therapym(Ng et al., 2004).

To minimize the inevitable postoperative pain following endodontic treatment, clinicians should work under optimal conditions and use the appropriate preparation technique, irrigation, and filling techniques for each case. Even under optimal conditions, postoperative pain can still occur due to several factors.

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# BÖLÜM 2

## ASSESSMENT OF ASYMPTOMATIC APICAL PERIODONTITIS, TREATMENT STRATEGIES

*Nesrin BEYAZASLAN*

*Neslihan Büşra KESKİN*

### Asymptomatic Apical Periodontitis

Symptomatic apical periodontitis can progress if the infection in the root canal is left untreated and may transition into an asymptomatic condition as its symptoms decrease. However, this does not mean that the disease has disappeared. Asymptomatic apical periodontitis is the result of the body's chronic inflammatory response to the infection (Neslihan et al.2013).

It is asymptomatic and is usually discovered incidentally during radiographic examination. It presents as a radiolucent periapical lesion on the radiograph. The affected tooth has a necrotic pulp. Rarely, an acute flare-up may occur in a chronic lesion, causing swelling and/or pain in the area. This is typically referred to as a Phoenix abscess or an acute flare-up of chronic apical periodontitis (Sigurdsson 2003).

### Etiology

Apical periodontitis is influenced by both endogenous and external causes. Microorganisms, their poisons, toxic metabolic byproducts, chemicals, mechanical damage, foreign substances, and physical injuries are examples of exogenous influences. On the other hand, endogenous factors include cytokines and other inflammatory mediators that activate osteoclasts, as well as metabolic products such urea and cholesterol crystals that come from the host (Stashenko 1990, Nair et al. 1998).

The infection of the pulp tissue caused by decay or other factors in the root canal system is the primary cause of apical periodontitis (Sundqvist 1976, MÖLLER et al. 1981, Nair 1997, Witherspoon 2008).

### Microbiology

In root canals that lack host protection because of pulp necrosis brought on by decay, trauma, periodontal disease, invasive surgical operations, or pulp removal for therapeutic reasons, endodontic infection arises. Endodontic infections have been linked to a variety of microbes, including viruses, fungi, and archaea, in addition to bacteria. However, bacteria are thought to be the main microorganisms involved in the pathophysiology of apical periodontitis due to their great prevalence, dominance, and high pathogenicity. Bacterial formations that resemble biofilms and are affixed to the canal walls are commonly seen in advanced stages of the endodontic infection process. Consequently, biofilm-related oral disorders have been linked to apical periodontitis (Berman et al. 2020).

Despite their ability to colonize the oral cavity, yeast fungus belonging to the Candida genus are rarely implicated in the etiology of primary apical periodontitis. According to Neelakantan et al. (2017), these fungi are typically found in situations of more resistant apical periodontitis.

Prokaryotes called archaea differ greatly from bacteria in their structure. Archaea are hard to find in samples from primary endodontic infections, however a phylotype that resembles Methanobrevibacter oralis has been found (Egan et al. 2002).

Root canal infections are typically associated with a microbial environment dominated by anaerobic bacteria. Molecular studies have shown that an average of 10-20 different bacterial species can be found in a root canal. Additionally, it has been demonstrated that the size of the apical periodontitis lesion is directly proportional to the types and amounts of bacteria in the root canal. In the case of primary apical periodontitis, the bacteria causing the infection include 9 out of 13 phyla found in the oral microbiota. These phyla include Firmicutes, Bacteroidetes, Fusobacteria, Actinobacteria, Proteobacteria, Spirochaetes, Synergistes, TM7, and SR1 (Kolenbrander et al. 2002).

Compared to the microbiota in primary infections, the microbiota of teeth with apical periodontitis and those that have had root canal therapy is significantly more restricted. Usually, 1–5 distinct bacterial species are detected in root canals that have been successfully filled; in canals that have not been properly filled, this number might increase to 10–20 species (Saito et al. 2006). Bacterial cells per root canal range from $10^3$ to $10^7$ in teeth where the infection continues after treatment (Roças et al. 2004). Enterococcus faecalis is the most frequent bacterial species found in root canals, with a prevalence rate of up to 90% in instances, according to numerous culture and molecular biology investigations (Pashley et al. 1985).

