

Elsevier Editorial System(tm) for Journal of Endodontics
Manuscript Draft

Manuscript Number:

Title: Antibiotic Use by Members of the Spanish Endodontic Society

Article Type: Clinical Research

Keywords: antibiotic therapy; prescribing habits; apical periodontitis; endodontist.

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Manuscript Region of Origin: Europe & Central Asia

Abstract: The purpose of this study was to determine the prescribing habits of active members of the Spanish Endodontic Society (AEDE) with regard to antibiotics. A one-page questionnaire was sent to the active members of the AEDE. Of the 508 surveys mailed, 158 surveys were returned, and 140 were found to be usable. The overall response rate was 31.1%. The data were analyzed using descriptive statistics and chi-square tests of independence. The average duration of antibiotic therapy was 6.8 \pm 1.8 days. In patients with no medical allergies most of responders (86.1%) selected amoxicillin as first-choice antibiotic, alone (44.3%) or associated to clavulanate (41.8%); metronidazole-spiramycin and clindamycin were prescribed by 7.6% and 3.7% of the respondents. The first drug of choice for patients with an allergy to penicillins was clindamycin 300 mgr (63.2%), followed by metronidazole-spiramycin (23.7%). For cases of irreversible pulpitis, 40.0 % of respondents prescribed antibiotics. For the scenario of a necrotic pulp, acute apical periodontitis,

and no swelling, 52.9% prescribed antibiotics. Almost 21.5% prescribed antibiotics for necrotic pulps with chronic apical periodontitis and a sinus tract. We conclude that, for the most part, the majority of the members of the AEDE were selecting the appropriate antibiotic for use in orofacial infections, but there are still many who are prescribing antibiotics inappropriately. The use of antibiotics for minor infections, or in some cases in patients without infections, could be a major contributor to the world problem of antimicrobial resistance.

Antibiotic Use by Members of the Spanish Endodontic Society

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ABSTRACT

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4 The purpose of this study was to determine the prescribing habits of active
5 members of the Spanish Endodontic Society (AEDE) with regard to antibiotics.
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7 A one-page questionnaire was sent to the active members of the AEDE. Of the
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9 508 surveys mailed, 158 surveys were returned, and 140 were found to be
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11 usable. The overall response rate was 31.1%. The data were analyzed using
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13 descriptive statistics and chi-square tests of independence. The average
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15 duration of antibiotic therapy was 6.8 ± 1.8 days. In patients with no medical
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19 antibiotic, alone (44.3%) or associated to clavulanate (41.8%); metronidazole-
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21 spiramycin and clindamycin were prescribed by 7.6% and 3.7% of the
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23 respondents. The first drug of choice for patients with an allergy to penicillins
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33 necrotic pulps with chronic apical periodontitis and a sinus tract. We conclude
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35 that, for the most part, the majority of the members of the AEDE were selecting
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39 who are prescribing antibiotics inappropriately. The use of antibiotics for minor
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41 infections, or in some cases in patients without infections, could be a major
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43 contributor to the world problem of antimicrobial resistance.
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57 **KEY WORDS:** antibiotic therapy, prescribing habits, apical periodontitis,
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INTRODUCTION

