Am J Transl Res 2024;16(7):2814-2827
www.ajtr.org /ISSN:1943-8141/AJTR0156370

Original Article

Drug sensitivity testing during dental pulp-dentin complex repair: its effect on treatment outcome and prognosis

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Received March 5, 2024; Accepted June 5, 2024; Epub July 15, 2024; Published July 30, 2024

Abstract: Objective: To assess the efficacy of targeted therapy based on drug sensitivity testing (DST) results in patients with acute pulpitis (AP). Methods: A total of 80 cases of AP were included retrospectively and divided into two groups: control (Ctrl) group (conventional drug palliative therapy, n=40) and experimental (Exp) group (DST + non-resistant drugs, n=40). The clinical data and laboratory examination data of patients, including bacterial culture data, drug sensitivity test results, Ca and P contents in dental pulp, visual analogue scale (AVS), treatment satisfaction, and dental pulp incidence, were collected and analyzed. Results: *Prevotella melaninogenica, Fusobacterium nucleatum*, and *Porphyromonas gingivalis* exhibited higher resistance rates (RS) to penicillin and amoxicillin but no resistance to imipenem and metronidazole. The content of Ca and P in the dental pulp of the Exp group patients was significantly higher than that of the Ctrl group (P=0.006). The total response rate (95% vs. 77.5%, P=0.018) and overall patient satisfaction (92.5% vs. 80%, P=0.021) were also significantly higher in the Exp group than in the Ctrl group. Additionally, when the follow-up duration exceeded 1 year, the incidence of dental pulp reactions in the Exp group was significantly lower than that of the Ctrl group (P=0.026). Conclusions: These findings suggest that Gram-negative anaerobes are the predominant oral pathogens in patients with AP. Imipenem and metronidazole demonstrate the most effective anti-infective properties against these anaerobes. Utilizing DST to select non-resistant drugs for treatment prior to therapy effectively enhances clinical outcomes for patients with AP.

Keywords: Drug sensitivity testing, acute pulpitis, conventional drug sedation therapy, total response rate, overall patient satisfaction

Introduction

Dental diseases such as dental caries, pulpitis, and periodontitis frequently present formidable challenges, compromising essential functions such as chewing, speech, and aesthetics, while also impeding social interaction and imposing a psychological burden [1]. Various oral diseases are common, manifesting as symptoms like bleeding, gingival swelling, and toothache. Acute pulpitis (AP) denotes inflammation of pulp tissue, typically originating from deep pulp regions, and represents a more severe form of pulpitis [2]. Clinical features of AP involve sharp, spontaneous pain or intermittent attacks exacerbated at night, often disrupting sleep patterns. As the disease progresses, pain duration lengthens, and stimuli such as temperature and food can trigger or exacerbate pain, persisting even after stimulus removal. Examination frequently reveals significant defects in dental hard tissues, such as deep caries, encroaching on the pulp. Microscopic perforations may be evident, with the perforation site potentially displaying fluid or blood seepage [3, 4]. Timely surgical interventions and anti-inflammatory treatments are imperative for managing pulpitis to prevent potential tooth loss, severe gingival pain, and a range of adverse reactions including fever and pyrexia [5, 6]. In severe cases, patients may endure intense headaches, dizziness, and fainting, harming overall health and affecting multiple organ functions. If left untreated over an extended duration, pulpitis may progress to bacterial inflammation in the periapical region,

https://doi.org/10.62347/ICYR9713

causing oral conditions such as gingivitis and periodontitis, thereby compromising dental health. This can result in diminished chewing ability and hormonal imbalances, precipitating various adverse reactions [7]. Throughout the course of AP, maintaining oral cleanliness and health is paramount to bolster tooth resilience, and avoid the deleterious effects of hot, acidic, and sugary substances. Untreated conditions may lead to complications associated with various oral inflammations, compromising oral safety and health [8-10]. Therefore, timely clinical intervention is necessary to prevent severe complications. Traditionally, conventional approaches to treating dental pulp diseases include root canal treatment, apical surgery, and tooth extraction, often followed by anti-inflammatory therapy postoperatively. However, these methods exhibit limitations such as drug resistance and uncertain prognosis. Hence, the quest for a more effective and personalized treatment strategy becomes imperative.

Previous studies show that dental pulp infections commonly manifest as mixed bacterial infections, as various bacterial species thrive in the oral cavity, including obligate anaerobes, facultative anaerobes, and aerobes [11-14]. Among these, obligate anaerobes are recognized as major pathogens. Obligate anaerobes comprise a bacterial subgroup that exclusively thrives in oxygen-deprived environments, predominantly inhabiting deep oral cavity regions like the dental pulp, where oxygen availability is limited [15, 16]. These bacteria can infiltrate the dental pulp, the tooth's inner soft tissue, through microcracks or dental caries, initiating infection. Facultative anaerobes and aerobes may also participate in dental pulp infection [17], as they can flourish in relatively oxygen-rich environments, contributing to mixed bacterial infections [18]. Hence, the treatment of dental pulp infections often necessitates broad-spectrum antibiotics to target various potential pathogens.

In recent times, a noticeable rise in resistance among clinically isolated anaerobic bacteria to beta-lactam antibiotics, beta-lactamase inhibitors, and metronidazole has been documented [19-21]. This trend has raised concern in clinical practice. Anaerobic bacteria commonly employ diverse resistance mechanisms, including the synthesis of beta-lactamases and other degrading enzymes, modification of drug targets or efflux mechanisms, and reduced cellular permeability to drugs [22-24]. These resistance mechanisms confer resistance to conventional therapeutic agents, posing challenges for treatment. For infections attributed to clinically isolated drug-resistant anaerobic bacteria, alternative antibiotics or combination therapy may be imperative to enhance augment treatment efficacy [25]. Physicians may consider using broader-spectrum antibiotics like aminoglycosides, quinolones, or peptide antibiotics [26, 27]. Moreover, adjunctive therapies such as phosphomycin and tigecycline could be options to explore. Nonetheless, antibiotic selection should be tailored to individual circumstances and guided by resistance testing and clinical assessment to ascertain the most suitable treatment regimen [28]. Therefore, preventive measures and prudent antibiotic usage are pivotal for mitigating the dissemination of drug-resistant strains.

