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ORIGINAL ARTICLE

The Outcome of Prescribing Antibiotics for the Management of Patients with Endodontic Infections

Masoud PARIROKH,[1] Anahita SAFFARZADEH,[2] Nouzar NAKHAEI,[3] Paul ABBOTT[4]

[1]Endodontology Research Center, Kerman University of Medical Sciences, Kerman, Iran
[2]Oral and Dental Diseases Research Center, Kerman University of Medical Sciences, Kerman, Iran
[3]Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran
[4]Department of Oral Restorative and Rehabilitative Sciences (P.A.), Faculty of Dentistry, University of Western Australia, Perth, Australia

ABSTRACT

Objective: This study aimed to evaluate the efficacy and duration of antibiotic therapy with different regimens of antibiotics for patients presenting with primary and secondary endodontic infections.

Methods: In a case series outcome study, all patients needing antibiotics due to endodontic infection were included. In patients with no history of hypersensitivity to penicillin, amoxicillin was used as the first-line antibiotic, followed by adding metronidazole if the symptoms did not show signs of recovery during the first 24 hours after prescribing the medication. If a patient did not respond to the combination of amoxicillin and metronidazole, amoxicillin was substituted with a parental penicillin G procaine. Patients who had sensitivity to penicillin received clindamycin. In cases where drainage was possible, the effect of the procedure on the success rate of antibiotic therapy was evaluated. All patients were asked to continue taking the antibiotic for up to two days following the relief of symptoms. Data were analysed by Chi-square, Fisher exact test, Independent t-test, and One-way ANOVA.

Results: Over a period of 6 years, 97 patients were eligible to be included in this study. In patients with no history of sensitivity to penicillin (95.9% of the patients), 52.7% of patients on amoxicillin and 43% of patients on amoxicillin plus metronidazole overcame the endodontic infections. In addition, drainage significantly increased the success rate of antibiotic therapy when amoxicillin was prescribed ($p=0.046$). There were no significant differences between the gender, age, type of tooth, need for primary or secondary endodontic treatment, previous history of infection, need for drainage or duration of antibiotic consumption ($p>0.05$), and the success of antibiotic prescription. However, patients who received a single antibiotic (either amoxicillin or clindamycin) had significantly shorter average times for the recovery of symptoms ($p<0.05$).

Conclusion: Amoxicillin helped patients recover from endodontic infection symptoms in more than half of the cases. However, it is necessary to monitor the patients to understand if they should be needed further treatment, such as another antibiotic or drainage.

Keywords: Amoxicillin, clindamycin, drainage, metronidazole, root canal

HIGHLIGHTS

- Prescribing appropriate antibiotics, drainage, and patient monitoring is essential when recovering from endodontic infections.
- More than half of the patients needing antibiotics recovered by only prescribing amoxicillin.
- Monitoring patients needing antibiotic therapy due to pulp and periapical infection is necessary to ensure the medication's efficacy. The medication should be switched if no sign of recovery is seen after 24 to 48 hours following the start of medication.
- The patients that received a combination of drainage and amoxicillin recovered significantly faster than those that just received antibiotics.

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Address for correspondence:
Anahita Saffarzadeh
Oral and Dental Diseases Research Center, Kerman University of Medical Sciences, Kerman, Iran
E-mail:
anahita.safarzadeh@gmail.com

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INTRODUCTION

Management of endodontic infections is mostly based on the disinfection of microorganisms and the breakdown of their by-products from within the root canal space and, if possible and necessary, via drainage through the tooth or a soft tissue incision (1). However, in some instances, it is necessary to prescribe antibiotics as adjunctive therapy. Some endodontic infections may be so severe that the patient has to be admitted to a hospital (2). Some reports with high levels of evidence have emphasised that antibiotics should only be prescribed if they are indicated to prevent further development of antibiotic-resistant microorganisms (3).