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4 The first antibiotic, penicillin, was discovered by Alexander Fleming in 1928.
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7 Florey, in 1940, introduced the use of antibiotics to clinical practice. Since then,
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10 antibiotics have been used extensively in dentistry. However, while many
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12 bacterial species were initially found to be sensitive to different types of
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14 antibiotics, there has been a gradual and sustained emergence of resistant
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16 strains (1). Antibiotic resistance is the ability of a microorganism to withstand
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18 the effects of antibiotics. We have now entered an era where some bacterial
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20 species, including those involved in endodontic infections (2), are resistant to
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22 the full range of antibiotics presently available.
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29 Dentistry's contributions to the problem of antibiotic resistance can be
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31 substantial because dentists prescribe approximately 10% of all common
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33 antibiotics (3). Odontogenic infections and, especially, endodontic infections,
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35 are polymicrobial involving a combination of Gram-positive, Gram-negative,
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37 facultative anaerobes and strict anaerobic bacteria (4, 5). Thus, antibiotics, with
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39 analgesics, account for the vast majority of medicines prescribed by dentists. In
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41 2004, a survey of over 6,000 general dental practitioners in the UK revealed
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43 that 40% of dentists were prescribing antibiotics on at least three occasions
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45 every week. The research also revealed that 15% of the dentists prescribed
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47 antibiotics on a daily basis. However, it is increasingly being accepted that such
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49 prescribing habits are often either inappropriate or unnecessary (1).
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In USA, several surveys have analyzed the use of antibiotic by diplomates of the American Board of Endodontics in the treatment of endodontic infections (6, 7, 8). Yingling *et al.* (2002) determined the prescribing habits of active members of the American Association of Endodontists (AAE) with regard to antibiotics concluding that the majority of the members of the AAE were selecting the appropriate antibiotic for use in orofacial infections, but there were still many who are prescribing antibiotics inappropriately. However, in Spain no study has analyzed the prescribing habits with regard to antibiotics between endodontists.

The purpose of this study was to investigate the antibiotic prescribing habits of the members of the Spanish Endodontic Society (Asociación Española de Endodoncia, AEDE).

MATERIALS AND METHODS

A one-page questionnaire was sent to the members of the AEDE (Fig. 1). A cover letter and postage-paid return envelope were also included. The 2007 mailing list of members was obtained from the AAE.

Some questions were based on those asked in the previous surveys developed in USA (6-9), and the questionnaire was reviewed by dental researchers and endodontic faculty for appropriateness and clarity. The data were analyzed using descriptive statistics and groups were compared by using a chi square test of independence.

RESULTS

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5 Of the 508 surveys mailed, 158 surveys were returned. A total of 18 were
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7 returned as undeliverable, and the others (n : 140) were found to be usable. The
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9 overall response rate was 31.1%.

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14 The demographics of the respondents are described in Table 1. Male
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16 respondents accounted for 63% and females 37% of the total. Fifty seven
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18 percent of the respondents were less than 35 years old and 36% more than 45
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20 years old. The mean age of the respondents was 34 ± 6 yr of age. The most
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22 frequent academic degree was DDS (62.9%). Stomatologist, medical doctor
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24 specialised in stomatology, represented 28.5% of total. Only 8.6% of the
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26 respondents were both MD and DDS. In relation with the percentage of time
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28 assigned to endodontic practice, the majority of respondents were in part-time,
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30 and only 21.4% declared themselves to be in full-time endodontic practice.
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32 However, 56% of the respondents dedicated to endodontics more than a half of
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34 their dental practice. The nation-wide proportion of respondents by region of
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36 Spain was evenly distributed (Fig. 2).

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46 The average duration of antibiotic therapy was 6.8 ± 1.8 days (Fig. 3). The
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48 standard deviation in this response indicated that majority prescribe for between
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50 6 and 8 days. There were no significant differences between respondents in
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52 relation with age, gender, academic degree, region, nor time dedicated to
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54 endodontics ($p > 0.05$).
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1 Most of responders (86.1%) chosen amoxicillin in patients with no medical
2 allergies (Table 2), alone (44.3%) or associated to clavulanic acid (41.8%).
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4 Metronidazole-spiramycin and clindamycin were prescribed as first-choice
5 antibiotic by 7.6% and 3.7% of the respondents. The first drug of choice for
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7 patients with an allergy to penicillin was clindamycin 300 mgr (63.2%), followed
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9 by metronidazole-spiramycin (23.7%) (Table 3).
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17 Table 4 lists the percentage of respondents who prescribed antibiotics for
18 various pulpal and periapical diagnoses. For cases of irreversible pulpitis with
19 moderate/severe symptoms and irreversible pulpitis with acute apical
20 periodontitis and moderate/severe symptoms, 11.4% and 28.6% of
21 respondents, respectively, prescribed antibiotics. In cases of a necrotic pulp,
22 chronic apical periodontitis, no swelling, and no other symptoms, antibiotics
23 were prescribed by 14.3%. In the scenario of necrotic pulp, acute apical
24 periodontitis, moderate/severe symptoms but no swelling, 52.9% prescribed
25 antibiotics. For a case of necrotic pulp, chronic apical periodontitis,
26 asymptomatic but with a sinus tract, 21.4% prescribe antibiotics. In the case of
27 a necrotic pulp, acute apical periodontitis, swelling, and other moderate/severe
28 symptoms, 94.3% of respondents prescribed antibiotics.
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48 There were no significant differences between respondents in prescribing habits
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50 endodontics ($p > 0.05$).
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DISCUSSION