**Histopathology**

The majority of the cells in asymptomatic apical periodontitis lesions are macrophages and lymphocytes. Giant cells and foamy macrophages, which are linked to cholesterol crystal deposits, especially those caused by broken cell membranes, can occasionally also be seen. About 18–44% of all apical periodontitis lesions include cholesterol crystals (Browne 1971, Jauregui Perez 1973).

The most noticeable sign of apical periodontitis is bone resorption. In resorptive Howship lacunae, multinucleated osteoclasts can occasionally be seen. Furthermore, asymptomatic apical periodontitis lesions frequently exhibit the growth of epithelial cell remains (Berman et al. 2020).

Information about cement alterations in apical periodontitis is extremely scarce. Simon and colleagues used scanning electron microscopy to analyze the uneven organization of cement fibers, extensions, and depressions during root canal infection. There was also a decrease in fibers and an increase in cement lacunae, mineralized extensions, and surface resorption. In extraradicular infection, all of these modifications might provide an environment that is more conducive to bacterial biofilm adhesion to the apical external root surface (Simon et al. 1981).

A considerable amount of nerve tissue is also present in teeth with chronic apical periodontitis, according to research using light and transmission electron microscopy (Lin et al. 1981, Martinelli et al. 1967). These results may help to explain why patients may feel pain when devices inadvertently come into contact with the periapical tissues in situations where local anesthetic is not used.

Asymptomatic apical periodontitis lesions frequently experience root resorption involving the cementum and dentin. Fortunately, compared to bone tissue, cementum and dentin tissues are more resilient to resorption brought on by inflammatory processes (Laux et al. 2000). On radiographs, however, a skilled clinician may interpret changes like a reduction in root mass (blunting and narrowing) as a sign of cementum and dentin resorption. In this instance, the non-surgical endodontic treatment's shaping and filling processing timeframes had to be modified appropriately. Numerous asymptomatic apical periodontitis lesions have been found to include bacteria, according to research employing light microscopy, transmission electron microscopy, and microbiological culturing techniques (Iwu et al. 1990, Abou-Rass et al. 1998).

In detailed transmission electron microscopy examinations, Nair (1987) was unable to detect bacteria in most asymptomatic apical periodontitis lesions (Nair, 1987). However, in cases where bacteria were found in inflamed periapical tissues, they were typically observed within phagocytes (Araujo-Pires et al. 2014).

It is crucial to remember that colonization—the simple presence of bacteria in periapical tissues that are inflamed—does not always signify a periapical infection. Non-surgical root canal therapy for teeth with apical periodontitis can have a good success rate as long as the root canal infection is under control. The majority of apical periodontitis lesions are not infected.

## Cell Biology

### Macrophages and Lymphocytes

The primary cellular constituents of asymptomatic apical periodontitis are macrophages and lymphocytes. Macrophages contribute to the host defense response in both directions (Hargreaves, 2010). Activated macrophages phagocytize pathogens, dead cells, and foreign objects as part of the innate immune response. They also strengthen defenses by generating pro-inflammatory cytokines and inflammatory mediators. However, lymphocytes are the only cells in the body that can identify and differentiate between many antigenic cues; they give the adaptive immune response important characteristics like memory and specificity (Dahlen, 2002).

### Dendritic Cells

In the pathophysiology of asymptomatic apical periodontitis, dendritic cells are crucial. They have been found in rats' apical periodontitis lesions (Kaneko et al., 2001). These immune cells, which belong to the mononuclear phagocyte family, are hematopoietic-derived and originate from the bone marrow. The mediator IL-12, which is produced by activated dendritic cells, is essential for the initiation of cellular immunity (Okiji et al., 1994).

### Osteoclasts

One of the main characteristics of asymptomatic apical periodontitis is peripheral bone deterioration. The periapical osteolytic lesion becomes stable in the chronic stage of apical periodontitis due to a decrease in osteoclast and osteoblast activity. Seven days after experimentally exposing tooth pulp to oral microbes, studies using animal models have shown bone deterioration. Days 10–20 see rapid bone resorption, which is followed by slower bone resorption. Asymptomatic apical periodontitis has been linked to the stationary phase of bone resorption activity. Active bone resorption has been associated with increased expression of bone resorptive cytokines, including TNF, IL-1, and IL-6.