Of all antibiotics prescribed, a range of 7–11% has been reported prescribed by dentists (4). The selection of the antibiotic prescribed when an endodontic infection presents mainly depends on the microorganisms isolated from the root canal and the periapical region. It has been recommended to use narrow-spectrum antibiotics as the first choice (5). The American Association of Endodontists (AAE) has recommended using amoxicillin with or without metronidazole for patients who do not have hypersensitivity to penicillin, and they recommend clindamycin for patients with hypersensitivity to penicillin (6). Most practitioners prescribe narrow-spectrum antibiotics to manage endodontic infections (5, 7, 8). However, in some countries, many dental practitioners have preferred broad-spectrum antibiotics instead of prescribing a narrow-spectrum antibiotic (9, 10). Several position statements and guidance have been introduced for prescribing systemic antibiotics in endodontics, including patients with apical abscess causing systemic signs and symptoms (localised fluctuant swellings, elevated body temperature >38°C, malaise, lymphadenopathy, trismus), patients with a history of severe systemic diseases and an acute apical abscess, rapidly spreading infections, soft tissue trauma in need of an antibiotic prescription, and replanted avulsed teeth (6, 11).

It has been reported that antibiotics have been prescribed for 10% of endodontic cases (7). Numerous investigations have focused on antibiotic prescription patterns in different regions of the world. These studies' results have shown that dental practitioners' knowledge of managing endodontic infection was insufficient (10, 12, 13). It has been reported that many cases had prescribed incorrect antibiotics, incorrect dosages, or inappropriate duration of therapy (14). The misuse and overuse of antibiotics results in the development of multidrug-resistant strains (1).

Unfortunately, only a few studies have reported the outcome of antibiotic prescriptions for managing endodontic infections (2, 15). In addition, due to the fear of facing progressive infection, many dental practitioners prescribe a broad-spectrum antibiotic at the first visit. Less evidence has been published regarding the course of antibiotic consumption to relieve the symptoms of infections. Investigations on the duration of antibiotic consumption have shown that dental practitioners prescribe a wide variety of course durations, ranging from either a short period of 2–3 days up to a long period of 7–10 days (6).

This study aimed to evaluate the outcome of antibiotic prescriptions on endodontic infections for patients attending a private practice office limited to endodontics in Kerman City in southeast Iran. A second aim was to evaluate the average time for symptom recovery when different antibiotic regimens were prescribed. Finally, other variables that might affect the success of different antibiotics and the average consumption course were also evaluated.

MATERIALS AND METHODS

The study followed the Helsinki Declaration (as revised in 2013) (16). In a case series outcome study with Ethics Committee reference number IR.KMU.REC.1398.235, all patients with the following inclusion criteria that attended a private office limited to endodontics in Kerman City in southeast Iran from February 2014 to January 2020 were included.

Inclusion criteria: Males and females without or with controlled systemic diseases, aged between 15 to 75 years old, presenting with an infection that was definitely of endodontic origin, and with one or more of the following clinical signs: progressive swelling, trismus, progressive diffuse swelling, facial cellulitis, infection involving a facial space, and systemic symptoms (fever, malaise, lymphadenopathy) (11, 17).

Exclusion criteria: Consumption of any systemic antibiotic (oral or parental) before attendance, taking any immunosuppressive medication, and uncontrolled diabetes. Any patients who did not follow the prescribed period of antibiotic consumption or did not respond to phone call follow-up during the treatment period and those with hypersensitivity to the antibiotic regimens used in this study were also excluded.

After evaluating the patient's medical history, clinical symptoms, root canal status, and periapical radiographs, an antibiotic was prescribed if it was considered needed. All patients received a loading dose of 1000 mg of amoxicillin followed by 500 mg of the same medication four times a day, and they were monitored for 24 hours. If the symptoms worsened, 500 mg of metronidazole was added to the previously prescribed amoxicillin in the same order of four times a day. If a patient's symptoms did not improve 24–48 hours after using the combination of amoxicillin and metronidazole, then four doses of parental penicillin G procaine 800000 IU over 48 hours were prescribed while still taking the metronidazole. In case of allergy to penicillin, patients received a loading dose of 600 mg clindamycin followed by 300 mg four times a day. All patients were monitored until they recovered from the symptoms. The time it took for symptoms to subside and the duration of the antibiotic consumption were recorded. In addition, the patients were monitored for any side effects or signs of allergy to the prescribed antibiotics. If necessary, drainage was also performed to help overcome the infection by opening an access cavity, cleaning the root canal space, and, if possible, a soft tissue incision (in case of fluctuant swelling). The following variables were evaluated: age, gender, root canal status, type of tooth, history of previous exacerbation, presence of periapical radiolucency, type of antibiotic and the

regimen, the need for drainage, development of symptoms of infection either following the treatment and patients who attended with symptoms.