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5 The survey instrument has historically been successful in obtaining pertinent
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7 information on the practice of endodontics. The population sampled in this study
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9 was large, 508 members of the AEDE. A large percentage of this target
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11 population was practicing endodontists, and it should be noted that no attempt
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13 was made to survey practicing endodontists who were *not* members of the
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15 AEDE. The overall response rate of 31.1% can be considered to be an
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17 acceptable rate of return for surveys. Other similar surveys published recently
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19 have reported response rates of 35% and 41% (10, 11). Questions were
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21 designed to collect a variety of information relative to the types of antibiotics
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23 used and the prescribing habits of endodontists as determined by age, gender,
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25 academic degree, area of the country, and percentage of time assigned to
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27 endodontics in their whole private dental practice.
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36 In relation with antibiotic therapy, an infection must be persistent or systemic to
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38 justify the need for antibiotics: i.e. fever, swelling, lymphadenopathy, trismus, or
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40 malaise in a healthy patient. Antibiotics are also more likely to be needed in an
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42 immunocompromised patient or a patient in poor health. The decision to
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44 prescribe antibiotics should not be influenced by patient demand, expectation of
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46 referring dentists, “just in case” situations, or because it is the day before a
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48 weekend or holiday. These reasons constitute inappropriate use of antibiotics.
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51 As it has been previously reported by Yingling *et al.* (9), some respondents
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53 submitted comments that patients and referring general practitioners often
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55 “demand” antibiotics be prescribed for every endodontic scenario. These
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endodontists felt compelled to prescribe them for “medical-legal” reasons and to decrease the risk of losing referrals.

Endodontic infections typically have a rapid onset and short duration, 2 to 7 days or less, particularly if the cause is treated or eliminated (12). The average length of antibiotic prescriptions in this study was 6.8 days with a range of 5 to 10 days. The proper dose and duration of an antibiotic is enough when there is sufficient evidence that the patient host defenses have gained control of the infection. When the infection is resolving or has resolved, then the drug should be terminated (9, 12). A 6 to 7 day course would probably be appropriate for most endodontic infections. An antibiotic loading dose should be used whenever the half-life of the antibiotic is longer than 3 h or whenever a delay of 12 h or more is unacceptable to achieve therapeutic blood levels (13).

The list of antibiotics included in the survey identifies those most often prescribed by Spanish dentists for the management of orofacial infections. The list included amoxicillin, alone or associated with clavulanic acid, clindamycin, lincomycin, erythromycin, azithromycin, and the association metronidazole-spiramycin. Amoxicillin 500 mg, alone (44.3%) or associated to clavulanic acid (41.8%), was the most prescribed antibiotic for patients who were not allergic to penicillin, being used by 86.1% of respondents (Table 2). Amoxicillin is a moderate-spectrum, bacteriolytic, β -lactam antibiotic that represents a synthetic improvement upon the original penicillin molecule. Amoxicillin is a good drug for orofacial infections because it is readily absorbed and can be taken with food. It is better able to resist damage from stomach acid so less of an oral dose is

