PATTERN OF ANTIBIOTIC PRESCRIPTION IN THE MANAGEMENT OF ENDODONTIC INFECTIONS AMONG SPANISH DENTISTS WITH PREFERENTIAL DEDICATION TO ORAL SURGERY

J. J. Segura-Egea[1], E. Velasco-Ortega[2], D. Torres-Lagares[3], J. M. Llamas-Carreras[4], M. C. Velasco-Ponferrada[2], F. J. López-Frías[2], A. García-Mendez[2], R. Medel-Soteras[2]

[1]Department of Endodontics, School of Dentistry, University of Seville, Spain.

[2]Department of Comprehensive Dentistry, School of Dentistry, University of Seville, Spain.

[3]Department of Oral Surgery, School of Dentistry, University of Seville, Spain.

[4]Department of Orthodontics, School of Dentistry, University of Seville, Spain.

Running title: antibiotic in endodontic infections.

Keywords: endodontic infections, apical periodontitis, irreversible pulpitis.

Corresponding author:

Prof. Juan J. Segura-Egea

School of Dentistry, University of Seville, C/ Avicena s/n, 41009-Seville (SPAIN)

e-mail: segurajj@us.es

ABSTRACT

Introduction. The purpose of this study was to identify antibiotic prescription practices in the treatment of endodontic infections among Spanish dentists with preferential dedication to Oral Surgery. **Methods**. Members of the Spanish Oral Surgery Society (SECIB) were surveyed on antibiotic prescription on six different pulpal and periapical diagnoses. A total of 200 questionnaires were delivered to the assistants but only 127 were returned properly answered (63.5%). **Results.** The average duration of antibiotic therapy was 7.0 ± 1.0 days. Ninety five percent of respondents selected amoxicillin as first-choice antibiotic in patients with no medical allergies, alone (33.9%) or associated to clavulanate (60.6%). The first drug of choice for patients with an allergy to penicillins was clindamycin 300 mg (65.4%), followed by azithromicyn (15.0%) and metronidazole-spiramycin (13.4%). For cases of irreversible pulpitis, 85.8 % of respondents prescribed antibiotics. For the scenario of a necrotic pulp, acute apical periodontitis, and no swelling, 70.9% prescribed antibiotics. Almost 60% of respondents prescribed antibiotics for necrotic pulps with chronic apical periodontitis and a sinus tract; in this clinical situation DDS prescribed more frequently antibiotics compared to MD ($p = 0.0080$; odds ratio = 8.0; C. I. 95% = 1.7 − 37.1). **Conclusions**. The majority of the members of the SECIB were selecting the appropriate antibiotic for use in endodontic 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.

INTRODUCTION

Odontogenic infections, especially endodontic infections such as apical periodontitis, are highly prevalent in Spain (Segura-Egea *et al*. 2005; Segura-Egea *et al*. 2008) and other countries (Frisk *et al*. 2008, Gulsahi *et al*. 2008). Endodontic infections are polymicrobial involving a combination of Gram-positive, Gram-negative, facultative anaerobes and strict anaerobic bacteria (Siqueira & Rôças, 2004). Thus, antibiotics, with analgesics, account for the vast majority of medicines prescribed by dentists. Al-Haroni & Skaug (2007) have analyzed 268,834 prescriptions issued by 4,765 dentists showed that the dentists' prescriptions of antibiotics contributed 8% of the total national consumption in Norway. In 2004, a survey of over 6,000 general dental practitioners in the UK revealed that 40% of dentists were prescribing antibiotics on at least three occasions every week (Lewis, 2008). The research also revealed that 15% of the dentists prescribed antibiotics on a daily basis. However, it is increasingly being accepted that such prescribing habits are often either inappropriate or unnecessary.

Antibiotic resistance is the ability of a microorganism to withstand the effects of antibiotics. Bacterial resistance to antimicrobials has been an ongoing challenge for clinicians ever since the discovery of antimicrobial agents because bacteria have succeeded in developing resistance to all antibacterial agents shortly after they had been marketed (Al-Haroni & Skaug, 2007; Lewis, 2008). We have now entered an era where some bacterial species, including those involved in endodontic infections, are resistant to the full range of antibiotics presently

available. Dentistry's contributions to the problem of antibiotic resistance can be substantial because dentists prescribe approximately 10% of all common antibiotics (Pallasch, 2000). Inappropriate prescribing and use have been identified as major factors in the emergence of antibiotic resistance. Several studies have analyzed the antibiotics prescribing habits of dentists showing that over prescription can be happening. 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. Between Flemish dentists, 48% prescribed antibiotics for acute apical periodontitis (Slaus & Bottenberg, 2002).