Currently, research predominantly focuses on bacterial culture and drug sensitivity testing (DST) in cases of pulpitis. Surgical interventions such as restorative treatments are employed in dental pulp repair. However, in the recovery process, preventing inflammation is crucial to ensure treatment efficacy, necessitating antibiotic therapy. Emerging evidence suggests that combining DST with sensitive antibacterial agents, characterized by minimal adverse effects, could improve treatment outcome [29]. Consequently, this study endeavors to address the therapeutic nuances inherent in the management of AP. Specifically, in this study, the reparative treatment of pulpitis necessitates the selection of appropriate drugs based on the type of infecting bacteria, underscoring a need to discern the microbial characteristics of oral infections in patients. This study aimed to investigate the impact of DST combined with targeted drug therapy on the efficacy of patients with AP, providing valuable insight for the clinical management of AP.

Materials and methods

Research subjects

This study retrospectively analyzed 80 patients with AP who received outpatient treatment in the Department of Stomatology and Endodontics, Wangjiang Hospital of Sichuan

University from May 2020 to January 2023. All patients comprised 48 males and 32 females aged from 20 to 66 years, with a disease duration ranging from 10 hours to 3 days. They were divided into an experimental group (Exp group) receiving targeted drug therapy based on DST results and control group (Ctrl group) receiving usual therapy, with 40 cases in each group.

The inclusion criteria for patient enrollment were as follows: (1) adults; (2) clinical presentation of paroxysmal spontaneous pain, nocturnal pain, and difficulty in self-localization of pain; (3) complete clinical information; (4) a history of pulpitis and periapical periodontitis.

Patients were excluded if they met any of the following conditions: (1) concomitant mental disorders; (2) antibiotic use within the past two months; (3) systemic diseases; (4) incomplete clinical information.

This study was approved by the Ethics Committee of Wangjiang Hospital, Sichuan University.

Sample size estimation

A comparison between two sample groups was conducted using SAS software, with two-tailed testing. The significance level (α) was set at 0.05, and the power of the test (1-β) was set at 0.80. The efficacy of treatment in the Ctrl group was assumed to be 75%, whereas in the Exp group it was set at 90%. Assuming a statistical difference exists, a minimum of 36 patients per group was required for the study. Therefore, a total of 80 patients were enrolled for comparison in this study.

Treatment method

The Ctrl group underwent conventional drug palliative therapy, involving pulp opening and decompression, followed by the placement of cotton pellets infused with metronidazole and dexamethasone into the pulp chamber, with daily replacement. Additionally, patients were orally administered compound sulfamethoxazole tablets twice daily, each dose comprising two tablets. Three days later, the decayed tooth tissue was removed, and the necrotic area was thoroughly irrigated with a solution containing metronidazole and dexamethasone. Cotton pellets containing the same solution were then inserted into the pulp chamber, sealed with eugenol zinc oxide, and replaced daily.

In contrast, patients in the Exp group received targeted drug therapy based on the results of DST, in addition to the aforementioned treatment methods.

Bacterial culture

After mouth rinsing, the patient's collection site was cleansed and sterilized. Utilizing a sterile pulp extirpation needle (manufactured by Huizhou Wodeya Technology Co., Ltd., China), intact vital pulp was meticulously selected, from which a sample was obtained. The collected pulp was then inoculated onto an aerobic blood agar plate and placed in a Yamato CO_2 incubator (Yamato Scientific Co., Ltd., Japan) for 24 hours. Subsequently, employing the three-zone streaking technique, the inoculum was streaked onto an anaerobic blood agar plate and introduced into an anaerobic gas pack system. The plates were incubated for an additional 24 hours in the CO_2 incubator.

Gram staining

The cultured colonies were selected using a disposable inoculating loop (manufactured by Guangzhou Biaomai Biotechnology Co., Ltd., China), and a small amount was transferred onto a glass slide containing physiological saline. The inoculum was evenly spread to create a thin layer of approximately 1 cm. After natural drying, the slide was held with forceps and passed through the flame of an alcohol lamp for 3 seconds. Subsequently, crystal violet solution (produced by Shanghai Sangon Biotechnology Co., Ltd., China) was applied to the slide and allowed to stand for 1 minute, followed by rinsing with running water. Iodine solution was then added to the slide to ensure complete coverage, and left for 1 minute before rinsing with running water. Next, 95% ethanol was added to the slide until the alcohol no longer exhibited a purple color, after which it was rinsed with water to remove the ethanol. Excess moisture was absorbed using absorbent paper. Afterwards, a 0.5% safranin solution was applied, left for 30 seconds, rinsed with running water, and allowed to air-dry. Finally, the slide was observed under an oil immersion lens (manufactured by Beijing Ruikexin Instrument Technology Co., Ltd., China).

Sample culture and identification

The bacteria obtained from microscopy were inoculated onto anaerobic plates and incubated at 37°C for 16 hours to assess oxygen tolerance. Following incubation, the colonies on the plates underwent Gram staining using both aerobic and anaerobic blood agar plates. Bacterial identification was conducted using the VITEK 2 COMPACT fully automated microbial identification system (BioMérieux, France). DST was performed on anaerobic bacteria, with Fusobacterium nucleatum 25285 employed as the quality control strain.

DST

The colony samples were inoculated onto an anaerobic culture medium and placed in an anaerobic incubator (manufactured by Shanghai Hengyue Medical Equipment Co., Ltd.) for a duration of 3 days. Subsequently, several pure colonies were selected and inoculated into 2 mL tubes containing physiological saline, with the bacterial suspension adjusted to a concentration of 0.55-0.65 McFarland units. A sterile cotton swab was immersed in a small amount of the bacterial suspension and streaked onto the agar surface three times, rotating the plate 60 degrees each time and spreading along the edge of the plate. Then the plates were partially air-dried at room temperature for 5 minutes, after which antibiotic paper discs were applied onto the agar surface and left to stand for 5 minutes. Finally, the plates were incubated at 35°C for 16 hours.

Bacterial drug susceptibility was determined using the Kirby-Bauer (KB) method, which involved testing for sensitivity to drugs such as penicillin (azithromycin), amoxicillin, gentamicin, piperacillin, ceftriaxone, imipenem, ciprofloxacin, levofloxacin, and metronidazole. The results were reported as susceptible (S), intermediate (I), or resistant (R) for each drug.