T cells outnumbered B cells in rats with adapted periapical wounds throughout the active phase of periapical bone degradation, while B cells outnumbered T cells during the stationary phase of bone destruction (Tazawa et al., 2022).

### Malassez Epithelial Cell Remnants (ERM)

Every tooth's periodontal ligament contains ERM. About 52% of inflammatory periapical lesions taken from removed teeth clearly show proliferation of ERM (Nair et al., 1996). This kind of abnormal (inflammatory) hyperplasia is what it is. Growth factors and cytokines generated during the inflammatory response are stimulated, leading to hyperplasia. When the causative stimulus is removed, this process reverses and possesses a self-limiting feature (Kumar et al., 2015).

### Fibroblasts

Cells called fibroblasts are essential for wound healing and persistent inflammation. Fibroblasts, which originate from undifferentiated mesenchymal cells, are present in all connective tissues. Proteoglycans, glycoproteins, different kinds of collagen, and elastin precursor molecules are all produced and secreted by them. Activated platelets, macrophages, endothelial cells, and inflammatory cells release fibrogenic cytokines like IL-1 and TGF-α, as well as growth factors like TGF-β, PDGF, EGF, and FGF, which cause fibroblast migration and proliferation in chronic inflammation. Leukocyte formation is influenced by a variety of cytokines produced by activated fibroblasts, including GM-CSF, IL-1, and IL-6. Additionally, by breaking down the proteins that make up the extracellular matrix, inflammation-stimulated fibroblasts generate matrix metalloproteinases.

One of the main characteristics of chronic apical periodontitis as a healing process is fibrovascular granulation tissue. Neovascularization is the process by which endothelial cells migrate and proliferate from pre-existing capillaries and venules to the site of chronic inflammation.

Activated macrophages, platelets, and endothelial cells release angiogenic molecules such vascular endothelial growth factor (VEGF) and TGF-β, which mediate this process.

### Chronic Apical Periodontitis Associated with Cyst Formation

Radicular cysts have a distinctive structure compared to other cysts in the body, as they do not share a similar pathogenesis. These cysts are most likely thought to form as a result of inflammatory proliferation due to epithelial cell remnants within the inflammatory periodontal ligament in chronic apical periodontitis lesions. A radicular cyst is a pathological cavity within an apical periodontitis lesion, typically surrounded by multi-layered, non-keratinized squamous epithelium of varying thicknesses, and often of large size (Lin et al., 2007).

Although they do not develop on their own, radicular cysts can be categorized as either "pocket cysts," which are connected to the apical foramen, or "true cysts," which are not connected to the root structure. As a result, radicular cysts and chronic apical periodontitis should not be viewed as distinct diseases (Nair, 1998). The radicular cyst is classified as an inflammatory lesion rather than an aberrant developmental or neoplastic lesion by the World Health Organization (WHO) in its histological categorization of odontogenic tumors, jaw cysts, and composite lesions (Kramer et al., 1992). Radicular cysts are found in 15-20% of apical periodontitis lesions in removed teeth (Nair et al., 1996).

### Reactive Bone Formation in Chronic Apical Periodontitis: Condensing Osteitis

Chronic osteomyelitis associated with proliferative periostitis is comparable to chronic apical periodontitis with reactive bone growth. Both illnesses' pathophysiology and causation are still poorly understood. It is believed that either high levels of local tissue resistance or protracted, moderate inflammation or infection cause these lesions. In the periapical region of the endodontically damaged tooth, inflammation causes reactive bone production in the alveolar trabecular or spongy bone rather than bone resorption (Berman et al., 2015).

### Post-Treatment Periapical Wound Healing

Understanding wound healing is as important as understanding the pathogenesis of the disease, as effective wound healing forms the primary goal of treatment.

In addition to cell-to-cell contacts, cell-extracellular matrix (ECM) interaction, and cell surface receptors, the wound healing process is closely controlled by a number of cytokines, growth factors, neuropeptides, and apoptosis, all of which have temporal and spatial expression (Brain, 1997). During wound healing, all of these humoral and cellular components are carefully controlled and can work in concert or antagonistically. The outcome is a very well-organized reaction that permits the restoration of the original tissue structure. According to some observations, wound healing is a predetermined process (Fouad et al., 1992).