Spain is one of the European countries with the highest antibiotic consumption rate and, therefore, with the highest percentages of bacterial resistance (Cars *et al*. 2000). This increased consumption rate is not justified by a greater prevalence of susceptible infections in this country compared to others; rather, there is a tendency to prescribe antibiotics against any infection, regardless of the underlying aetiology (Sancho-Puchades *et al*. 2009). Ten percent of global antibiotic prescription in Spain is made by dentists (Bascones *et al*. 2004).

Recently, Rodríguez-Núñez *et al*. (2009) have reported that, with regards to irreversible pulpitis and necrotic pulps with no systemic involvement, the Spanish endodontists are overprescribing antibiotics. Odontogenic infections must be treated not only by endodontists, but also by general dentists and oral

surgeons. The purpose of this study was to identify the pattern of antibiotic prescription in the treatment of endodontic infections among Spanish dentists with preferential dedication to Oral Surgery.

MATERIALS AND METHODS

During the VII Congress of the Spanish Oral Surgery Society held in 2009, members were randomly requested to answer a one-page questionnaire (Fig. 1) surveying about antibiotics use in the treatment of endodontic infections. The questions were based on those asked in the previous surveys developed in USA (Whitten *et al.* 1996; Yingling et al. 2002) and Spain (Rodríguez-Núñez et al. 2009). Two hundred questionnaires were delivered to the assistants. The only participation requirement was Spanish Oral Surgery Society membership. Only 127 questionnaires were returned properly answered (63.5%).

A database was created for further analysis using version 15.0 of the Statistical Package for Social Sciences (SPSS, SPSS inc., Chicago, IL, USA). Data description was carried out by frequency tables. When obtaining the numerical representation by percentages, the total number of answers for each query was taken into account. Data were analyzed using descriptive statistics, chi square test of independence and logistic regression. Statistically significant differences were considered for $p < 0.05$.

RESULTS

The demographics of the respondents are described in Table 1. Male respondents accounted for 49% and females 51% of the total. Seventy six percent of the respondents were less than 36 years old and 11% more than 45 years old. The mean age of the respondents was 34 ± 6 yr of age. The most frequent academic degree was DDS (88.2%). Stomatologist, medical doctor specialized in stomatology, represented 7.9% of total. Only 3.9% of the respondents were both MD and DDS. In relation to postgraduate formation, 47% of the respondents had completed postgraduate training in oral surgery. The nation-wide proportion of respondents by regions of Spain was evenly distributed (Fig. 2).

The average duration of antibiotic therapy was 7.0 ± 1.0 days (Fig. 3). The standard deviation in this response indicated that majority prescribe for between 6 and 8 days. There were no significant differences between respondents in relation with age, gender, academic degree, postgraduate formation, nor region ($p > 0.05$).

Most of respondents (94.5%) chosen amoxicillin in patients with no medical allergies (Table 2), alone (33.9%) or associated to clavulanic acid (60.6%). Amoxicillin/Clavulanic acid 875/125 mg was prescribed as first choice antibiotic by 41.7% of respondents, whereas 18.1%, 8.7%, 3.1% and 0.8% selected amoxicillin 750 mg, amoxicillin 500 mg, clindamycin and metronidazole-spiramycin, respectively. The first drug of choice for patients with an allergy to

penicillin was clindamycin 300 mg (65.4%), followed by azithromicyn (15.0%) and metronidazole-spiramycin (13.4%) (Table 3).

Table 4 lists the percentage of respondents who prescribed antibiotics for various pulpal and periapical diagnoses. For cases of irreversible pulpits with moderate/severe symptoms and irreversible pulpitis with acute apical periodontitis and moderate/severe symptoms, 31.5% and 54.3% of respondents, respectively, prescribed antibiotics. In cases of a necrotic pulp, chronic apical periodontitis, no swelling, and no other symptoms, antibiotics were prescribed by 30.7%. In the scenario of necrotic pulp, acute apical periodontitis, moderate/severe symptoms but no swelling, 70.9% prescribed antibiotics. For a case of necrotic pulp, chronic apical periodontitis, asymptomatic but with a sinus tract, 59.8% prescribe antibiotics. In the case of a necrotic pulp, acute apical periodontitis, swelling, and other moderate/severe symptoms, 94.5% of respondents prescribed antibiotics.