Observation indicators

Primary outcomes: The therapeutic efficacy was evaluated by categorizing the treatment outcomes of the patients into the following categories: cured, effective, and ineffective. “Cured” meant that the patients experienced no pain, restored normal chewing function, and exhibited good root absorption after treatment. A treatment outcome was considered “effective” if the patients had mild toothache, significant improvement in chewing function, and good root absorption after treatment. Conversely, it was deemed “ineffective” if patients still experienced significant toothache, redness and swelling of the gums, and exhibited poor root absorption, necessitating retreatment. The total response rate (TRR) was calculated based on these categories.

Additionally, patient satisfaction with the treatment in both groups was assessed, with categories ranging from highly satisfied, and satisfied, to dissatisfied. The treatment satisfaction rate was calculated based on these responses.

Post-treatment follow-up: Following the treatment, patients were followed up via WeChat, phone calls, and in-person consultations to observe the incidence of dental pulp reactions.

Secondary outcome: Analysis of pulp composition in patients before and one week after dental treatment was as follows. The X-ray photoelectron spectrometer (XPS) (Kratos Scientific Inc., UK) was used to analyze and calculate the surface calcium (Ca) and phosphorus (P) contents, as well as the Ca/P ratio in the patient’s pulp.

Moreover, visual analog scale (VAS) was employed to record visual analog pain scores of patients in the Exp and Ctrl groups before treatment and at one week post-treatment. The scores were categorized as follows: relief (a decrease in VAS score by more than 2 points compared to pre-treatment), no change (an increase or decrease in VAS score of no more than 2 points compared to pre-treatment), and exacerbation (an increase in VAS score by 2 points or more compared to pre-treatment). Furthermore, the time to onset of analgesic effect was also recorded for both groups of patients.

Statistical analysis

In this study, data analysis was carried out using SPSS 27.0 statistical analysis software. Quantitative data were presented as mean ± standard deviation. Paired-sample t-tests were used for within-group comparisons, while inde-

Table 1. General data of patients in different groups

Indicator		Exp group	Ctrl group	*P*
Gender	Males	25	23	0.961
	Female	15	17	
Age (years old)		36.29 ± 10.05	38.15 ± 6.95	0.597
Height (cm)		159.02 ± 13.46	162.35 ± 11.07	0.634
Weight (kg)		61.33 ± 5.93	58.48 ± 4.75	0.109
Duration of symptoms (days)		1.51 ± 0.48	1.72 ± 0.45	0.098

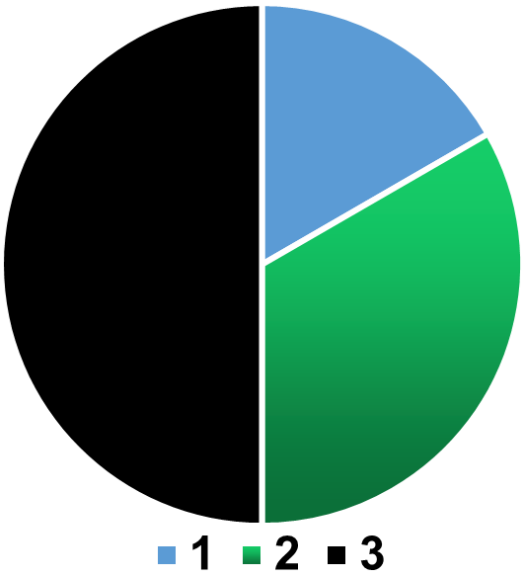

Figure 1. Distribution of pathogenic bacteria among the patients. Tags 1-3 indicate Gram-negative anaerobic bacteria, Gram-positive aerobic bacteria, and Gram-positive anaerobic bacteria, respectively.

pendent-sample t-tests were conducted for between-group comparisons. Counted data were expressed as percentages (%), and intergroup analysis was performed using χ^2 tests. $P < 0.05$ was considered significant.

Results

General data of patients in different groups

As detailed in **Table 1**, the Exp group comprised 25 males and 15 females, with an average age of 36.29 ± 10.05 years, an average duration of symptoms of 1.51 ± 0.48 days, a mean height of 159.02 ± 13.46 cm, and a mean weight of 61.33 ± 5.93 kg. Meanwhile, the Ctrl group included 23 male and 17 female patients, with an average age of 38.15 ± 6.95 years, an average duration of symptoms of 1.72 ± 0.45 days, a mean height of 162.35 ± 11.07 cm, and a mean weight of 58.48 ± 4.75 kg. No significance was observed between Exp and Ctrl groups regarding gender distribution, age, duration of symptoms, height, or weight ($P > 0.05$).

Bacterial distribution

As illustrated in **Figure 1**, 115 bacterial strains were isolated, including 69 strains of Gram-negative anaerobic bacteria (60%), 37 strains of Gram-positive aerobic bacteria (32.17%), and 9 strains of Gram-positive anaerobic bacteria (7.83%), which were marked with 1, 2, and 3 in the figure.

Figure 2 illustrates the specific proportions of patients with different bacteria. Among the Gram-negative anaerobic bacteria (**Figure 2A**), *Prevotella melaninogenica* was found in 45 cases, *Fusobacterium nucleatum* in 16 cases, *Porphyromonas gingivalis* in 8 cases, and *Peptostreptococcus micros* in 2 cases. Among the Gram-positive aerobic bacteria (**Figure 2B**), *Staphylococcus aureus* was found in 24 cases, *Enterococcus faecalis* in 10 cases, and *Enterococcus coli* in 3 cases. Furthermore, among the Gram-positive anaerobic bacteria (**Figure 2C**), only 9 cases of anaerobic Streptococcus were detected.

Main results of DST for Gram-negative anaerobic bacteria

As depicted in **Figure 3**, *Prevotella melaninogenica* exhibited resistance to penicillin in 29 strains with a resistance rate (RS) of 64.44%. It also showed resistance to amoxicillin in 21 strains with an RS of 46.67%. Resistance to piperacillin was observed in 11 strains with an RS of 24.44%. Moreover, three strains showed resistance to ceftriaxone with an RS of 6.67%. However, there were no strains resistant to imipenem or metronidazole, with an RS of 0% for both antibiotics. Therefore, *Prevotella melaninogenica* exhibited a higher RS to penicillin and amoxicillin, a lower RS to ceftriaxone, and no resistance to imipenem and metronidazole.