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wasted, does have a much broader spectrum against the Gram negative cell wall, and is able to last a bit longer. However, amoxicillin is susceptible to degradation by β -lactamase-producing bacteria, and often is given with clavulanic acid to increase its spectrum against staphylococcal bacteria. Amoxicillin/ clavulanic acid is one of the antibiotics recommended for the treatment of odontogenic infections due to its wide spectrum, low incidence of resistance, pharmacokinetic profile, tolerance and dosage (14, 15). Due to the longer half-life and more sustained serum levels, amoxicillin is taken 3 times a day and costs only slightly more than penicillin. However, its broad spectrum is more than is required for endodontic needs, and its use in a healthy individual may contribute to the global antibiotic resistance problem (16). In Spain, the leading antibiotic prescribed in 2007 was amoxicillin plus clavulanic acid, 5.15 doses per 1,000 inhabitants and day (DID), followed by amoxicillin alone (2.95 DID) (17). Amoxicillin is also the principal antibiotic prescribed in dental clinic for both adult and child patients in other European countries (18). On the contrary, in USA, amoxicillin is prescribed only by 27.5% of members of the American Association of Endodontists (AAE) (9), who selected mainly penicillin VK as the first choice antibiotic (68.5%). Thus, penicillin VK is the principal antibiotic prescribed by dentist in USA (19). Penicillin is a narrow spectrum antibiotic for infections caused by aerobic Gram-negative cocci and anaerobes. However, penicillin is not well absorbed from the intestinal tract meaning that at least 70% of an oral dose is wasted. Penicillin is also a short-acting medication, with half of the amount circulating being removed from the body every half hour. In Spain, the doses per 1,000 inhabitants and day of penicillin V were 0.034 in

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2007, more than a hundred lower than that of amoxicillin-clavulanate (5.15 DID).

In our study, other antibiotics prescribed were metronidazole-spiramycin (7.6%) and clindamycin (3.7%). In the study of Yingling et al. (9), clindamycin was the second prescribed antibiotic for nonpenicillin-allergic patients (45.26%). Clindamycin is a broader spectrum antibiotic than penicillin but is still narrow in its specificity toward oral pathogens. It is bacteriostatic or bactericidal, depending on drug concentration, infection site, and microorganism. It is 90% absorbed from the gastrointestinal tract in the oral form and has peak serum concentration within 60 min. The recommended dose for adults is 150 to 450 mg, 4 times a day for orofacial infections (20). Considering that clindamycin has a low but serious risk of pseudomembranous colitis (21), broader spectrum, and being 2 to 3 times more costly than amoxicillin, there seem to be logical to prefer amoxicillin, as the results of this survey indicated, because amoxicillin is effective with less risk, less cost, and less contribution to antimicrobial resistance. Nevertheless, if an infection were found to be resistant to amoxicillin, with or without the adjunct of metronidazole, one could change to clindamycin.

The first drug of choice for patients with an allergy to penicillins was clindamycin (63.2%). In USA the study of Whitten *et al.* (19) reported a 21.6% for clindamycin as first choice antibiotic, but a posterior study carried out by Yingling *et al.* (9) found a percentage (57.03%) similar to that reported in the present study.

