Original Research

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Comparative evaluation of success rates in endodontic therapy versus oral medicine interventions in the management of chronic periapical lesions

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Abstract

INTRODUCTION. Chronic periapical lesions are an outcome of pulpal necrosis that necessitates final treatment. Although the traditional endodontic treatment is still the gold standard, the use of adjunctive interventions based on oral medicine and conservative pharmacological approaches as potential modes of treatment have been proposed.

MATERIALS AND METHODS. A prospective comparative study was performed on 180 patients with chronic periapical lesions who were grouped as Group A (conventional endodontic therapy only, $n = 60$), Group B (endodontic therapy plus systemic pharmacological intervention, $n = 60$) and Group C (conservative oral management and delayed endodontic intervention, $n = 60$). The main outcomes were the level of healing success, reduction of the size of the lesion, and the resolution of the symptoms measured at 3, 6, and 12 months. Secondary outcomes were pain scores, quality of life and treatment complications.

RESULTS. 12 months overall success rates were: Group A (83.3%), Group B (91.7%), Group C (45.0%), $p < 0.001$. The lesion size reduction in terms of the mean was also 4.82 ± 1.24 mm (Group A), 5.67 ± 1.18 mm (Group B) and 2.14 ± 1.52 mm (Group C), $p < 0.001$. Total periapical healing Group A (76.7), Group B (85.0) and Group C (33.3), $p < 0.001$. The Group B (4.2 + 1.8 days) and the Group C (12.6 + 4.8 days) had significantly shorter pain resolution times when compared to Group A (6.8 + 2.4 days), $p < 0.001$. The highest level of patient satisfaction was obtained in Group B (8.64 + 1.12) in comparison to Group A (7.92 + 1.34) and Group C (5.28 + 1.86), $p = 0.001$. Group A, 10.0%: Group B, 5.0%: Group C, 41.7%: treatment failure requiring surgical intervention was found.

CONCLUSIONS. Endodontic therapy with systemic pharmacological intervention has better results compared to endodontic therapy or conservative oral medicine treatment. The outcome of conservative pharmacological treatment without conclusive endodontic therapy is far worse and thus there is a need to treat the infectious etiology to achieve success in treating periapical lesions.

Keywords: periapical lesion, endodontic therapy, oral medicine, antibiotics, anti-inflammatory drugs, treatment outcome, periapical healing, root canal treatment

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Сравнительная оценка показателей успеха эндодонтической терапии и вмешательств в области оральной медицины при лечении хронических периапикальных поражений

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Резюме

ВВЕДЕНИЕ. Хронические периапикальные поражения являются следствием некроза пульпы и требуют окончательного лечения. Несмотря на то что традиционное эндодонтическое лечение остается «золотым стандартом», в качестве возможных терапевтических подходов предлагается применение вспомогательных вмешательств в рамках оральной медицины и консервативной фармакотерапии.

МАТЕРИАЛЫ И МЕТОДЫ. Проведено проспективное сравнительное исследование с участием 180 пациентов с хроническими периапикальными поражениями, распределенных на три группы: группа A (только традиционная эндодонтическая терапия, $n = 60$), группа B (эндодонтическая терапия в сочетании с системной фармакологической терапией, $n = 60$) и группа C (консервативное оральное лечение с отсроченным эндодонтическим вмешательством, $n = 60$). Основными оцениваемыми параметрами являлись уровень заживления, уменьшение размеров очага поражения и купирование симптомов через 3, 6 и 12 месяцев. Вторичные показатели включали выраженность болевого синдрома, качество жизни и осложнения лечения.

РЕЗУЛЬТАТЫ. Через 12 месяцев общие показатели успеха составили: группа A – 83,3%, группа B – 91,7%, группа C – 45,0% ($p < 0,001$). Среднее уменьшение размеров очага поражения составило 4,82 ± 1,24 мм в группе A, 5,67 ± 1,18 мм в группе B и 2,14 ± 1,52 мм в группе C ($p < 0,001$). Полное периапикальное заживление наблюдалось у 76,7% пациентов группы A, 85,0% – группы B и 33,3% – группы C ($p < 0,001$). Время купирования болевого синдрома было достоверно меньше в группе B (4,2 ± 1,8 дня) и группе C (12,6 ± 4,8 дня) по сравнению с группой A (6,8 ± 2,4 дня), $p < 0,001$. Наивысший уровень удовлетворенности пациентов отмечен в группе B (8,64 ± 1,12) по сравнению с группой A (7,92 ± 1,34) и группой C (5,28 ± 1,86), $p = 0,001$. Частота неудач лечения, потребовавших хирургического вмешательства, составила: группа A – 10,0%, группа B – 5,0%, группа C – 41,7%.