Fusobacterium nucleatum displayed resistance to penicillin in 16 strains, with an RS of 100%. It indicated resistance to amoxicillin in

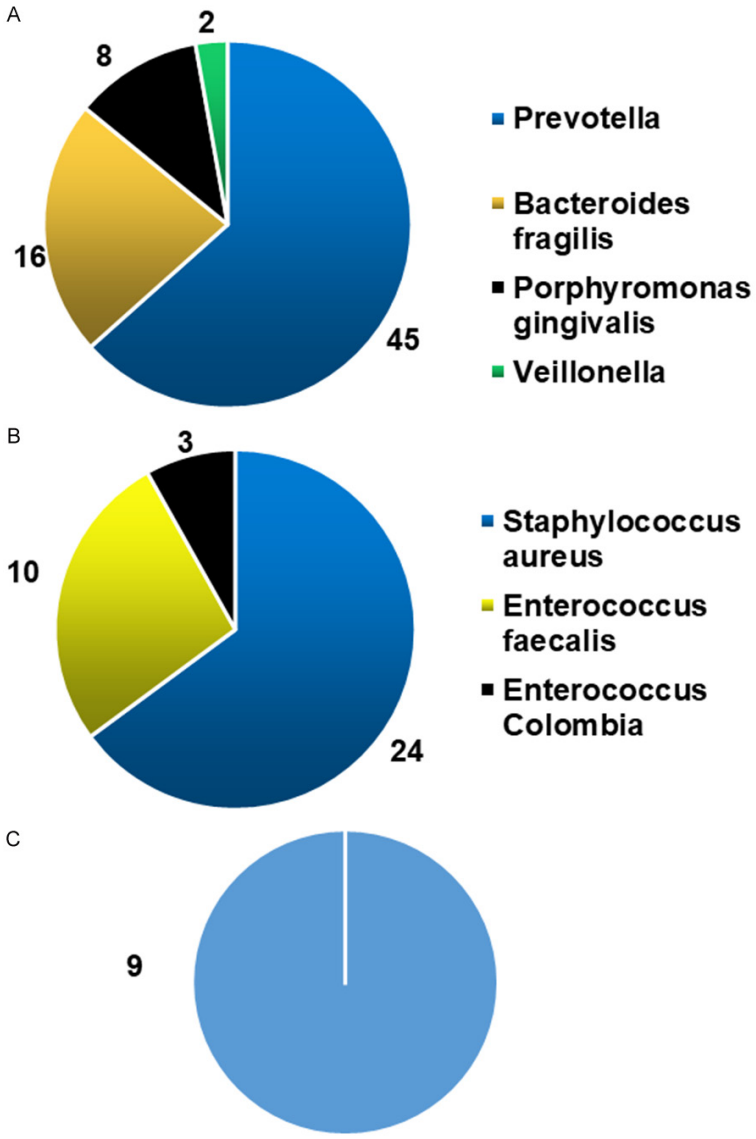

Figure 2. Proportions of different types of pathogenic bacteria. (A) represents the proportion of Gram-negative anaerobic bacteria; (B) represents the proportion of Gram-positive aerobic bacteria; and (C) represents the proportion of Gram-positive anaerobic bacteria.

14 strains, with an RS of 87.5%. Resistance to piperacillin was observed in 5 strains, with an RS of 31.25%. Additionally, resistance to ceftriaxone was found in 3 strains, with an RS of 18.75%. However, no resistance to imipenem or metronidazole was observed, with an RS of 0%. These results indicate that *Fusobacterium nucleatum* has a higher RS to penicillin and amoxicillin, while demonstrating no resistance to imipenem and metronidazole. These results are shown in **Figure 4**.

Figure 5 illustrates the RS of *Porphyromonas gingivalis* to different drugs. It revealed that *Porphyromonas gingivalis* exhibited resistance to penicillin in 5 strains, with RS of 62.5%. It exhibited resistance to amoxicillin in 4 strains, with an RS of 50%. Resistance to piperacillin was observed in 1 strain, with an RS of 12.5%. Additionally, resistance to ceftriaxone was found in 1 strain, also with an RS of 12.5%. However, no resistance to imipenem or metronidazole was observed, with an RS of 0%. These results indicate that *Porphyromonas gingivalis* has a relatively high RS to penicillin and amoxicillin, while demonstrating a lower RS to piperacillin and ceftriaxone. Furthermore, it exhibits no resistance to imipenem and metronidazole.

Comparison of dental pulp composition

The changes in dental pulp composition before and after treatment were observed (**Figure 6**). There was no significant difference in the content of dental pulp composition between the two groups before treatment (P=0.335). However, it was found that after treatment, the content of Ca and P in the dental pulp of patients significantly increased (P=0.006), while the Ca/P ratio significantly decreased (P=0.023).

Therapeutic effects of patients after different treatments

Figure 7 compares the therapeutic effects of patients in various groups. **Figure 7A** summarizes the numbers of cases with different results, and **Figure 7B** compares the TRR in different groups. In the Exp group, 23, 15, and 2 cases were cured, effective, and ineffective, respectively, resulting in a TRR of 95%. In the Ctrl group, 11, 20, and 9 cases were cured, effective, and ineffective, respectively, resulting in a TRR of 77.5%. It is evident that the Exp group had a higher TRR than the Ctrl group (P=0.018).

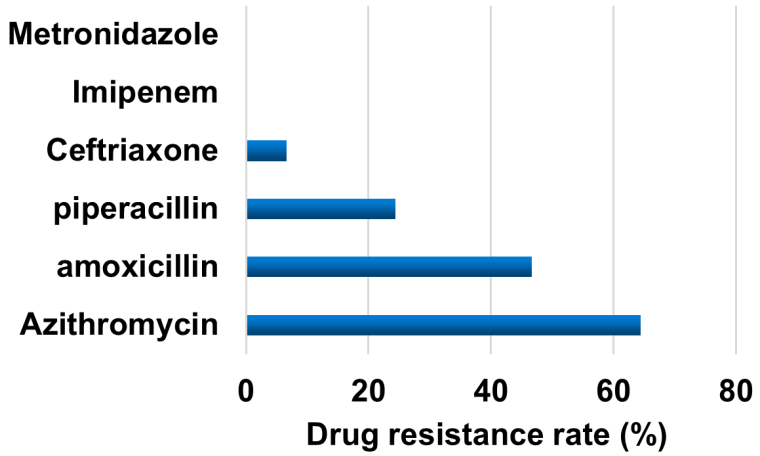

Figure 3. RS of *Prevotella melaninogenica* to penicillin, amoxicillin, piperacillin, ceftriaxone, imipenem, and metronidazole. RS, resistance rate.