Patients were monitored by telephoning them every 24 hours. Telephoning was done by the office receptionist, who was trained to ask questions regarding the symptoms, including the patient's systemic condition (fever, chilling, pain, tenderness to percussion or chewing, and the spread of swelling). If necessary, patients were asked to return to the office to be assessed by the practitioner. In addition, some patients sent an explanation of their symptoms or photographs to the practitioner via social networks, at first by Telegram (Telegram, Dubai, United Arab Emirates) and later by WhatsApp (WhatsApp, Mountain View, California). One week after commencing the antibiotics, the patients were examined to be certain about their recovery from all symptoms and clinical signs of the infection. Treatment was defined as being successful when the patient no longer had acute signs or symptoms after taking the first-line antibiotic (i.e. either amoxicillin or clindamycin).

Data were analysed with Chi-square, Fisher exact, Independent t-test, and One way ANOVA. Statistical analysis was performed using SPSS version 22 (IBM Corp, Armonk, NY, USA). The comparisons were considered significant if $p<0.05$.

RESULTS

Of one hundred-seven patients who could be included in this study, four were excluded because of missing data on follow-up. Four other patients were excluded due to either prescribing antibiotic regimens different from the practitioner's recommendation or not following the antibiotic course they had been prescribed. Two patients reported complications after antibiotic consumption. One male patient with no history of taking clindamycin previously had respiratory distress after taking the antibiotic, while the other patient was a female who reported an orange to red colour of her urine after taking metronidazole. Hence, these two patients were prescribed different antibiotic regimens and excluded from the final evaluation. A total of 97 patients were eligible to be included in this study. The outcomes of antibiotic therapy related to the different variables are summarised in Table 1.

There were 4.1% of the patients who had a history of hypersensitivity to penicillin; therefore, they received clindamycin as the first-line antibiotic. Of the remaining 93 patients with no sensitivity to the penicillin, 52.7% responded well to amoxicillin as the first-line antibiotic, whereas 43% had to have metronidazole to assist their recovery from symptoms. Only 4.3% of the patients needed parental penicillin G procaine because neither the amoxicillin nor the amoxicillin plus metronidazole could manage their symptoms (Table 2). The patients who were treated with either amoxicillin or clindamycin had significantly less average times of antibiotic consumption compared to the other antibiotic regimens (Table 3, 4). None of the other variables (such as age, gender, pulp status, type of tooth, history of previous exacerbation, presence of periapical radiolucency, type of antibiotic regimen, need for drainage, and development of symptoms before attending the clinic or after receiving endodontic therapy) had any significant influence on the duration of antibiotic therapy (Table 5).

For 17.5% of the patients, drainage was performed either through a soft tissue incision or through the access cavity of the teeth. When the practitioner performed drainage, the success rate of the antibiotic therapy significantly improved compared to treatment without drainage ($p=0.046$).

In retreatment cases, the percentage of patients needing another antibiotic in addition to amoxicillin was higher than for teeth in need of antibiotics for a primary infection; however, the difference was not statistically significant ($p=0.4$).

Regardless of which antibiotic regimens were prescribed, 52.6% of the patients reported significant improvement in recovery from the symptoms by 24 hours after commencing the antibiotics, whereas 34% reported significant improvement after 48 hours and 13.4% after 72 hours.

DISCUSSION

The results of this study show that either amoxicillin or clindamycin as the first-line antibiotic can improve the signs and symptoms of endodontic infections in more than half of the patients. However, the remaining patients needed another oral antibiotic or parental penicillin G procaine to assist their recovery.