1 Other antibiotics prescribed for patients with an allergy to penicillins were
2 metronidazole-spiramycin, erythromycin, lincomycin and azithromycin.
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4 Erythromycin, a macrolide, has a similar spectrum of activity to that of penicillin.
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6 Azithromycin is semisynthetic derivative of erythromycin that has been modified
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8 to create a broader spectrum of antibacterial activity and improved tissue
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10 penetration (22). Metronidazole, prescribed in Spain and USA as (Flagyl®), is an
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12 antibiotic that is very effective against obligate anaerobes but not against
13
14 facultative anaerobic bacteria. If amoxicillin is not effective after 2 to 3 days of
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16 use, then metronidazole has been recommended as a supplemental medication
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18 (16). Metronidazole has excellent activity against anaerobes but no activity
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20 against aerobes and therefore requires to be used in conjunction with other
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22 agents (antimicrobial combination) for chemotherapy of oral infections.
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24 Spiramycin, a macrolide antibiotic used especially to treat toxoplasmosis, was
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26 chosen as a possibility because of its good activity against both aerobes and
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28 anaerobes and its pharmacokinetics was found to be suitable and could achieve
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30 high concentrations in alveolar bone and gingival tissue which exceeded serum
31
32 levels. Moreover, the combination metronidazole-spiramycin is potentially
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34 synergic and appropriate for treatment of odontogenic abscesses (23). The
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36 combination of spiramycin and metronidazole is commonly used in Europe as
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38 well as in Canada and Mexico, but it is still considered an experimental drug in
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40 the United States, even though can sometimes be obtained by special
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42 permission from the FDA for toxoplasmosis in the first trimester of pregnancy. In
43
44 Spain, metronidazole-spiramycin (Rhodogyl®) is commonly used. In the present
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46 study, metronidazole-spiramycin was prescribed by 23.7% of the respondents
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48 for patients with an allergy to penicillins.
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Table 4 lists the percentage of respondents who prescribe antibiotics for various pulpal and periapical diagnoses. Because a medical history could not be provided and specific details of the symptoms could not be included in every question, interpretation of this data must be considered in light of these limitations (9). The first category was for irreversible pulpitis with moderate/severe symptoms and the second category was for the same with an acute apical periodontitis component. Combined, 40.0% of the respondents prescribed antibiotics for these cases. These pulps are still vital. There is no infection or signs of systemic involvement. Antibiotics are not indicated in either situation. This number is similar to the results found by Whitten *et al.* (19). These findings are almost 50% more than those found by Dorn *et al.* (6), Gatewood *et al.* (8), and Yingling *et al.* (9).

The third situation was necrotic pulp, chronic apical periodontitis, no swelling, and no or mild symptoms. Again, in a healthy patient, there is no indication for antibiotic use, and treatment should be limited to nonsurgical root canal therapy. In this survey 14.3% prescribed antibiotics. Although is a minor percentage, it indicates that exists an inappropriate usage of antibiotics that must been corrected. In previous surveys developed in USA higher percentages has been reported (9, 19) indicating that this problem is widespread.

The fourth category was necrotic pulp, acute apical periodontitis, no swelling, and moderate/severe symptoms. The proper treatment for this case is debridement of the root canal space and analgesics. Again, comparing the Dorn *et al.* (7), Gatewood *et al.* (8), Yingling *et al.* (9), and Whitten *et al.* (19) studies,

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which reported 30.0%, 33.1%, 53.9%, and 67.3% prescription for antibiotics respectively, this survey's result was 52.9%, which fits in the same range as previous studies. This again is over-usage of antibiotics. Interestingly, 21.4% still prescribed antibiotics for asymptomatic cases of necrotic pulp, chronic apical periodontitis, and cases with sinus tracts (the fifth scenario). This result is almost twice of 11.9% in Yingling *et al.* (9). Although reduced from 29.2% in Whitten *et al.* (19), indicated treatment should consist of nonsurgical root canal therapy with analgesics if needed for pain but no antibiotics. If the patient was medically compromised and the sinus tract did not close within a few weeks or the patient experienced a flare up with systemic involvement, then antibiotics would be indicated.

The last situation described a case of a necrotic pulp, acute apical periodontitis (abscess), swelling, and moderate to severe symptoms of an infection. Those prescribing antibiotics in the previous studies (7, 8, 9, and 19) ranged from 87.6% to 99.2%. The results of the present survey were comparable at 94.3% and appropriately so. If one interprets that systemic involvement was present in this case, then antibiotics are indicated in conjunction with debridement of the root canal space and an incision and drainage (I & D) procedure (9).

The interesting point in this survey is that, with regards to irreversible pulpitis, necrotic pulps with no systemic involvement, and sinus tracts, the members of the AEDE are over-prescribing. Why are the respondents prescribing antibiotics for any of the first five scenarios in Table 4? If it were because the patient was immunocompromised, then maybe this would be acceptable (16). If it was