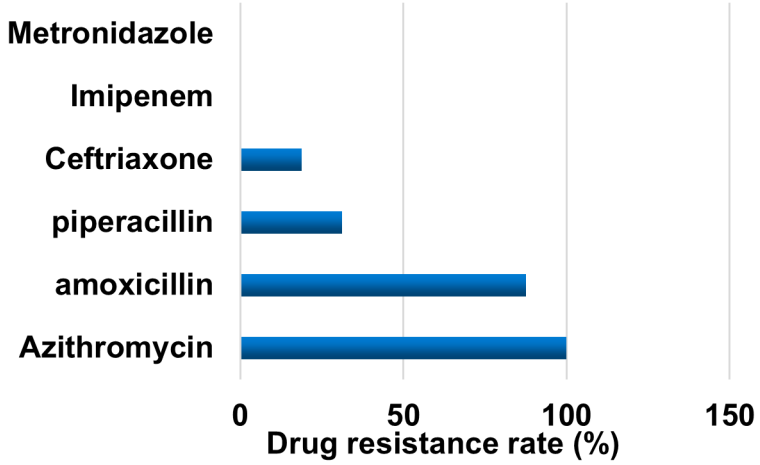

Figure 4. RS of *Fusobacterium nucleatum* to penicillin, amoxicillin, piperacillin, ceftriaxone, imipenem, and metronidazole. RS, resistance rate.

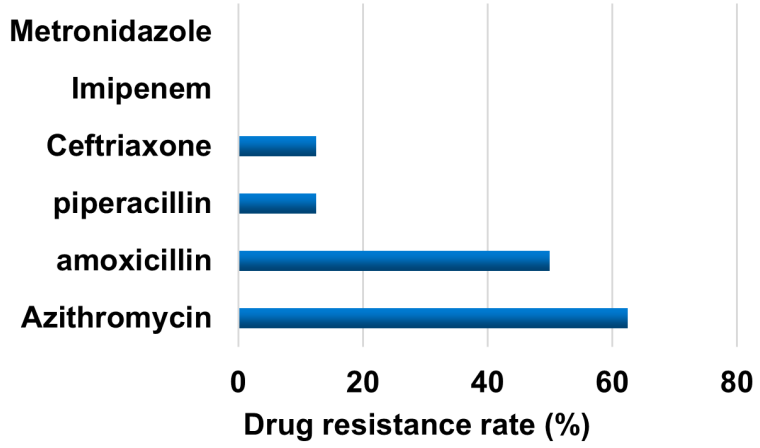

Figure 5. RS of *Porphyromonas gingivalis* to penicillin, amoxicillin, piperacillin, ceftriaxone, imipenem, and metronidazole. RS, resistance rate.

VAS score and pain relief rate of patients after different treatments

The VAS scores of patients before and after different treatments were compared in **Figure 8**. In the Exp group, the pretreatment and posttreatment VAS scores were 5.35 ± 0.87 points and 1.19 ± 0.24 points, respectively. In the Ctrl group, the pretreatment and post-treatment VAS scores were 5.44 ± 0.95 points and 2.81 ± 0.41 points, respectively. It is evident that difference in the pretreatment VAS score was insignificant between patients in the Exp and the Ctrl groups (P=0.385). However, the post-treatment VAS score was markedly lower in the Exp group than in the Ctrl group (P= 0.016).

Figure 9 depicts the pain relief conditions of patients after different treatments. In the Exp group, there were 35 cases showing pain relief, 4 cases with no change, and 1 case with aggravated pain. Meanwhile, in the Ctrl group, there were 28 cases showing pain relief, 13 cases with no change, and 9 cases with aggravated pain, as illustrated in **Figure 9A**. Furthermore, the pain relief rate was 87.5% in the Exp group and 70% in the Ctrl group, suggesting that the pain relief rate in the Exp group was significantly higher than that in the Ctrl group (P=0.007), as shown in **Figure 9B**.

Overall patient satisfaction (OPS) in different groups

As summarized in **Figure 10A**, 30 cases were very satisfied, 7 cases were satisfied, and 3 cases were dissatisfied in the