In this study, in addition to the phone call made by the receptionist, some patients sent a brief explanation of their clinical symptoms or a photograph showing the site of infection if the clinician asked for one by social networks. The explanation gave the practitioner confidence about the treatment progress and an indication as to whether the infection was being controlled. The Covid-19 outbreak has made this type of communication between dentists and their patients essential because a practitioner can monitor patients carefully and limit their clinic attendance to just when necessary (18).

In most countries, amoxicillin is the first choice antibiotic for endodontic infections for patients who have no allergy to penicillin, while clindamycin is the first choice antibiotic for patients who are allergic to penicillin (8, 19, 20). It has been reported that about 8–11% of the population is allergic to penicillin or its derivatives, although there are also some misinterpretations regarding penicillin allergy (5). It should be noted that a misrepresented penicillin allergy could lead to the use of an alternative antibiotic that may not be as effective as penicillin, as well as being more toxic and with a higher price (21).

The AAE has recommended using narrow-spectrum antibiotics as the first-line therapy since broad-spectrum antibiotics may cause changes in the gastrointestinal microbiota (6). In addition, extended or broad-spectrum antibiotics should only be prescribed if a persistent infection indicates the presence of microorganisms resistant to narrow-spectrum antibiotics (22, 23). A systematic review and meta-analysis reported lower bacterial resistance to amoxicillin in bacteria isolated from

TABLE 1. The patients' variables and outcome of antibiotic therapy

Effectiveness	The success of first-line antibiotics		Need more antibiotics to overcome infection		p
	n	%	n	%	
Variables					
Age	53	54.64	44	45.36	0.475
Gender					
Male	18	60	12	40	0.478
Female	35	52.2	32	47.8	
Presence of a systemic condition					
No	28	48.3	30	51.7	0.125
Yes	25	64.1	14	35.9	
Root canal status					
Necrosis	32	61.5	20	38.5	0.103
Gutta-percha	18	47.4	20	52.6	
Paste	1	50	1	50	
Partial necrosis	2	50	2	50	
Previous surgery	0	0	1	100	
Presence of symptoms					
No	33	57.9	24	42.1	0.442
Yes	20	50	20	50	
History of abscess					
No	28	58.3	20	41.7	0.469
Yes	25	51	24	49	
Presence of periapical radiolucency					
No	14	63.6	8	36.4	0.335
Yes	39	52	36	48	
Drainage performed					
No	40	50	40	50	0.046
Yes	13	76.5	4	23.5	
Type of treatment					
RCT	34	60.7	22	39.3	0.400
Retreatment	18	48.6	19	51.4	
No treatment	1	33.3	2	66.7	
IR	0	0.0	1	100	
Type of teeth					
Anterior max	5	38.5	8	61.5	0.129
Premolar max	12	50	12	50	
Molar max	11	61.1	7	38.9	
Anterior man	7	100	0	0.0	
Premolar man	6	42.9	8	57.1	
Molar man	12	57.1	9	42.9	

RCT: Root canal treatment, IR: Intentional replantation, Max: Maxilla, Man: Mandible

acute endodontic infections than other antibiotics (24). Amoxicillin may be considered a broad-spectrum antibiotic; however, when used alone, it has a narrower spectrum than when it is combined with clavulanic acid and when it is combined with metronidazole.

In this study, the previous recommendations of the AAE and the current European Society of Endodontology (ESE) position statement were considered as the criteria for prescribing antibiotics for endodontic infections (11, 17). However, recent AAE guidance and an American Dental Association's expert panel have recommended that antibiotics should only be prescribed if there are systemic signs of an endodontic infection (6, 25).

Due to the lack of guidelines for an antibiotic prescription for overcoming endodontic infections, the AAE and ESE have published clinical guidance and position statements, respectively. The AAE guidance encourages using amoxicillin combined with clavulanic acid. In contrast, the ESE supported using amoxicillin plus metronidazole for endodontic infections that were not responding well to amoxicillin alone. In a study conducted by Segura-Egea et al. (19) regarding the worldwide pattern of antibiotic prescription, amoxicillin plus metronidazole has been used as the first choice for overcoming infection due to endodontic reasons in Asia and Africa. However, metronidazole has been the second choice for treating endodontic infections in Europe and the Middle East.