Lesions caused by apical periodontitis often recover by regeneration and, to a lesser extent, repair. Osteocytes in the alveolar bone, osteoblasts, mesenchymal cells in the bone marrow, and stem cells in the periodontal ligament are some of the local tissue-specific cells engaged in periapical wound healing (Seo et al., 2004).

Following its entry into the new regeneration process, the periodontal ligament will eventually undergo remodeling to become a mature periodontal ligament, in which a group of collagen fibers known as Sharpey's fibers will enter the newly produced cementum and another group will enter the newly formed alveolar bone. This will finish the regeneration of the injured periapical tissues, such as the alveolar bone, cementum, and periodontal ligament (Berman et al., 2015).

According to reports based on molecular cell biology, pocket cysts in apical periodontitis lesions may shrink after non-surgical root canal therapy due to apoptosis or programmed cell death (Lin et al., 2007). On the other hand, real apical cysts have a lesser chance of healing during non-surgical root canal therapy because of their autonomous structure and kinds (Nair et al., 1990).

**Treatment Strategies**

The treatment of periapical lesions varies depending on the size, type, and clinical condition of the patient. Endodontic treatment is the primary approach for controlling the lesions and preserving the tooth; however, in some cases, surgical interventions may be required. Additionally, in recent years, emerging tissue healing technologies, such as biological treatment options like Platelet-Rich Plasma (PRP), have been used to accelerate the healing of lesions and support regeneration at the root apices.

A study by Keskin et al. (2023) examined how intracanal cryotherapy affected the levels of proteolytic enzymes, inflammatory cytokines, and post-operative discomfort in teeth with asymptomatic apical periodontitis. 44 patients with a diagnosis of asymptomatic apical periodontitis had their mandibular premolar teeth treated with endodontics over the course of two sessions. ELISA was used to measure the levels of TNF-α, PGE2, MMP-8, IL-1β, IL-2, IL-6, and IL-8. The degree of pain following root canal therapy may be predicted by IL-1β and PGE2 levels, as there was a positive association between these biomarker levels and discomfort between sessions. They discovered that for teeth with asymptomatic apical periodontitis, intracanal cryotherapy was useful in minimizing pain in the near term following root canal therapy. Cryotherapy stopped IL-1β, IL-2, and IL-6 levels from rising in comparison to the control group (Keskin et al., 2023).

Karaoğlan et al. (2022) followed up on the results of single-session or two-session root canal retreatments in teeth with periapical lesions. In the 24-month follow-up of retreatments completed in one or two sessions in asymptomatic teeth with periapical lesions, no statistically significant difference in healing was observed. They reported that the size of the peri-

apical lesion and the initial apical level of the root canal filling affected the outcome of root canal retreatment (Karaoğlan et al., 2022).

In a study examining the antibacterial efficacy of calcium hydroxide alone or in combination with ibuprofen and ciprofloxacin in teeth with asymptomatic apical periodontitis, Karataş et al. reported that, when used in vivo as an intracanal medication during root canal treatment, the combination of ciprofloxacin and calcium hydroxide provided higher antibacterial efficacy (Karataş et al., 2020).

It was found that in vivo functional loading (IFL) of full crown prostheses delayed periapical healing in mandibular molar teeth with pulp necrosis and asymptomatic apical periodontitis that had received endodontic treatment. This study examined the impact of functional loading timing on periapical healing in these teeth (Kangjam et al., 2024).

In a study examining the effect of photodynamic therapy on periapical lesion healing after root canal retreatment, it was reported that photodynamic therapy applied with passive ultrasonic activation had similar effects on periapical lesion healing (Pažin et al., 2024).

The first clinical safety and efficacy data on the use of allogeneic umbilical cord mesenchymal stem cells for endodontic treatment comes from a randomized controlled Phase I/II clinical study that assessed the safety and effectiveness of human umbilical cord mesenchymal stem cells for regenerative endodontic procedures in mature permanent teeth with apical lesions based on 12-month follow-up results. Based on biological principles that promote dentin-pulp regeneration, this novel technique shows promise as a therapy option for periapical diseases (Brizuela et al., 2020).