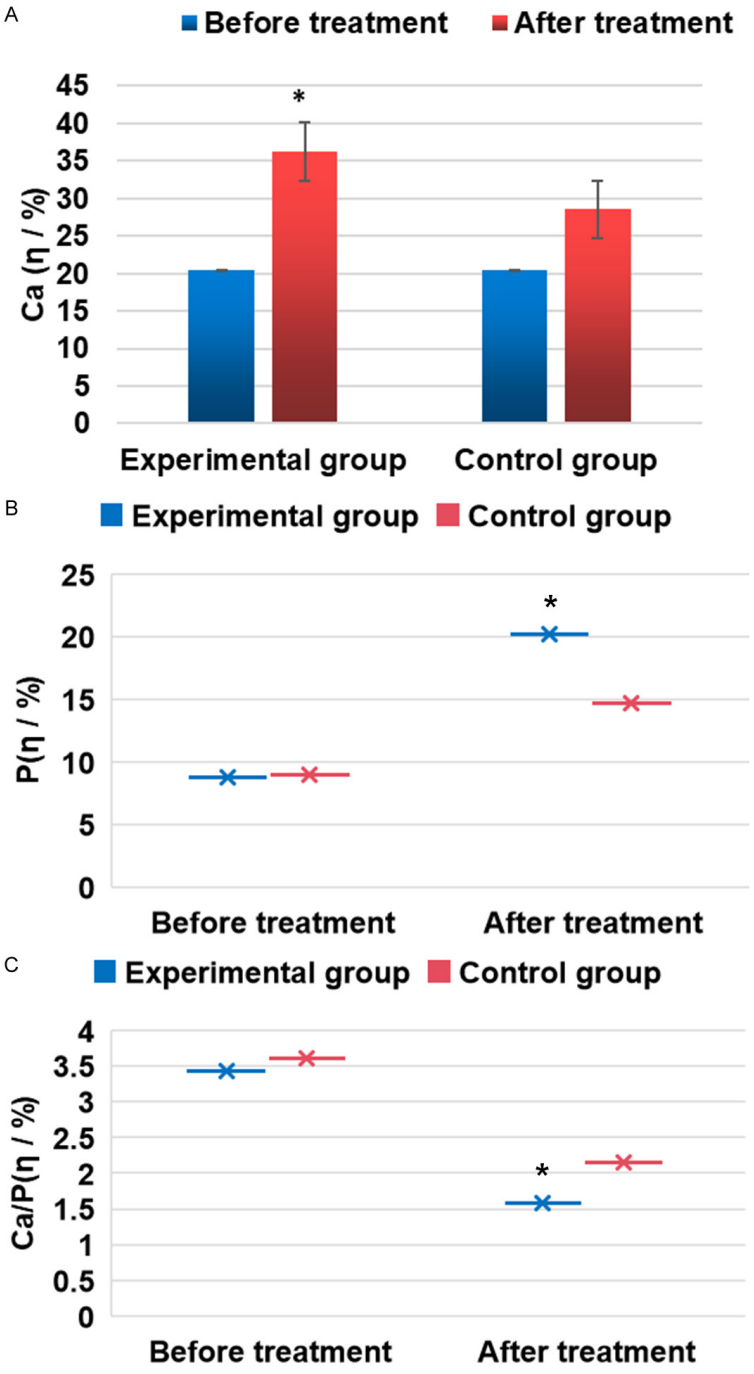

Figure 6. The content of dental pulp composition. A: Ca content; B: P content; C: Ca/P content. Note: *$P < 0.05$.

Exp group. In contrast, in the Ctrl group, 17 cases were very satisfied, 15 were satisfied, and 8 cases were dissatisfied. Thus, the OPS in the Exp and Ctrl groups was 92.5% and 80%, respectively (**Figure 10B**). These results show that the OPS in the Exp group was markedly higher (P=0.021).

Incidence of endodontic reaction in patients

After post-treatment follow-up of patients (**Figure 11**), it was observed that 2 patients in the Ctrl group and 1 patient in the Exp group were lost to follow-up. Since the number of patients lost to follow-up was less than 5%, there was no need to supplement the cases. Also, among patients with follow-up periods less than a year, there was no significant difference in the rate of sensitive dental pulp reactions between the Exp and the Ctrl groups (P=0.139). However, among patients with follow-up periods over a year, the rate of sensitive dental pulp reactions was significantly lower in the Exp group than in the Ctrl group (P=0.026). This indicates that the medication extends the time before sensitive dental pulp reactions occur in patients.

Discussion

Acute pulpitis (AP) commonly arises from congested dental pulp or acute exacerbation of chronic pulpitis. Its hallmark symptom is severe pain, characterized by sudden onset of intense pain without external stimulus. The pain may manifest as continuous or intermittent, with paroxysmal episodes or exacerbations [30]. If left untreated, AP can result in pulp degeneration, pulp necrosis, and may even precipitate angina in patients with coronary heart disease, potentially leading to cardiovascular events. The primary etiology of pulpitis is infection. When the hard tissues of the tooth sustain damage due to various factors, bacteria can infiltrate and infect the dental pulp [31-33]. Dental caries represents the most prevalent cause of tooth hard tissue loss, with

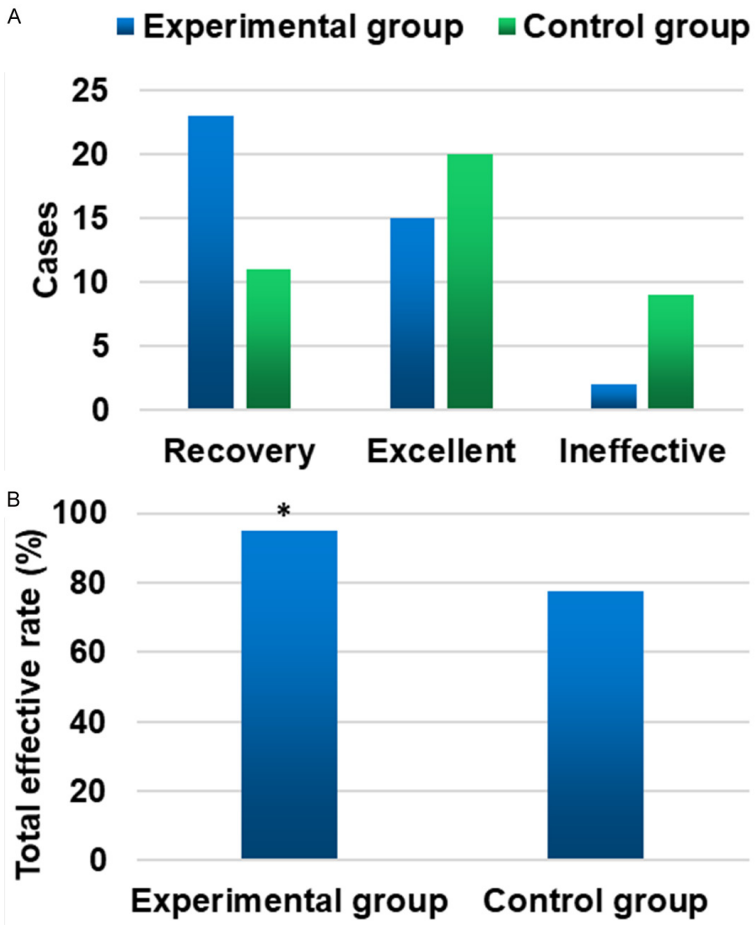

Figure 7. Therapeutic effects of patients after different treatments. (A) represents the number of recovered, effective, and ineffective cases; (B) is the total effective rate of treatment. *$P < 0.05$.