Establishing drainage through the tooth or via a soft tissue incision is recommended whenever possible since drainage helps to eliminate the accumulated pus, inflammatory me-

TABLE 2. Outcome of antibiotic therapy based on the prescribed medication regimens

Effectiveness	The success of first-line antibiotic		Need more antibiotics to overcome infection	
	n	%	n	%
Treatment regimen				
Amoxicillin	49	52.68	44	47.32
Amoxicillin and metronidazole	40	90.90	4	9.10
Amoxicillin and metronidazole followed by parental penicillin	4	100	0	0.00
Clindamycin	4	100	0	0.00

TABLE 3. Average medication consumption periods for the different antibiotic regimens

Statistics	n	Min (days)	Max (days)	Mean (days)	SD	p
Antibiotic regimens						
Amoxicillin	49	3	10	4.2653	1.20374	0.001
Amoxicillin and metronidazole	40	4	8	5.6750	1.04728	
Amoxicillin and metronidazole followed by parental penicillin	4	6	8	7.0000	0.81650	
Clindamycin	4	3	5	4.0000	0.81650	

Min: Minimum, Max: Maximum, SD: Standard deviation

diators, and irritants from the periapical space (11, 17). However, it is not always possible to achieve drainage through the tooth, such as when a post and crown are in place. Drainage via the soft tissues also may not always be possible. In the present study, 17.5% of the cases received drainage in addition to antibiotic therapy. This study showed a significantly higher successful outcome when amoxicillin was prescribed, and drainage was established compared to the other antibiotic regimens (p=0.046). Based on the results of this study, it could be hypothesised that providing drainage may decrease the need to prescribe broad-spectrum antibiotics and potentially prevent the development of resistance amongst the microorganisms. This needs to be investigated further.

The recent Covid-19 outbreak, in some instances, has restricted dentistry's approach to emergency treatments due to the high chance of aerosol production during dental treatment. It has been recommended to manage urgent endodontic patients with suspected or confirmed Covid-19 infection with antibiotics in case of swelling (26). The results of the present study show that endodontic infections can be managed by prescribing antibiotics in 82.5% of the cases without the need to perform any other intervention. Monitoring the patients daily and adding or changing antibiotics whenever needed could successfully manage their endodontic infections. Moreover, choosing appropriate antibiotic regimens and establishing drainage whenever possible resulted in no need to send patients to a hospital because of failure to manage the infections.

Several studies have confirmed that amoxicillin (23, 27) and penicillin G procaine are appropriate antibiotics for endodontic infections (23). However, there are also some reports of infections being resistant to penicillin G and clindamycin (28, 29). In this study, four patients whose symptoms did not resolve when taking amoxicillin and metronidazole received parental penicillin G procaine. The reason that parental penicillin G procaine was used instead of amoxicillin was to have a higher concentration of the penicillin derivatives in the patient's blood to overcome the infection. The results revealed that all treated endodontic infections could be managed with narrow-spectrum antibi-

TABLE 4. Comparison of the periods of medication consumption for the different antibiotic regimens

Comparisons	Mean difference	SD	p
Antibiotic regimens			
Amoxicillin			
Amoxicillin and metronidazole	–1.40969*	0.23832	0.001
Amoxicillin and metronidazole followed by parental penicillin	–2.73469*	0.58158	0.001
Clindamycin	0.26531	0.58158	0.968
Amoxicillin and metronidazole			
Amoxicillin	1.40969*	0.23832	0.001
Amoxicillin and metronidazole followed by parental penicillin	–1.32500	0.58649	0.115
Clindamycin	1.67500*	0.58649	0.027
Amoxicillin and metronidazole followed by parental penicillin			
Amoxicillin	2.73469*	0.58158	0.001
Amoxicillin and metronidazole	1.32500	0.58649	0.115
Clindamycin	3.00000*	0.79083	0.001
Clindamycin			
Amoxicillin	–0.26532	0.58158	0.968
Amoxicillin and metronidazole	–1.67500*	0.58649	0.027
Amoxicillin and metronidazole followed by parental penicillin	–3.00000*	0.79083	0.001