There were no significant differences between respondents in antibiotics prescribing habits in relation with age, gender, post-graduate formation nor region (p > 0.05). To further study the possible association between these factors and the pattern of antibiotic prescription in the different clinical situations, multivariate logistic regression analyses were carried. When multivariate logistic regression was run with gender (female/male), age (< 35 years / ≥ 35 years), post-graduate formation (no formation / training in oral surgery), and academic degree (MD / DDS) as independent variables, and "antibiotics prescription in the fifth situation" (absent / present) as the dependent

variable (Table 5), the analysis suggested that prescription of antibiotics in this clinical situation was significantly associated to academic degree: DDS prescribed more frequently antibiotics in the fifth situation (i.e., NP with CAP; sinus tract present; no/mild pre-op symptoms) compared to MD ($p = 0.0080$; odds ratio = 8.0; C. I. 95% = 1.7 – 37.1). In fact, 18.7% and 65.2% of MD and DDS, respectively, prescribed antibiotics in the fifth clinical situation.

DISCUSSION

The survey instrument has historically been successful in obtaining pertinent information on the practice of general dentistry and endodontics. The population sampled in this study was Spanish dentists with preferential dedication to Oral Surgery. So, during the annual congress, the members of the Spanish Oral Surgery Society (SECIB) were randomly requested to answer the one-page questionnaire surveying about antibiotics use in the treatment of endodontic infections. The questions and the six endodontic treatment situations proposed were based on those asked in the previous surveys developed in USA (Whitten *et al.* 1996; Yingling *et al.* 2002) and Spain (Rodríguez-Núñez *et al.* 2009). Questions were designed to collect a variety of information relative to the types of antibiotics used and the prescribing habits of dentists with preferential dedication to Oral Surgery, as determined by age, gender, academic degree, post-graduate formation, and area of the country.

The overall response rate of 63.5% can be considered to be an acceptable rate of return for surveys. Other similar surveys published recently have reported

response rates of 31.1% (Rodríguez-Núñez *et al*. 2009), 35% (Lee *et al*. 2009), 41% (Creasy *et al*. 2009), 75% (Madarati *et al*. 2009), and 87% (Koch et al. 2009).

Antibiotic therapy is an important part of routine dentistry practice. Dentist use of antibiotics is characterized by a number of particularities. In effect, antibiotic prescription is empirical, i.e., the clinician does not know what microorganism is responsible for the infection, since pus or exudates cultures are not commonly made. Based on clinical and bacterial epidemiological data, the germs responsible for the infectious process are suspected, and treatment is decided on a presumptive and probabilistic basis. As a result of the above, broad spectrum antibiotics are typically prescribed.

In relation with antibiotic therapy, an infection must be persistent or systemic to justify the need for antibiotics: i.e. fever, swelling, lymphadenopathy, trismus, or malaise in a healthy patient (Yingling *et al*. 2002). Antibiotics are also more likely to be needed in an immunocompromised patient or a patient in poor health. The decision to prescribe antibiotics should not be influenced by patient demand, expectation of referring dentists, "just in case" situations, or because it is the day before a weekend or holiday. These reasons constitute inappropriate use of antibiotics. As it has been previously reported by Yingling *et al*. (2002), some respondents submitted comments that patients and referring general practitioners often "demand" antibiotics are prescribed for every endodontic scenario. These dentists 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 (Pallasch, 1993). The average length of antibiotic prescriptions in this study was 7.0 ± 1.0 days, in accordance with the result (6.8 days) reported previously by Rodríguez-Núñez *et al*. (2009) between Spanish endodontists. The proper dose and duration of an antibiotic is enough when there is sufficient evidence that the patient host defences have gained control of the infection. When the infection is resolving or has resolved, then the drug should be terminated (Pallasch, 1993; Yingling *et al*. 2002). 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 (Montgomery & Kroeger, 1984). Confusion about prescribing antibiotics and inappropriate prescribing practices, however, were reported by respondent dentists. The majority of endodontic infections resolve in three to seven days (Epstein *et al*. 2000) thus, the 18.0 percent of respondents who routinely prescribe antibiotics for more than seven days should reassess how they prescribe antibiotics.