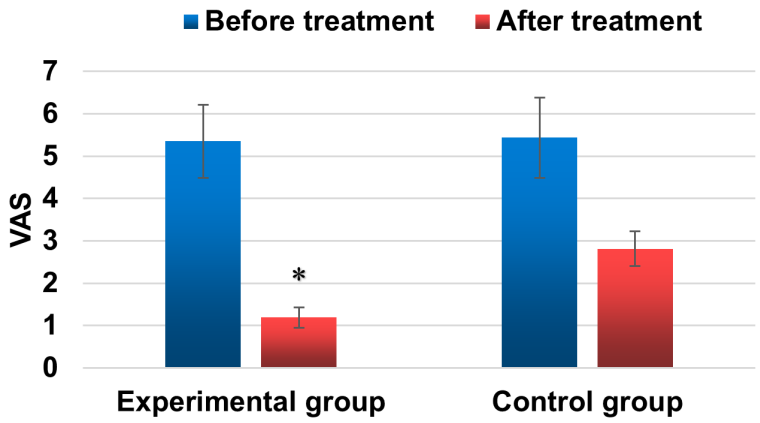

Figure 8. Pretreatment and posttreatment VAS scores of patients in various groups. *$P < 0.05$. VAS, visual analog scale.

other contributing factors including dental defects stemming from abnormal tooth development, and dental pulp exposure due to accidents (e.g., crown fractures, wedge-shaped defects, malformed cusps, aberrant lingual grooves, hidden cracks in teeth, severe dental wear, and vertical root fractures) [34, 35]. Furthermore, in cases of severe periodontal disease, the periodontal pocket may extend to the apical region, facilitating bacterial ingress into the pulp cavity by apical foramina or small branches of the tooth root, thereby provoking pulp inflammation [36]. Hence, this study selected 80 patients diagnosed with AP, treated at the outpatient department from May 2020 to January 2023, as the study population. This study isolated a total of 115 bacterial strains, with Gram-negative anaerobic bacteria being the most prevalent, followed by Gram-positive aerobic bacteria and Gram-positive anaerobic bacteria. This suggests that oral infections in patients with AP are primarily dominated by Gram-negative anaerobic bacteria.

Prevotella melaninogenica is a black anaerobic bacterium belonging to the Prevotella genus and Bacteroidetes phylum. This bacterium is commonly found in the normal flora of the upper respiratory tract and is often implicated as an important pathogen in various anaerobic infections, frequently occurring in conjunction with other aerobic and anaerobic bacteria [37-40]. In this study, it was observed that *Prevotella melaninogenica* exhibited a higher RS to penicillin and amoxicillin, a lower RS to ceftriaxone, and an RS of 0 to imipenem and metronidazole. This suggests that imipenem or metronidazole may be more effective in preventing and treating *Prevotella melaninogenica* infections.

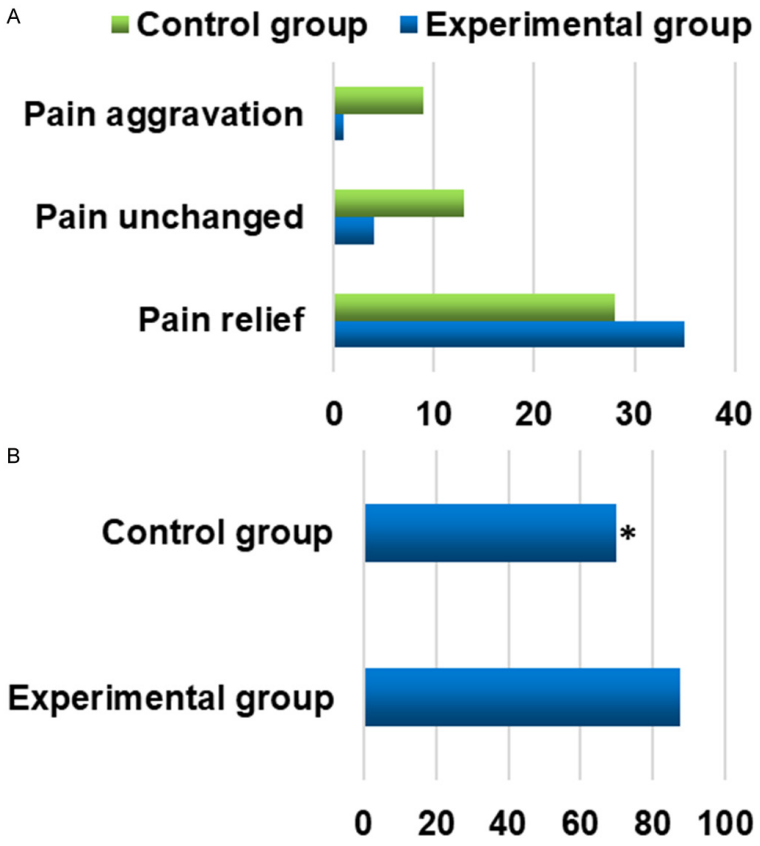

Figure 9. Pain relief rates of patients. (A) represents the number of cases of pain relief, unchanged, or aggravation; (B) is the pain relief rate. *$P < 0.05$.

Additionally, *Fusobacterium nucleatum* and *Porphyromonas gingivalis* exhibited high resistance to penicillin and amoxicillin, suggesting the consideration of alternative antibiotics when treating gingival infections caused by these pathogens. Moreover, despite the resistance rates of *Fusobacterium nucleatum* to cefuroxime and imipenem being 0%, vigilance is still necessary regarding possible resistance to other drugs changing over time and with increasing usage pressure. Additionally, a study incorporating 12 articles found a significant occurrence of antibiotic-resistant isolates of various bacteria including *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella denticola*, *Prevotella melaninogenica*, Actinomyces, Capnocytophaga, Streptococcus, Veillonella, Neisseria, and Fusobacterium among patients with periodontitis. Among these species, the highest resistance frequencies were observed against amoxicillin, clindamycin, and metronidazole [41]. Another investigation revealed resistance of periodontal bacteria from periodontitis patients to tetracycline, metronidazole, and azithromycin upon pre-treatment [42]. These findings are akin to those of our study and may be attributed to the biological characteristics and mechanisms of action of these bacterial species and antibiotics. *Fusobacterium nucleatum* is a commensal bacterium that colonizes the mammalian intestinal tract and is also commonly linked with clinical infection cases as an opportunistic pathogen [43, 44]. *Porphyromonas gingivalis* possesses pathogenicity and expresses various virulence factors such as lipopolysaccharides, peptidoglycans, and gingipains [45-47].