ВЫВОДЫ. Эндодонтическая терапия в сочетании с системной фармакологической поддержкой демонстрирует более высокую эффективность по сравнению с изолированной эндодонтической терапией или консервативным лечением методами оральной медицины. Консервативная фармакотерапия без окончательного эндодонтического вмешательства характеризуется значительно худшими результатами, что подтверждает необходимость устранения инфекционной этиологии для достижения успешного лечения периапикальных поражений.

Ключевые слова: периапикальное поражение, эндодонтическая терапия, оральная медицина, антибиотики, противовоспалительные препараты, исход лечения, периапикальное заживление, лечение корневых каналов

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INTRODUCTION

Chronic periapical lesions are inflammation diseases that occur in the periradicular tissues of the tooth apices and are caused by the presence of the bacteria that were initially embedded into the tooth necrot pulp tissue [1]. These lesions are a huge burden in clinical endodontics since they occur in about 5–10 percent of teeth and are among the most frequent causes of tooth loss among adults [2]. Chronic periapical pathology is radiographically evident as periapical radiolucencies and clinically, may be either asymptomatic or may be accompanied by intermittent symptoms such as tenderness to percussion, mild discomfort, and swelling [3].

The pathogenesis of the chronic periapical lesions is the combination of host-microbial interactions in which the products and metabolites of bacteria of the infected root canals stimulate the chronic inflammatory response of the periapical tissues [4]. This is an inflammatory event, which is mediated by complex immunological cascades and cytokines, prostaglandins and matrix metalloproteinases which eventually culminate in bone resorption and the development of granulomatous tissue/radicular cysts [5]. Chronic periapical infections have a polymicrobial microbiology with obligate anaerobes such as Porphyromonas endodontalis, Prevotella species, Fusobacterium nucleatum, and Peptostreptococcus species [6].

Traditional endodontic therapy that includes pulpectomy, biomechanical preparation, chemomechanical debridement, and three-dimensional obturation of the root canal system is the conventional treatment option of tooth with chronic periapical lesions [7]. The goals of this intervention are to get rid of the infectious agent, avoid reinfection, and provide an environment that would allow periapical healing. The systematic review and meta-analysis show a success rate of between 74 and 86 of primary endodontic treatment of periapical lesion teeth [8]. But there is a group of cases, which shows infiltrating infection or failure of treatment, which requires a retreat treatment or surgery.

It has been demonstrated that adjunctive oral medicine interventions, including systemic antibiotics and anti-inflammatory medication, could improve the outcomes of treatment in a number of ways: a decrease of a bacterial load, regulation of inflammatory reactions, the prevention of complications in the procedure, and the stimulation of periapical healing [9]. The most used antibiotics are amoxicillin, amoxicillin-clavulanate, metronidazole, and azithromycin which have been chosen according to their efficacy in endodontic pathogens [10]. Corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) could also help to mitigate the production of inflammatory mediators and prevent post-operative symptoms.

It still is a controversial issue whether systemic antibiotics are essential in standard endodontic therapy [11]. Guidelines usually prescribe antibiotics when patients have systemic manifestation (fever, malaise, lymphadenopathy) or spreading infection, but there is no evident agreement on the use of antibiotics with uncomplicated chronic periapical lesion [12]. Issues of antibiotic resistance, side effects and cost-effectiveness require prudent use of antibiotics. Nevertheless, the adjunctive antibiotic treatment might be applicable to selected cases (extensive lesions), immunocompromised patients, or anatomical considerations.

Another solution that has been considered is conservative oral medicine management which is followed by delayed definitive endodontic therapy especially in areas with limited resources or where a patient cannot undergo endodontic therapy immediately [13]. It involves the use of systemic antibiotics and anti-inflammatory drugs, which are used temporarily to manage infection and symptoms before a final endodontic treatment. Nevertheless, the effectiveness of this conservative methods and their long-term effect are not sufficiently described.

There has been recent research into the comparative effectiveness of various treatment modalities of chronic periapical lesions. A systematic review conducted by Segura-Egea et al. revealed that the treatment protocols and methods of outcomes assessment had a significant level of heterogeneity among the studies [14]. The majority of comparative studies performed so far are concerned with technical differences in endodontic care (use of instruments, irrigation regime, use of intracanal agents) as opposed to comparative studies of underlying philosophies of treatment [15]. There is a scanty body of evidence that directly compares traditional endodontic treatment with any of the other endodontic-pharmacological interventions or self-treatment conservative oral care treatments.