A study conducted in 2020 evaluated the effects of a single-cone technique with a reciprocating single-file system on apical periodontitis healing and postoperative pain after endodontic treatment. The study found that the single-cone technique with reciprocating file, when compared to manual instrumentation followed by lateral condensation technique, yielded similar results in terms of periapical healing and postoperative pain (de-Figueiredo et al., 2020).

In order to speed up the healing of periapical lesions, the Apexum technique (Apexum Ltd, Or-Yehuda, Israel) involves the minimally invasive excision of periapical chronic inflammatory tissues via root canal access. A study examining the effectiveness and safety of the Apexum method was carried out by Metzger et al. According to the research findings, the Apexum approach offers faster periapical healing than traditional root canal treatment and results in much less postoperative pain and suffering

than either apical surgery or traditional root canal treatment (Metzger et al., 2009).

Ahmed et al. studied the effects of conventional endodontic treatment with PRP on pain and healing after revascularization in necrotic mature permanent mandibular molars with periapical periodontitis. The study found that, except for the 12-hour post-treatment period, there was no statistically significant difference in pain intensity between the two groups across all time points. However, the revascularization group demonstrated a statistically significant higher prevalence of pain-free status compared to the endodontic treatment group. In terms of healing, periapical lesions significantly reduced in size in both groups compared to preoperative lesion sizes, but no significant difference was observed between the two groups (Ahmed et al., 2023).

In a study conducted by Alshahhoud et al. (2024), the applications of natural chitosan-based scaffolds and enzymatically modified chitosan-based scaffolds in single-rooted teeth with apical lesions were compared with clinical and radiographic evaluations to assess the effectiveness of pulp regeneration.

According to the results of the study, the group treated with enzymatically modified chitosan and blood clot showed superior results in pulp regeneration after six months and demonstrated higher healing compared to the other groups (Alshahhoud et al. 2024).

In a study by Kurt et al., the healing of mandibular molar teeth with large periapical lesions was assessed and contrasted with the outcomes of a traditional two-session root canal treatment, which served as the control group. The single-session root canal treatment used 2% CHX as the final irrigation. In mandibular molars with extensive periapical lesions, the study found that a single-session root canal treatment with 2% CHX as the final irrigation had positive healing outcomes, comparable to the two-session calcium hydroxide therapy (Kurt et al. 2022).

The study conducted by Uluköylü et al. in 2019 investigates the effects of calcium hydroxide (Ca[OH]2) and agents such as ibuprofen or ciprofloxacin added to this treatment on the levels of receptor activator of nuclear factor kappa B ligand (RANKL) and osteoprotegerin (OPG), which influence bone resorption in the treatment of periapical lesions. The study found that the addition of these drugs to Ca(OH)2 did not provide any additional benefit in lowering the levels of RANKL and OPG (Uluköylü et al. 2019). This result emphasizes that studies involving the addition of intracanal medications should carefully assess treatment strategies, particularly in situations like periapical lesions, where bone resorption is significant.

Fonzar et al. conducted a study evaluating whether endodontic treatment is more effective in a single session or in two sessions with one week of intracanal calcium hydroxide therapy in symptomatic teeth and teeth with periapical lesions. In the study, patients were randomized to receive either a single visit (99 patients) or two visits with one week of intracanal calcium hydroxide therapy (100 patients) at two centers. After treatment, patients were followed for one year, and the outcome measures included tooth loss, radiographic healing, complications, post-treatment pain, and analgesic consumption. At the end of the year, treatment outcomes were found to be similar in both groups, but patients who received single-session treatment experienced less postoperative pain and used fewer analgesics than those who underwent two-session treatment (Fonzar et al. 2017). These findings suggest that single-session endodontic treatment leads to less pain and reduced medication use, indicating that single-session treatment should be preferred. This is an important indicator in clinical practice for reducing treatment time and improving patient comfort.

Asymptomatic apical periodontitis is a condition that does not present clinical symptoms but can be detected through radiographic examinations. With early diagnosis and appropriate endodontic intervention, complications can be prevented, and the long-term preservation of the tooth is possible. In this regard, treating asymptomatic apical periodontitis is crucial for dental professionals.

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