In antibiotic therapy, persistent inflammatory responses may arise due to antimicrobial resistance. This study found that combining DST with targeted antibiotic therapy yielded significant efficacy. Sng et al. (2022) [48] proposed the phenomenon of collateral sensitivity, wherein increased resistance to one antibiotic is associated with increased sensitivity to a second antimicrobial agent, indicating that enhancing antimicrobial drug sensitivity can improve the efficiency of antimicrobial therapy. In a study applying DST + targeted drug therapy to mesothelioma treatment, high-throughput drug sensitivity and resistance testing were conducted on five established PM cell lines using 527 anticancer drugs in a 2D environment. Treatment based on cell sensitivity to drugs resulted in a notable activity within the cell lines [49]. This parallels the methodology employed in our study. Furthermore, patients in the Exp group exhibited a notable decrease in VAS pain scores. This suggests that the combination of DST and CDST can effectively alleviate pain and improve patient comfort. In terms of patient satisfaction, the Exp group showed significantly higher OPS compared to the Ctrl group. This indicates that the combination of DST and targeted antimicrobial therapy can effectively

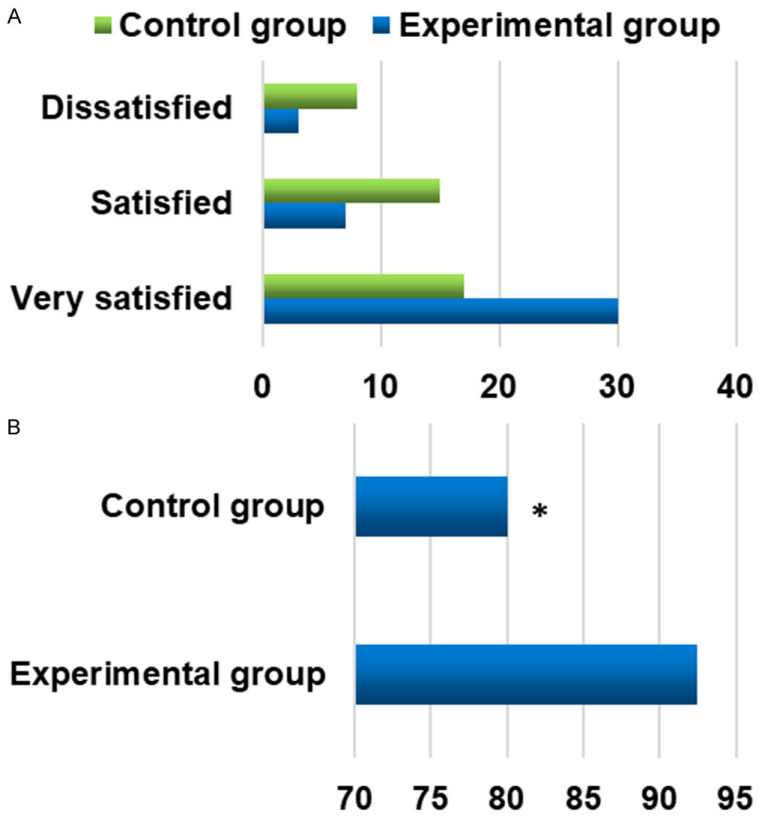

Figure 10. OPS of patients in different groups. (A) represents the number of very satisfied, satisfied, and dissatisfied cases; (B) represents overall satisfaction. *$P < 0.05$. OPS, overall patient satisfaction.

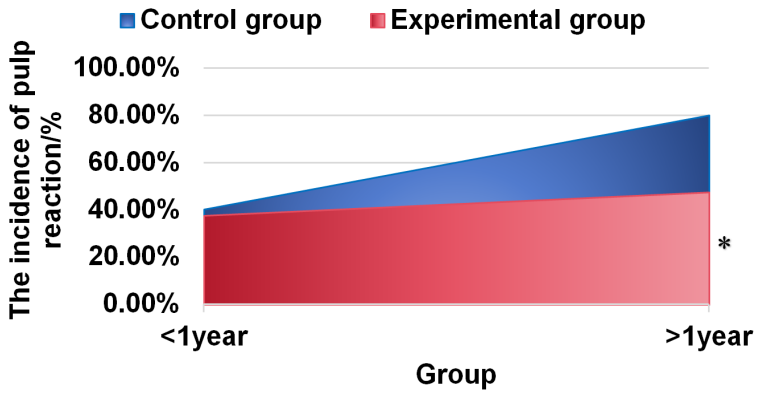

Figure 11. Relationship between the duration of follow-up and the incidence of endodontic reaction after treatment. *$P < 0.05$.

improve patient treatment satisfaction. A study using novel antimicrobial agents for the treatment of pulp diseases included 69 patients scheduled for endodontic retreatment. Microbial quantification from the pre-existing canals was conducted followed by antimicrobial therapy. Results showed a significant reduction in postoperative pain within 48 and 72 hours after the application of antimicrobial agents [50]. This finding resonates with the outcomes of our current investigation.

In this study, observations revealed an increase in the content of Ca and P in both the Ctrl group and the Exp group. Repeated irrigation of the necrotic site with a solution containing metronidazole and dexamethasone was conducted to achieve anti-inflammatory and antibacterial effects, promote tissue repair and healing, and alleviate pain. However, the efficacy of this approach may significantly diminish if bacteria in the necrotic site develop resistance to the drugs. Tailoring drug administration based on DST markedly enhances the formation of crystalline hydroxyapatite layers comprising active Ca and P components. Additionally, studies proposed spectral antibacterial therapy and second-generation sequencing targeted therapy for bacterial infections, which share similarities with the antimicrobial comparison methods employed in this study [51]. Furthermore, research suggested that the formation of hydroxyapatite crystal layers enhances their sealing effect on dentinal tubules and alleviates pain [52], consistent with the aforementioned results. Extended follow-up after patient discharge revealed that conducting DST to guide drug usage could prolong the interval before patients experience dental pulp reactions.

Conclusions

Targeted drug therapy based on DST results significantly improves the therapeutic outcome

of patients with AP, alleviates pain, increases the content of Ca and P in the pulp, and enhances patient satisfaction. However, this study had a limited and homogeneous patient sample. Future research should broaden the sample sources and increase the sample size to further investigate the impact of DST on pulpitis treatment. The findings of this study provide valuable insight for the clinical management of patients with AP.

Disclosure of conflict of interest

None.

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