1 because of insufficient training or fear of litigation, then this is clearly an
2 inappropriate use of antibiotics (9). Nonsurgical root canal therapy without
3 antibiotics is usually adequate to treat cases of irreversible pulpitis, acute and
4 chronic apical periodontitis, draining sinus tracts, and localized swellings (16).
5
6 The pulpal circulation is compromised in these cases, and systemic antibiotics
7 will not reach therapeutic concentrations in the pulp. Removing the source of
8 the infection by performing nonsurgical root canal therapy will usually allow
9 healing of any periradicular lesion or inflammation to occur. Analgesics are
10 indicated for pulpitis pain and pain from periapical inflammation, not antibiotics
11 (9, 16).
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26 Antibiotic therapy is an art and a science (9). There are so many confounding
27 variables, such as suspected pathogen, ability to establish drainage,
28 pharmacokinetic properties of the drug, mechanism of action of the antibiotic,
29 virulence of the infection, the current health status of the host, and host defense
30 mechanisms, that it is not possible to make antibiotic therapy into a mechanistic
31 technological science (24). The most important decision for the dental
32 practitioner to make is not which antibiotic to use but *whether to use one at all*.
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46 The prevalence of teeth with apical periodontitis amongst the Spanish
47 population is high (25). Nonsurgical root canal treatment is the treatment of
48 choice. Moreover, most of endodontic situations are resolved by nonsurgical
49 endodontics and accompanying incision and drainage procedures when
50 indicated (9). Spanish endodontists must take into account that, when the
51 decision is made to use an antibiotic, it is important to adhere to basic principles
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of antibiotic dosing: (a) use high doses for short durations; (b) use an oral antibiotic loading dose; (c) achieve blood levels of the antibiotic at 2 to 8 times the minimum inhibitory concentration; (d) use frequent dosing intervals; and (e) determine duration of therapy by remission of disease (12). However, it is important that not only the dental profession but the general public understand the importance of restricting the use of antibiotics to those true cases of severe infection that require them (1). The use of antibiotics for minor infections, or in some cases in patients without infections, could be a major contributor to the world problem of antimicrobial resistance.

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Figure 1. Antibiotic survey sent to members of the AEDE.

Figure 2. Distribution of respondents by Spain's regions.

Figure 3. Distribution of respondents by treatment duration.

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Table 1. Description of respondents

Gender	Male	62.9 %
	Female	37.1 %
Age (yr)	25 - 35	57.1 %
	35 - 45	7.2 %
	> 45	35.7 %
Mean age (yr)		34 ± 6
Academic degree	DDS	62.9%
	MD (stomatologist)	28.5%
	MD+DDS	8.6%
Time assigned to endodontics	Full-time	21.4%
	Part-time (75-95%)	10.0%
	Part-time (50-75%)	24.3%
	Part-time (< 50%)	44.3%

Table 2. Antibiotic preference in patients with no medical allergies.

Antibiotic		%
Amoxicillin	500 mgr	20.3
	750 mgr	15.2
	1000 mgr	8.8
Amoxicillin / Clavulanic acid	500 / 125 mgr	15.2
	875 / 125 mgr	26.6
Metronidazole / Spiramicyn	125 mgr / 750.000 UI	7.6
Clindamicyn	300 mgr	3.7
Azithromicyn	500 mgr	1.3
Other		1.3

Table 3. Antibiotic preference in patients with medical allergies.

Antibiotic		%
Clindamicyn	300 mgr	63.2
Metronidazole / Spiramicyn	125 mgr / 750.000 UI	23.7
Erythromicyn	500 mgr	3.9
Lincomicyn	500 mgr	3.9
Azithromicyn	500 mgr	2.6
Other		2.6

Table 4. Situation in which antibiotic were prescribed.

Situation	Prescribe antibiotics (%)
IP; mod/severe pre-op symptoms	11.4
IP with AAP; mod/severe pre-op symptoms	28.6
NP with CAP; no swelling, no/mild pre-op symptoms	14.3
NP with AAP; no swelling, mod/severe pre-op symptoms	52.9
NP with CAP; sinus tract present; no/mild pre-op symptoms	21.4
NP with AAP; swelling present; mod/severe pre-op symptoms	94.3

IP: Irreversible pulpitis.

NP: Necrotic pulp.

AAP: Acute Apical Periodontitis.

CAP; Chronic Apical Periodontitis.