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, azithromicyn, and the association metronidazole-spiramycin.

Traditionally, β-lactam antibiotics have been used as first-line therapy in odontogenic infections (Abu Fanas *et al*. 1991). In the present survey, amoxicillin, alone (33.97%) or associated to clavulanic acid (60.6%), was the most prescribed antibiotic for patients who were not allergic to penicillin, being used by 94.5% of respondents. 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 wasted, does have a much broader spectrum against the Gram negative cell wall, and is able to last a bit longer. However, studies suggest that amoxicillin antimicrobial activity against some bacteria involved in odontogenic infection is declining due to the increasing emergence of β-lactamase producing bacteria. Consequently, some authors consider the combination of a β-lactam antibiotic with a β-lactamase inhibitor, such as amoxicillin plus clavulanic acid, (Gilbert *et al*. 2003; Maestre Vera 2004). Amoxicillin/ clavulanic acid is an up-to-date first-line treatment option for odontogenic infections due to its wide spectrum, low incidence of resistance, pharmacokinetic profile, tolerance and dosage (Kuriyama et a. 2007; Stein et al. 2007). 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) (Llor *et al*. 2009). In this survey, amoxicillin associated to clavulanic acid was prescribed by 60.6% of respondents.

In a previous report on prescribing antibiotics habits between Spanish endodontists, amoxicillin alone, followed by amoxicillin associated to clavulanic acid, were the first choice antibiotic in patients without penicillin-allergies (Rodríguez-Núñez *et al*. 2009). Amoxicillin was also the principal antibiotic prescribed in dental clinic for both adult and child patients in other European countries (Tulip & Palmer, 2008) and in Kuwait (Salakoa *et al*. 2004). On the contrary, in Yemen (Al-Haroni & Skaug 2006) and in Norway penicillin is the first choice antibiotic in the treatment of endodontics infections, although there were only a few oral surgeons in the sample of this study (Demirbas *et al*. 2006). In USA, a similar feature can be seen. Amoxicillin was prescribed only by 27.5% of members of the American Association of Endodontists (AAE) (Yingling *et al*. 2002), who selected mainly penicillin VK as the first choice antibiotic (68.5%). Thus, penicillin VK is the principal antibiotic prescribed by dentist in USA (Whitten *et al*. 1996). 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. Penicillins are not predictive when used against endodontic diseases due to the composition of and resistance to antibiotics in bacterial biofilms adhering to the root canal surface (Mohammadi & Abbott, 2009).

In our study, the second prescribed antibiotic for nonpenicillin-allergic patients was clindamycin 300 mg (3.7%), in accordance with the study of Yingling *et al*. (2002). 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 (Wynn *et al*. 2001). Considering that clindamycin has a low but serious risk of pseudomembranous colitis (Jaimes 1991), 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.

Other antibiotics prescribed for non-allergic patients were azithromicyn 500 mg (1.6%) and metronidazole-spiramycin (0.8%). On the contrary, in the previous report of Rodríguez-Núñez *et al*. (2009), metronidazole-spiramycin was the second prescribed antibiotic in non-penicillin allergic patients (7.8%).

The first drug of choice for patients with an allergy to penicillins was clindamycin (65.4%), in accordance with the result previously found between Spanish endodontists (63.2%) (Rodríguez-Núñez *et al*. 2009). In the United States the study of Whitten *et al*. (1996) reported a 21.6% for clindamycin as first choice antibiotic, but a posterior study carried out by Yingling *et al*. (2002) found a percentage (57.03%) similar to that reported in the present study.

Other antibiotics prescribed for patients with an allergy to penicillins were metronidazole-spiramycin, erythromycin, lincomycin and azithromicyn. Erythromycin, a macrolide, has a similar spectrum of activity to that of penicillin. Is the first choice prescribed antibiotic for patients with an allergy to penicillins in Kuwait (Salakoa *et al*. 2004). Azithromycin is semisynthetic derivative of erythromycin that has been modified to create a broader spectrum of antibacterial activity and improved tissue penetration (Bahal & Nahata 1992). Metronidazole, prescribed in Spain an the United States as Flagyl® (Sanofi Aventis, S.A., Alcorcón, Madrid, Spain), is an antibiotic that is very effective against obligate anaerobes but not against facultative anaerobic bacteria. If amoxicillin is not effective after 2 to 3 days of use, then metronidazole has been recommended as a supplemental medication (AAE 1999). Metronidazole has excellent activity against anaerobes but no activity against aerobes and therefore requires to be used in conjunction with other agents (antimicrobial combination) for chemotherapy of oral infections. Spiramycin, a macrolide antibiotic used especially to treat toxoplasmosis, was chosen as a possibility because of its good activity against both aerobes and anaerobes and its pharmacokinetics was found to be suitable and could achieve high concentrations in alveolar bone and gingival tissue which exceeded serum levels. Moreover, the combination metronidazole-spiramycin is potentially synergic and appropriate for treatment of odontogenic abscesses (Roche & Yoshimori 1997). The combination of spiramycin and metronidazole is commonly used in Europe as well as in Canada and Mexico, but it is still considered an experimental drug in the United States, even though can sometimes be obtained by special permission from the FDA for toxoplasmosis