Knowledge of the relative performance of these modes of treatments has significant clinical, economic, and population health consequences [16]. The evidence-based guidance, resource allocation optimization, and patient outcomes could be informed by the identification of the best treatment strategies. Moreover, the description of the effectiveness of conservative pharmacological management would serve as valuable information in the case when the immediate endodontic intervention is not possible [17].

Thus, the purpose of this scrutiny was to compare the success rates and clinical outcome of conventional endodontic treatment, combined endodontic treatment and systemic pharmacological intervention in the treatment of chronic periapical lesions compared to each other, to determine the effectiveness of adjunctive pharmacological interventions on healing parameters and symptom resolution, to determine the feasibility of conservative oral medicine treatment as interim or alternative treatment of chronic periapical lesions, as well as determine the factors that might be linked to the success or failure of treatments in different intervention modalities.

MATERIALS AND METHODS

Study design and setting

This prospective, parallel-group, comparative clinical trial was conducted at the Department of Conservative Dentistry and Endodontics from March 2021 to April 2023.

Sample size determination

Sample size was calculated using G*Power software version 3.1.9.7 for comparing three independent groups, considering an effect size of 0.40 based on pilot study data, alpha error of 0.05, and power of 90%. The minimum required sample size was determined to be 51 participants per group. Accounting for 15% potential dropout rate, 60 participants were recruited for each group, yielding a total sample of 180 patients.

Study population and allocation

The study population comprised 180 adult patients presenting with single-rooted teeth exhibiting chronic periapical lesions. Participants were allocated using computer-generated randomization (1:1:1 ratio) into three treatment groups:

Group A (Conventional Endodontic Therapy): Standard root canal treatment without systemic medications ($n = 60$).

Group B (Combined Intervention): Root canal treatment with adjunctive systemic antibiotics and anti-inflammatory medications ($n = 60$).

Group C (Conservative Oral Medicine): Initial pharmacological management with antibiotics and anti-inflammatory drugs, delayed endodontic intervention after 6 weeks ($n = 60$).

Allocation concealment was maintained using sequentially numbered, sealed, opaque envelopes opened only after patient enrolment.

Inclusion criteria

1. Age 18–60 years.
2. Single-rooted permanent teeth (incisors, canines, premolars) with chronic periapical lesions.
3. Radiographic periapical radiolucency ⩾3 mm in diameter.
4. Non-vital pulp confirmed by negative response to electric pulp testing and cold testing.
5. Teeth restorable with adequate coronal structure.
6. No previous endodontic treatment.
7. Willingness to comply with treatment protocol and follow-up.

Exclusion criteria

1. Systemic conditions affecting healing (uncontrolled diabetes mellitus, immunosuppressive disorders).
2. Pregnancy or lactation.
3. Allergy to penicillin, cephalosporins, or NSAIDs.
4. Antibiotic use within previous 3 months.
5. Acute periapical abscess with systemic manifestations.
6. Vertical root fractures or extensive external resorption.
7. Teeth with inadequate periodontal support (>4 mm bone loss).
8. Inability to achieve adequate isolation.
9. Multi-rooted teeth.
10. Previous endodontic treatment (retreatment cases).

Treatment protocols

Group A – Conventional Endodontic Therapy:

1. Single-visit or multiple-visit root canal treatment based on clinical presentation.
2. Access cavity preparation under rubber dam isolation.
3. Working length determination using electronic apex locator and radiographic confirmation.
4. Cleaning and shaping using ProTaper Universal rotary system to size F3.
5. Irrigation protocol: 2.5% sodium hypochlorite (NaOCl) between instruments, final irrigation with 17% EDTA followed by 2.5% NaOCl.
6. Obturation using lateral compaction technique with gutta-percha and AH Plus sealer.
7. Coronal seal with composite resin restoration.
8. No systemic medications prescribed.

Group B – Combined Endodontic-Pharmacological Intervention:

1. Identical endodontic protocol as Group A.
2. Adjunctive pharmacological regimen:

– amoxicillin 500 mg three times daily for 7 days (or Azithromycin 500 mg once daily for 3 days if penicillin-allergic);
– metronidazole 400 mg three times daily for 5 days;
– ibuprofen 400 mg three times daily for 5 days.