*: Statistically significant. SD: Standard deviation

TABLE 5. Effect of various variables on duration of antibiotic therapy

P value of effectiveness	p
Variables	
Age	0.470
Gender	0.470
Presence of a systemic condition	0.230
Root canal status	0.963
Presence of symptoms	0.993
History of abscess	0.944
Presence of periapical radiolucency	0.166
Drainage performed	0.114
Type of treatment	0.912
Type of tooth	0.684

otics. However, sometimes a higher dosage of antibiotics may be needed. Poeschl and associates (2) reported that aerobic and anaerobic microorganisms in deep space odontogenic infections were less resistant to penicillin G than to clindamycin. Several studies show that a combination of amoxicillin and clavulanic acid is more effective than amoxicillin used with metronidazole when the first narrow-spectrum antibiotic (i.e. amoxicillin) did not eliminate symptoms in the early period following the commencement of the antibiotic (2, 23, 28, 30). In this study, due to the broader spectrum of the combination of amoxicillin and clavulanic acid, the narrower spectrum antibiotics (amoxicillin and metronidazole) were prescribed. However, this was one of the limitations of this study since it might be possible to prescribe a combination of amoxicillin and clavulanic acid when amoxicillin and metronidazole do not resolve the symptoms. This could be useful since some patients may object to having parental penicillin injections.

There were some side effects from the antibiotics that practitioners should be aware of and note to prevent further problems. Two patients reported side effects associated with the antibiotics. One male patient reported severe acute respiratory distress that started after using the second dose of clindamycin and had no history of taking this medication. This side effect emphasises two key points. Firstly, in addition to monitoring the patients to determine whether their symptoms are resolving, it is necessary to advise them not to continue an antibiotic if they encounter any side effects, and they should contact their doctor immediately. Secondly, no history of taking a specific antibiotic does not mean there is no chance of hypersensitivity to that medication. The other patient reported red to orange urine after taking metronidazole. This is one of the rare side effects of this antibiotic (31). This side effect is significant because patients may make a mistake and think it is a sign of haematuria. Therefore, the practitioner should be aware of that side effect and reassure the patient.

This study showed that when the infection was managed with one antibiotic, a significantly shorter course of the medication was necessary (Table 3). There are different recommendations for the duration of courses of antibiotics. The AAE and ESE position statements recommend taking antibiotics for 3–7 days (6, 11). However, some authors believe 2–3 days would be enough if either soft tissue drainage or extraction were performed (15). In this study, the average period of antibiotic consumption varied when different antibiotic regimens were prescribed (Table 3). Most respondents of a survey conducted in the USA and other countries recommended an average of 5–7 days for their patients (5, 8). However, the results of the present study showed that 95.9% of the patients could be managed by taking antibiotics for less than 7 days. In this study, the patients were asked to continue their antibiotics for up to 2 days following relief from their acute symptoms. None of the patients reported a rebound of the symptoms after they stopped taking the antibiotics. Only one patient reported a rebound but stopped taking the antibiotic only one day after recovery from the symptoms. Due to the exclusion criteria, that patient had to be excluded from the analysis.

The results of this study show that most patients reported appropriate recovery during the first 72 hours following the commencement of the antibiotics. This follows the AAE's recommendation that emphasised the use of shorter courses of antibiotics (6). Therefore, in patients who are responding well either to amoxicillin or clindamycin, a shorter course of antibiotics could be recommended. Even in patients who had to be given parental penicillin to overcome their symptoms, there was no need to use the medication for more than a week.

A limitation of this study is that the results relate to patients who attended the office with no history of previous intervention. Therefore, the actual number of patients in need of antibiotic therapy that visited the practitioner was much greater than the sample in this study, but many patients could not be included because of the strict inclusion and exclusion criteria.

CONCLUSION

In conclusion, prescribing antibiotics for patients with an endodontic infection should be associated with monitoring, adding another antibiotic, or switching to other antibiotics whenever needed. More than half of the patients with no history of allergy to penicillin responded well to the currently recommended narrow-spectrum first-choice antibiotic (i.e., amoxicillin). In addition, when drainage and antibiotic therapy were combined, the need to add or change antibiotics was significantly reduced.

Disclosures

Conflict of interest: The authors deny any conflict of interest.

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