in the first trimester of pregnancy. In Spain, metronidazole-spiramycin (Rhodogyl®, Sanofi Aventis, S.A., Alcorcón, Madrid, Spain) is commonly used. Twenty three percent of Spanish endodontists selected metronidazole-spiramycin for penicillin-allergic patients (Rodríguez-Núñez *et al*. 2009). In the present study, metronidazole-spiramycin was prescribed by 13.5% of the respondents for patients with an allergy to penicillins.

Table 4 lists the percentage of respondents who prescribe antibiotics for various pulpal and periapical diagnoses. The majority of chronic or even acute dental infections can be successfully treated by eliminating the source of infection, pulp extirpation, drainage of abscess, or tooth extraction without the need for antibiotics. Exceptions are when there is evidence of systemic involvement and gross, rapid, and diffuse spread of infection (Al-Haroni M & Skaug 2006). 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 (Yingling *et al*. 2002).

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. Thirty one percent and 54.3% of the respondents prescribed antibiotics for the first and second situation, respectively. These pulps are still vital. There is no infection or signs of systemic involvement. Antibiotics are not indicated in either situation (Keenan *et al*. 2005). This number is similar to those reported by Dorn *et al.* (1977), Gatewood *et al*. (1990), Whitten *et al*. (1996), Yingling *et al*. (2002), Salakoa *et al*. (2004), Al-Haroni M & Skaug (2006), but is

almost twice than those found by Rodríguez-Núñez *et al*. (2009). Our findings indicate that the scientific basis for prescribing antimicrobial agents was neglected by the majority of the respondents.

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, but, in this survey 30.7% of respondents prescribed antibiotics. On the contrary, only 14.3% of Spanish endodontists prescribed antibiotics in such situation (Rodríguez-Núñez et al. 2009). However, in previous surveys developed in USA higher percentages have been reported (Whitten *et al*. 1996; Yingling *et al*. 2002). In the study developed in Yemen, a large proportion of the surveyed dentists (72%) indicated they would prescribe antimicrobial agents for treatment of chronic apical infections. These results indicate 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*. (1977), Gatewood *et al*. (1990); Slaus & Bottenberg 2002; Rodríguez-Núñez *et al*. (2009), Whitten *et al*. (1996), and Yingling *et al*. (2002) studies, which reported 30.0%, 33.1%, 48%, 52.9%, 53.9%, and 67.3% prescription for antibiotics respectively, this survey's result was 70.9% which, again is very high compared to all previous published studies. This again is over-usage of antibiotics.

The general tendency of respondents to over-prescribe antimicrobials for irreversible pulpitis and acute apical periodontitis may be motivated because, unfortunately, patients presenting with dental pain also routinely expect an antibiotics for the treatment of 'toothache'. It is difficult to explain to the patient, and occasionally their relatives, that dental pain is an inflammatory condition that is appropriately managed by use of analgesics and local measures and not a bacterial infection that requires provision of an antibiotic. The same problematic situation is frequently encountered in general medical practice, where patients with dental pain request the provision of an antibiotic. There is no doubt that achieving low prescribing rates will be a considerable challenge to the profession due to the pressure exhibited by patients expecting antibiotic therapy (Lewis, 2008).