3. Medications initiated on day of endodontic treatment.

Group C – Conservative Oral Medicine Management:

1. Initial pharmacological management without immediate endodontic intervention:

– amoxicillin-clavulanate 625mg three times daily for 7 days;
– metronidazole 400 mg three times daily for 7 days;
– diclofenac sodium 50 mg twice daily for 7 days.

2. Clinical and radiographic re-evaluation at 6 weeks.
3. Definitive endodontic therapy performed at 6 weeks using protocol identical to Group A.
4. No systemic medications at time of delayed endodontic treatment.

Outcome assessment

Clinical and radiographic evaluations were performed by calibrated examiners (inter-examiner reliability $\kappa = 0.89$) blinded to group allocation at baseline, 3-, 6-, and 12-months post-treatment.

Primary outcomes

Overall Success Rate: Composite outcome including clinical success (absence of symptoms, no tenderness to percussion/palpation, no sinus tract) and radiographic success (complete or substantial healing of periapical lesion).

Periapical Healing: Assessed using Periapical Index (PAI) scoring system and categorized as:

– complete healing: PAI score reduction to 1–2;
– partial healing: PAI score reduction but remaining at 3–4;
– failure: No change or progression (PAI score ⩾4).

Lesion Size Reduction: Measured on standardized periapical radiographs using digital analysis software (ImageJ), calculating maximum lesion diameter.

Secondary outcomes

Clinical parameters:

– pain: assessed using Visual Analog Scale (VAS, 0-10) at baseline, 24 hours, 48 hours, 7 days, and each follow-up;

– tenderness to percussion and palpation;

– presence of sinus tract or swelling;

– tooth mobility (Miller's classification).

Patient-reported outcomes:

– patient satisfaction: 10-point Likert scale;

– quality of life: Oral Health Impact Profile-14 (OHIP-14);

– treatment acceptability.

Adverse events:

– procedural complications;

– drug-related adverse effects;

– need for additional interventions.

Radiographic assessment

Standardized periapical radiographs were obtained using paralleling technique with XCP positioning devices and consistent exposure parameters. Digital radiographs were analyzed using ImageJ software version 1.53k. Periapical Index (PAI) scoring was performed according to Orstavik criteria (1–5 scale). Two independent calibrated observers assessed all radiographs, with disagreements resolved through consensus.

Statistical analysis

Data were analyzed using SPSS version 28.0 and R software version 4.2.2. Intention-to-treat analysis was performed for all randomized participants. Normality was assessed using the Shapiro-Wilk test and Q-Q plots. Continuous variables were expressed as mean ± standard deviation and compared using one-way ANOVA with post-hoc Tukey's HSD test. Non-normally distributed variables were compared using Kruskal-Wallis test with post-hoc Dunn's test. Categorical variables were presented as frequencies and percentages and analyzed using chi-square test or Fisher's exact test. Repeated measures ANOVA was employed to assess temporal changes within and between groups. Time-to-event outcomes (pain resolution, healing achievement) were analyzed using Kaplan-Meier survival analysis with log-rank test. Binary logistic regression was performed to identify independent predictors of treatment success. Statistical significance was set at $p < 0.05$.

RESULTS

Participant flow and baseline characteristics

A total of 203 patients were screened, with 180 meeting eligibility criteria and completing randomization. Overall, 172 patients (95.6%) completed the 12-month follow-up: Group A (58/60, 96.7%), Group B (59/60, 98.3%), Group C (55/60, 91.7%). Dropouts were due to loss to follow-up ($n = 5$) and withdrawal of consent ($n = 3$).

Baseline characteristics were comparable across groups. Mean age was 38.4 ± 11.2 years overall (Group A: 37.8±10.9, Group B: 38.6 ± 11.4, Group C: 38.8 ± 11.5, $p = 0.891$). Gender distribution showed 98 males (54.4%) and 82 females (45.6%), with no significant difference across groups ($p = 0.742$). Mean baseline lesion size was 5.86±1.42 mm (Group A: 5.78 ± 1.38 mm, Group B: 5.92 ± 1.46 mm, Group C: 5.88 ± 1.44 mm, $p = 0.834$).

Treatment success rates and periapical healing

Table 1 presents the primary outcome measures including overall success rates and periapical healing outcomes at 12 months.