ANTIBIOTIC SURVEYGENDER: Male Female AGE (ys): 25-35 35-45 More than 45 ACADEMIC DEGREE: MD DDS MD & DDS

PERCENTAGE OF TIME DEDICATED TO ENDODONTIC PRACTICE: _____%

1. Which antibiotic do you prescribe most often for an adult patient with no medical allergies?:

- Amoxicillin (Clamoxyl®): 500mg 750mg 1g
- Amoxicillin + Clavulanic Acid (Augmentine®): 250mg / 62.5mg 500mg / 125mg 875mg/125mg
- Clindamicyn (Dalacin®): 300mg
- Azithromicyn (Zitromax®): 150mg 200mg 250mg 500mg 1g
- Metronidazole + Spiramicyn (Rhodogyl®):
- Other: _____

2. For how many days do you prescribe antibiotics?: _____**3. Which antibiotic do you prescribe most often for an adult patient with allergy to penicillin?:**

- Clindamicyn (Dalacin®): 300mg
- Azithromicyn (Zitromax®): 150mg 200mg 250mg 500mg 1g
- Metronidazole + Spiramicyn (Rhodogyl®):
- Erythromicyn (Pantomicina®):
- Lincomycin (Lincocin®):
- Other: _____

4. In which of the following situations would you prescribe antibiotics? Check all that apply.

- Irreversible pulpitis; mod/severe pre-op symptoms
- Irreversible pulpitis with Acute Apical Periodontitis; mod/severe pre-op symptoms
- Necrotic pulp with Chronic Apical Periodontitis; no swelling, no/mild pre-op symptoms
- Necrotic pulp with Acute Apical Periodontitis; no swelling, mod/severe pre-op symptoms
- Necrotic pulp with Chronic Apical Periodontitis; sinus tract present; no/mild pre-op symptoms
- Necrotic pulp with Acute Apical Periodontitis; swelling present; mod/severe pre-op symptoms

Return address:

Dr. A. Rodriguez Núñez.
C/ Jiménez Aranda 19, Esc.5, 2ºE.
Sevilla-41011.

Figure
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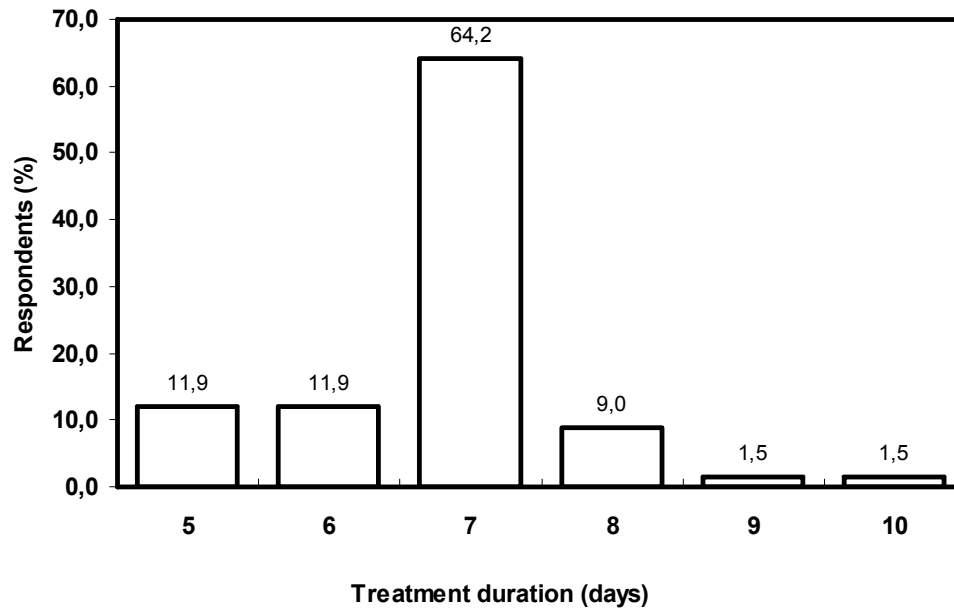


Fig. 3. Distribution of respondents by treatment duration.