Interestingly, 59.8% of respondents still prescribed antibiotics for asymptomatic cases of necrotic pulp, chronic apical periodontitis, and cases with sinus tracts (the fifth scenario). This result is more than twice of 21.4% in Rodríguez-Núñez *et al*. (2009) and five-times higher than results of 11.9% in Yingling *et al*. (2002). However, Whitten *et al*. (1996) reported that 47% of surveyed dentists prescribed antibiotics in this clinical situation. Unless there is a systemic involvement, management of uncomplicated abscesses is effective drainage and removal of the cause. Furthermore, clinical audits have shown that prescribing an antibiotic makes no difference to the outcome of treatment of acute dental infection if drainage is established (Lewis, 2008). Indicated treatment should consist of nonsurgical root canal therapy with analgesics if

needed for pain but no antibiotics. In majority of localized or diffuse odontogenic infection, removal of the course and/or drainage would usually lead to a complete resolution of the problem. However, in some situations, drainage or removable of the cause may not be feasible immediately. In such situations, and especially when there is an evidence of systemic involvement, antibiotic use can be instituted to prevent or limit local and metastatic spread of infection (Martin *et al.* 2000; Siqueira 2002). 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.

Logistic regression analysis indicated that in the fifth clinical situation, DDS prescribed more frequently antibiotics compared to MD (p = 0.0080; odds ratio = 8.0; C. I. 95% = 1.7 − 37.1). In fact, 18.7% and 65.2% of MD and DDS, respectively, prescribed antibiotics in the fifth clinical situation. In the study sample only 11.8% of surveyed dentists were MD. On the contrary, in the previous study carried out by Rodríguez-Núñez *et al*. (2009) between Spanish endodontists the proportion of MD in the sample was 37.1%. The different composition of the sample respect academic degree could explain the difference observed in the antibiotic prescription pattern in the fifth situation in that study (21.4%) respect to the present study (59.8%). Whitten *et al*. (1996) found significant differences between general dentists and endodontists in the antibiotics prescription pattern in several clinical situations, such as irreversible pulpitis with chronic apical periodontitis, no/mild preoperative symptoms; irreversible pulpitis with acute apical periodontitis, moderate/severe preoperative symptoms; and asymptomatic cases of necrotic pulp, chronic

apical periodontitis, and cases with sinus tracts. Significantly more general dentists respondents prescribed antibiotics in cases of irreversible pulpitis or when a draining sinus tract was present, conditions for which relatively few endodontists indicated antibiotic use. These results, together with the present results, may indicate that there is an overuse of antibiotics among general dentists and dentists with preferential dedication to Oral Surgery. A new consensus statement by Spanish specialists in microbiology and odontology is needed to establish useful recommendations in the clinical management an antibiotic use of endodontic infections.

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 (Dorn *et al*. 1977; Gatewood *et al*. 1990; Whitten *et al*. 1996; Yingling *et al*. 2002; Rodríguez-Núñez *et al*. 2009) ranged from 87.6% to 99.2%. The results of the present survey were comparable at 94.5% 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 (Yingling et al. 2002). The consensus statement on antimicrobial treatment of odontogenic bacterial infections published in 2004 (Bascones *et al*. 2004) stated that periapical abscess comprises a clear indication for debridement and surgical drainage complemented with systemic antibiotics.

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 SECIB 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 (AAE 1999). If it was because of insufficient training or fear of litigation, then this is clearly an inappropriate use of antibiotics (Yingling *et al*. 2002). Nonsurgical root canal therapy without antibiotics is usually adequate to treat cases of irreversible pulpitis, acute and chronic apical periodontitis, draining sinus tracts, and localized swellings. The pulpal circulation is compromised in these cases, and systemic antibiotics will not reach therapeutic concentrations in the pulp. Removing the source of the infection by performing nonsurgical root canal therapy will usually allow healing of any periradicular lesion or inflammation to occur. Analgesics are indicated for pulpitis pain and pain from periapical inflammation, not antibiotics (AAE 1999; Martin *et al.* 2000).

Antibiotic therapy is an art and a science (Yingling *et al*. 2002). There are so many confounding variables, such as suspected pathogen, ability to establish drainage, pharmacokinetic properties of the drug, mechanism of action of the antibiotic, virulence of the infection, the current health status of the host, and host defence mechanisms, that it is not possible to make antibiotic therapy into a mechanistic technological science (Pallasch 1986). The most important decision for the dental practitioner to make is not which antibiotic to use but whether to use one at all. Bascones *et al*. (2004) suggested that treatment should be provided in some acute situations of odontogenic infection of pulp

origin as a complement to root canal treatment. Poveda-Roda *et al*. (2007) are in accordance with this criterion.