Table 1. Treatment success rates and periapical healing outcomes at 12 months

Таблица 1. Показатели успешности лечения и исходы периапикального заживления через 12 месяцев

Outcome parameter	Group A ($n = 58$)	Group B ($n = 59$)	Group C ($n = 55$)	p-value*
Overall Success Rate, *n* (%)	50 (86.2)	54 (91.5)	25 (45.5)	< 0.001†
Clinical Success, *n* (%)	54 (93.1)	57 (96.6)	38 (69.1)	< 0.001
Radiographic Success, *n* (%)	51 (87.9)	55 (93.2)	27 (49.1)	< 0.001
Periapical Healing Status:				
Complete Healing, *n* (%)	44 (75.9)	50 (84.7)	18 (32.7)	< 0.001
Partial Healing, *n* (%)	7 (12.1)	5 (8.5)	9 (16.4)	< 0.001
No Healing / Failure, *n* (%)	7 (12.1)	4 (6.8)	28 (50.9)	< 0.001
Mean PAI Score Reduction ± SD	2.42 ± 0.86	2.78 ± 0.74	1.24 ± 1.12	< 0.001‡
Mean Lesion Size Reduction (mm) ± SD	4.82 ± 1.24	5.67 ± 1.18	2.14 ± 1.52	< 0.001‡
Percentage Lesion Reduction (%) ± SD	83.4 ± 18.6	95.8 ± 12.4	36.4 ± 28.6	< 0.001‡
Need for Surgical Intervention, *n* (%)	6 (10.3)	3 (5.1)	23 (41.8)	< 0.001
Tooth Extraction, *n* (%)	2 (3.4)	2 (3.4)	7 (12.7)	0.046

Note: * Chi-square test or Fisher's exact test unless otherwise indicated; † Primary outcome; ‡ One-way ANOVA with post-hoc Tukey's test showing significant differences between all group pairs ($p < 0.05$ for Group A vs. B, $p < 0.001$ for Groups A and B vs. C)

Примечание: * Критерий хи-квадрат или точный критерий Фишера, если не указано иное; † Первичная конечная точка; ‡ Однофакторный дисперсионный анализ (ANOVA) с пост-хок тестом Тьюки, выявившим статистически значимые различия между всеми парами групп ($p < 0,05$ для группы А по сравнению с группой В; $p < 0,001$ для групп А и В по сравнению с группой С)

Kaplan-Meier analysis revealed significant differences in time to complete healing across groups (log-rank $\chi^2 = 42.38$, $p < 0.001$), with median healing times of 4.2 months (Group A), 3.6 months (Group B), and healing not achieved in majority of Group C patients by 12 months.

Clinical parameters and symptom resolution

Table 2 demonstrates the comparison of clinical parameters and temporal patterns of symptom resolution across treatment groups.

Treatment complications and adverse events

Table 3 presents treatment-related complications and adverse events across the three groups.

Predictors of treatment success

Binary logistic regression analysis identified independent predictors of overall treatment success:

1. Treatment modality Group B vs. Group C: OR = 14.82 (95% CI: 5.84–37.62), $p < 0.001$.
2. Treatment modality Group A vs. Group C: OR = 8.36 (95% CI: 3.52–19.87), $p < 0.001$.
3. Baseline lesion size <5 mm vs. ⩾5 mm: OR = 3.24 (95% CI: 1.42–7.39), $p = 0.005$.
4. Age <40 years vs. ⩾40 years: OR = 2.18 (95% CI: 1.04–4.57), $p = 0.039$.
5. Anterior teeth vs. posterior teeth: OR = 2.67 (95% CI: 1.21–5.89), $p = 0.015$.

Economic considerations

Mean total treatment cost (including medications, procedures, and follow-up) was: Group A: $285 ± 45, Group B: $348 ± 52, Group C: $524 ± 128 (includes initial conservative management, delayed endodontic treatment, and higher rate of additional interventions), $p < 0.001$.

DISCUSSION

This future comparative trial assessed three different management methods of chronic periapical lesions showing significant variations in clinical results, healing rates, as well as patient subjective outcome. This research shows that endodontic therapy with adjunctive pharmacological intervention would give a better result than the traditional endodontic therapy, whereas conservative oral medicine management without prompt definitive endodontic therapy would give a very poor outcome.

The total success rate of conventional endodontic therapy (Group A), which is 86.2% in this research, is consistent with the literature that gives success rates of 74–86% of primary endodontic treatment on teeth with periapical lesions [1]. This coherence confirms that we used a methodological approach and the results of the control group were enough to compare them with published standards. The prevalence rate indicates the effectiveness of the modern endodontic practice such as rotary instrumentation, superior irrigation regimens and better obturation systems in treating the infective etiology of periapical pathology [2].

Table 2. Clinical parameters and symptom resolution

Таблица 2. Клинические параметры и динамика купирования симптомов

Parameter	Group A (*n* = 58) Mean ± SD	Group B (*n* = 59) Mean ± SD	Group C (*n* = 55) Mean ± SD	*p*-value*
Baseline Pain Score (VAS 0–10)	5.84 ± 1.92	5.96 ± 1.88	5.78 ± 2.04	0.862
Pain Score at 24 hours	4.12 ± 1.64	2.86 ± 1.38	5.92 ± 1.86†	<0.001‡
Pain Score at 48 hours	2.94 ± 1.42	1.74 ± 1.12	4.68 ± 1.94†	<0.001‡
Pain Score at 7 days	0.86 ± 0.94	0.42 ± 0.68	2.84 ± 1.62†	<0.001‡
Time to Pain Resolutio, *n* (days)	6.8 ± 2.4	4.2 ± 1.8	12.6 ± 4.8§	<0.001‡
Percussion Tenderness at 12 months, *n* (%)	3 (5.2)	2 (3.4)	17 (30.9)	<0.001
Palpation Tenderness at 12 months, *n* (%)	4 (6.9)	2 (3.4)	14 (25.5)	<0.001
Sinus Tract at 12 months, *n* (%)	1 (1.7)	0 (0.0)	8 (14.5)	0.001
Post-operative Flare-up, *n* (%)	8 (13.8)	3 (5.1)	18 (32.7)¶	<0.001
Baseline OHIP-14 Score	18.6 ± 5.4	19.2 ± 5.8	18.4 ± 5.6	0.726
OHIP-14 Score at 12 months	6.4 ± 3.2	4.8 ± 2.6	11.8 ± 4.8	<0.001‡
OHIP-14 Improvement	12.2 ± 4.6	14.4 ± 5.2	6.6 ± 4.2	<0.001‡
Patient Satisfactio, n Score (0–10)	7.92 ± 1.34	8.64 ± 1.12	5.28 ± 1.86	<0.001‡

Note: * One-way ANOVA unless otherwise indicated; † Pain scores for Group C represent values during initial conservative management phase (before delayed endodontic intervention); ‡ Post-hoc Tukey's test showed significant differences between most group pairs; § Time to pain resolution in Group C calculated from delayed endodontic intervention; || Chi-square test; ¶ Includes flare-ups during both conservative management and delayed endodontic phases

Примечание: * Однофакторный дисперсионный анализ (ANOVA), если не указано иное; † Показатели болевого синдрома в группе С отражают значения в период первичного консервативного ведения (до отсроченного эндодонтического вмешательства); ‡ Пост-хок тест Тьюки выявил статистически значимые различия между большинством пар групп; § Время до купирования болевого синдрома в группе С рассчитывалось с момента проведения отсроченного эндодонтического вмешательства; || Критерий хи-квадрат; ¶ Включены случаи обострений как на этапе консервативного лечения, так и в период отсроченного эндодонтического вмешательства

Table 3. Treatment complications and adverse events

Таблица 3. Осложнения лечения и нежелательные явления

Complication / Adverse event	Group A (*n* = 58), *n* (%)	Group B (*n* = 59), *n* (%)	Group C (*n* = 55), *n* (%)	*p*-value*
Overall Complication Rate	12 (20.7)	18 (30.5)	34 (61.8)	< 0.001
Procedural Complications:				
Instrument separation	1 (1.7)	1 (1.7)	2 (3.6)	0.739
Perforation	0 (0.0)	0 (0.0)	1 (1.8)	0.323†
Apical extrusion	2 (3.4)	1 (1.7)	3 (5.5)	0.529†
Drug-Related Adverse Events:	0 (0.0)	14 (23.7)	16 (29.1)	< 0.001
Gastrointestinal disturbances	0	9 (15.3)	11 (20.0)	0.005
Allergic reactions (mild)	0	2 (3.4)	2 (3.6)	0.332†
Diarrhea	0	5 (8.5)	7 (12.7)	0.024
Nausea	0	4 (6.8)	6 (10.9)	0.056
Post-treatment Complications:				
Persistent infection	4 (6.9)	2 (3.4)	18 (32.7)	< 0.001
Symptomatic recurrence	3 (5.2)	1 (1.7)	12 (21.8)	< 0.001
Progressive lesion enlargement	2 (3.4)	1 (1.7)	9 (16.4)	0.005
Treatment Discontinuation Due to Adverse Events	0 (0.0)	3 (5.1)	5 (9.1)	0.065†
Additional Treatment Required:				
Endodontic retreatment	3 (5.2)	2 (3.4)	11 (20.0)	0.003
Surgical endodontics	6 (10.3)	3 (5.1)	23 (41.8)	<0.001
Tooth extraction	2 (3.4)	2 (3.4)	7 (12.7)	0.046