The prevalence of apical periodontitis amongst the Spanish population is high (Jiménez-Pinzón *et al*. 2004). Nonsurgical root canal treatment is the treatment of choice. Moreover, most of endodontic situations are resolved by nonsurgical endodontics and accompanying incision and drainage procedures when indicated (Bascones *et al*. 2004). Spanish dentists must take into account that, when the decision is made to use an antibiotic, it is important to adhere to basic principles 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 (Pallasch, 1993).

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 (Lewis, 2008). 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.

REFERENCES

AAE (American Association of Endodontists) (1999) Prescription for the future. Responsible use of antibiotics in endodontic therapy. Accessed July 14, 2009. Available at: http://www.aae.org/NR/rdonlyres/9DE9C7C7-B50B-45DA-ABFF-244F2A5C290B/0/ss99ecfe.pdf.

Abu Fanas SH, Drucker DB, Hull PS (1991) Amoxycillin with clavulanic acid and tetracycline in periodontal therapy. *Journal of Dentistry*, **19**:97-9.

Al-Haroni M, Skaug N (2007) Incidence of antibiotic prescribing in dental practice in Norway and its contribution to national consumption. *Journal of Antimicrobial Chemotherapy*, **59:**1161–66.

Al-Haroni M, Skaug N (2006) Knowledge of prescribing antimicrobials among Yemeni general Dentists. *Acta Odontologica Scandinavica*, **64**:274-280.

Bahal N, Nahata MC (1992) The new macrolide antibiotics: azithromycin, clarithromycin, dirithromycin, and roxithromycin. *Annals of Pharmacotherapy,* **26**:46–55.

Bascones Martinez A, Aguirre Urizar JM, Bermejo Fenoll A, Blanco Carrion A, Gay-Escoda C, Gonzalez-Moles MA (2004). Consensus statement on antimicrobial treatment of odontogenic bacterial infections. *Medicina Oral Patología Oral Cirugía Bucal*, **9**:369-76.

Cars O, Molstad S, Melander A (2001) Variation in antibiotic use in the European Union. *Lancet,* **357**:1851-3.

Creasy JE, Mines P, Sweet M (2009) Surgical trends among endodontists: the results of a web-based survey. *Journal of Endodontics*, **35**:30-4.

Demirbas F, Gjermo PE, Preus HR (2006) Antibiotic prescribing practices among Norwegian dentists. *Acta Odontologica Scandinavica*, **64**:355-9

Dorn SO, Moodnik RM, Feldman MJ (1977) Treatment of the endodontic emergency: a report based on a questionnaire. Part I. *Journal of Endodontics*, **3**:94–100.

Epstein JB, Chong S, Le ND (2000) A survey of antibiotic use in dentistry. *Journal of the American Dental Association*, **131**:1600-9.

Frisk F, Hugoson A, Hakeberg M (2008) Technical quality of root fillings and periapical status in root filled teeth in Jönköping, Sweden. *International Endodontic Journal*, **41**:958-68.

Gatewood RS, Himel VT, Dorn SO (1990) Treatment of the endodontic emergency: a decade later. *Journal of Endodontics*, **16**:284–91.

Gilbert DN, Moellering RC, Sande MA (2003) Clinical approach to inicial choice of antimicrobial therapy. In: Gilbert DN, Moellering RC, Sande MA, eds. The Sanford Guide to antimicrobial therapy 2003. Hyde Park, VT: Antimicrobial Therapy Inc..

Gulsahi K, Gulsahi A, Ungor M, Genc Y (2008) Frequency of root-filled teeth and prevalence of apical periodontitis in an adult Turkish population. *International Endodontic Journal*, **41**:78-85.

Jaimes EC (1991) Lincocinamides and the incidence of antibiotic-associated colitis. *Clinical Therapeutics*, **13**:270–80.

Jiménez-Pinzón A, Segura-Egea JJ, Poyato M, Velasco E, Ríos JV (2004) Prevalence of apical periodontitis and frequency of root-filled teeth in an adult Spanish population. *International Endodontics Journal*, **37**:167-73.

Keenan JV, Farman AG, Fedorowicz Z, Newton JT (2005) Antibiotic use for irreversible pulpitis. *Cochrane Database Systematic Reviews*:CD004969.

Koch M, Eriksson HG, Axelsson S, Tegelberg A (2009) Effect of educational intervention on adoption of new endodontic technology by general dental practitioners: a questionnaire survey. *International Endodontic Journal*, **42**:313-21.