Note: * Chi-square test; † Fisher's exact test

Примечание: * Критерий хи-квадрат; † Точный критерий Фишера

The materially better success rate of 91.5% in Group B (endodontic-pharmacological intervention) means that the use of adjunctive systemic medications has a meaningful clinical benefit. Although this improvement of 5.3 percent is apparently small, this is a 38 percent relative decrease in failure rate with conventional therapy used alone. The improved results are probably due to the work of synergistic mechanisms: endodontic treatment will focus on the initial source of infection in the root canal system, and systemic antibiotics will focus on the extraradicular infection and the decrease in bacterial load in periapical tissues [3]. With an excellent antiprolkaryotic effect against obligate anaerobes that are the leading agents in endodontic infections, metronidazole, which augments the spectrum of amoxicillin, offers complete antimicrobial coverage [4].

The anti-inflammatory (ibuprofen) of Group B possibly enhanced better results via several different mechanisms other than symptom management [5]. NSAIDs prevent the activity of enzymes of cyclooxygenase, blocking the production of prostaglandins and altering the course of the inflammatory process. It is possible that this inflammatory suppression can save the architecture of the periapical bone, decrease activity in osteoclastic cells, and cause more favorable conditions of healing. The tangible benefit of adjunctive anti-inflammatory therapy to patients is demonstrated by the significantly shorter pain resolution time in Group B (4.218 days) than in Group A (6.82.4 days).

The objective radiographic data of Group B (reduced lesion size by a significant margin of 95.8 12.4% vs. Group A 83.4 18.6% of the lesion area) support the positive impact of the combination intervention. The near full remission of lesions in Group B predicts that a pharmacological adjunctive therapy can support the more thorough periapical bone regeneration. Research has shown that residual peri apical inflammation may be present despite technically satisfactory endodontic treatment, and this may limit healing [6]. Systemic drugs can be used to address this residual inflammation better.

These results (dramatically poor in Group C: conservative oral medicine management with delayed endodontic intervention) highlight an essential principle of the endodontic treatment: the definitive treatment of the infectious source in the root canal system [7]. Antibiotics are only able to temporarily suppress the population of bacteria and control the symptoms, but without controlling the sources with endodontic debridgement and obturation, infections always come back. The success rate of 45.5 percent of Group C, which is less than 50 percent of Groups A and B, shows that pharmacological treatment is not sufficient in the treatment of chronic periapical lesions.

Group C shows a high level of failure to treat (50.9) and surgical operation (41.8) which are the outcomes of failure to administer decisive treatment. The bacterial populations were probably adapted, biofilms deve-

loped, and periapical destruction might have occurred even with the antibiotic treatment during the 6-week conservative management period [8]. The biological environment might be unfavorable to healing by the time delayed endodontic treatment was given than with immediate endodontic treatment. The implications of this finding to clinical practice and resource allocation are significant since the conservative and cost-saving measures aimed at postponing costs or the complexity of treatment eventually caused an increase in failures and the necessity to undergo costly surgical operations.

The fact that the complication rate was much higher in Group C (61.8) should be taken seriously. In addition to the anticipated increased prevalence of persistent infection and relapse of treatment, this group had an increase in post-operative flare-ups (32.7% vs. 13.8% in Group A and 5.1% in Group B, respectively). Such exacerbations can be caused by the pressure of selection of bacteria during the course of antibiotics, which causes more virulent or resistant colonies. Moreover, untimely treatment could have provided more tissue to be exposed to the infection, and this is more likely to lead to complications in the future during endodontic therapy [9].

In Group B, the adverse events were drug related in 23.7 percent and 29.1 percent of Group C patients, mostly mild gastrointestinal events. Although these undesirable events were typically self-limiting and did not affect the treatment outcomes, they are significant factors to be considered during the benefit-risk analysis. The wise use of antibiotics should be based on the therapeutic value versus the side effects, the issue of antimicrobial resistance and expenditure of healthcare funds [10]. These two facts indicate that, in the case of teeth with chronic periapical lesions, the advantages of adjunctive antibiotics over these issues are even stronger in Group B. Nevertheless, the unfavorable results of antibiotic therapy in Group C prove that antibiotic treatment cannot be a replacement of the final endodontic therapy.

The data on the quality of life, assessed with the means of OHIP-14 showed significant improvement in Group B (14.4 ± 5.2 points), as opposed to Group A (12.2 ± 4.6 points) and Group C (6.6 ± 4.2 points). This patient outcome validates the fact that the clinical and radiographic benefits are translated into meaningful improvements in the daily functioning and wellbeing of the patients. The increased patient satisfaction rates in Group B (8.64 ± 1.12) present the level of appreciation by the patients towards the promptness in symptom solving and the overall outcomes [11].

Economic analysis also showed some curious paradox, whereby Group B was incurring greater initial treatment costs in terms of amounts (348 vs. 285 for Group A) in terms of amount of duetomedication, but Group C experienced the highest total costs (524) although initial conservative management was less expensive. The failure rate of Group C was very high which required further interventions such as retreatment, surgical endodontics, and extractions which increased total spending. This observation proves that the cost savings caused by conservative management at the very beginning are compensated by the costs incurred downstream brought about by failure to treat [12].

The value of the identification of the baseline lesion size, patient age, and the location of the tooth determining the success of the treatment is based on the prognostic information. Big lesions (⩾5mm) had a lower probability of healing, which may reflect a higher tissue destruction, higher bacterial load, or possibly a cystic conversion [13]. Better results were observed in younger patients (< 40 years), which is probably attributed to the increased capacity to heal and immune response. A higher success rate was observed with anterior teeth as compared to the posterior teeth which may be associated with easier anatomy, easier access and lower occlusal pressure [14].

There are a number of limitations that should be considered. The research did not include multi-rooted teeth which are prone to generalization to the molars which comprise a big percentage of teeth which are subjected to endodontic treatment. The 12 months follow up though significant, might not be effective in reflecting long term outcomes as some failures are not exhibited until a few years [15]. The ethical reason why the study design lacked a placebo-controlled arm, was that it would have made it impossible to evaluate the placebo effects. The type of antibiotic and anti-inflammatory regimens that have been used is just one of several possible protocols; alternate medication options, dosages, or respective durations may have varied outcomes. Also, the article failed to determine the behavior of antimicrobial resistance, which is of great concern in light of the contemporary issues regarding the stewardship of antibiotics [16].

The future studies are aimed at long-term studies (3–5 years) to evaluate sustained results, microbiological examination such as antimicrobial resistance profiling, exploration of alternative pharmacological regimens, research of biomarkers, to determine the patients who are most inclined to respond to adjunctive medications, cost-effectiveness studies, both at the societal and healthcare system level, and special populations such as immunocompromised patients [17–20].

CONCLUSION

The prospective comparative study proves that the endodontic therapy in conjunction with adjunctive systemic pharmacological intervention yields better clinical and radiographic results than endodontic therapy in the context of chronic periapical lesions alone. The integrated strategy generates increased success rates (91.5% vs. 86.2%), lesion size reduction, quicker symptoms improvement, and increased patient satisfaction and life quality. Such advantages seem to far surpass the slight growth in treatment expenses and acceptable adverse event profile.

More importantly, there is a significantly lower level of success in conservative oral medicine management with delayed endodontic interventions as compared to immediate endodontic techniques, with success rates that are half as high. The high failure rate, rising surgical

intervention requirement and finally the economic cost of the conservative management highlight the principal rule that conclusive treatment that removes the infectious source is crucial in the management of periapical lesions. Antibiotics and anti-inflammatory drugs, although useful as helper drugs, cannot replace proper endodontic treatment.

The clinical implications of these results are as follows: in the endodontic treatment of teeth with chronic periapical lesions, adjunctive systemic antibiotics (amoxicillin plus metronidazole) and anti-inflammatory drugs (NSAIDs) should be considered on a regular basis, indefinite endodontic treatment of these lesions should not be treated conservatively except in the limited cases where endodontic treatment is contraindicated or contraindicated, initial cost savings due to the use of conservative treatment should not be considered, and treatment.

The paper underlines the value of timely and definitive endodontic intervention as the foundation of chronic periapical lesion therapy, and adjunctive pharmacological treatment as a valuable addition to the use of optimal endodontic intervention. These insights, based on evidence, must be reflected in clinical choices, guideline writing, and so advice to a patient on the best management of chronic periapical pathology.

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