Kuriyama T, Williams DW, Yanagisawa M, Iwahara K, Shimizu C, Nakagawa K, Yamamoto E, Karasawa T (2007) Antimicrobial susceptibility of 800 anaerobic isolates from patients with dentoalveolar infection to 13 oral antibiotics. *Oral Microbiology and Immunology*, **22**:285-8.

Lee M, Winkler J, Hartwell G, Stewart J, Caine R (2009) Current trends in endodontic practice: emergency treatments and technological armamentarium. *Journal of Endodontics*, **35**:35-9.

Lewis MA (2008) Why we must reduce dental prescription of antibiotics: European Union Antibiotic Awareness Day. *British Dental Journal,* **205**: 537-8.

Llor C, Cots JM, Gaspar MJ, Alay M, Rams N (2009) Antibiotic prescribing over the last 16 years: fewer antibiotics but the spectrum is broadening. *European Journal of Clinical Microbiology and Infectious Diseases,* **28**:893-7.

Maestre Vera JR (2004) Therapeutic options in the odontogenic infection. *Medicina Oral Patología Oral Cirugía Bucal*, **9** Suppl:S19-31.

Madarati AA, Watts DC, Qualtrough AJ (2009) Opinions and attitudes of endodontists and general dental practitioners in the UK towards the intra-canal fracture of endodontic instruments. Part 2. *International Endodontic Journal*, **41**:1079-87.

Martin MV, Longman LP, Palmer NAO (2000) Adult antimicrobial prescribing in primary dental care for general dental practitioners. Faculty of general dental practitioners, UK: *The Royal College of Surgeons of England*.

Mohammadi Z, Abbott PV (2009) The properties and applications of chlorhexidine in endodontics. *International Endodontic Journal*, **42**:288-302.

Montgomery EH, Kroeger DC (1984) Use of antibiotics in dental practice. *Dental Clinics of North America*, 2**8**:433–53.

Pallasch TJ (1986) Antibiotic myths and reality. *Journal of Californian Dental Association*, **14**: 40–5.

Pallasch TJ (1993) How to use antibiotics effectively. *Journal of the Californian Dental Association*, **21**:46–50.

Pallasch TJ (2000) Global antibiotic resistance and its impact on the dental community. *Journal of Californian Dental Association*, **28**:215–33.

Poveda-Roda R, Bagán JV, Sanchis-Bielsa JM, Carbonell-Pastor E (2007) Antibiotic use in dental practice. A review. *Medicina Oral Patología Oral Cirugía Bucal*, **12**:E186-92.

Roche Y, Yoshimori RN (1997) In-vitro activity of spiramycin and metronidazole alone or in combination against clinical isolates from odontogenic abscesses. *Journal of Antimicrobial Chemotherapy*, **40**:353-7.

Rodriguez-Núñez A, Cisneros-Cabello R, Velasco-Ortega E, Llamas-Carreras JM, Tórres-Lagares D, Segura-Egea JJ (2009) Antibiotic use by members of the Spanish Endodontic Society. *Journal of Endodontics*, **35**:1198-203

Salakoa NO, Rotimib VO, Adibb, Al-Mutawac S (2004) Pattern of antibiotic prescription in the management of oral diseases among dentists in Kuwait. *Journal of Dentistry*, **32**:503–9.

Sancho-Puchades M, Herráez-Vilas JM, Valmaseda-Castellón E, Berini-Aytés L, Gay-Escoda C (2009) Analysis of the antibiotic prophylaxis prescribed by Spanish Oral Surgeons. *Medicina Oral Patología Oral Cirugía Bucal* **14**:E533-7,

Segura-Egea JJ, Jiménez-Pinzón A, Ríos-Santos JV, Velasco-Ortega E, Cisneros-Cabello R, Poyato-Ferrera M (2005) High prevalence of apical periodontitis amongst type 2 diabetic patients. *International Endodontic Journal*, **38**:564–69.

Segura-Egea JJ, Jiménez-Pinzón A, Ríos-Santos JV, Velasco-Ortega E, Cisneros-Cabello R, Poyato-Ferrera MM (2008) High prevalence of apical periodontitis amongst smokers in a sample of Spanish adults. *International Endodontic Journal*, **41**:310–16.

Siqueira JF (2002) Endodontic infections: Concepts, paradigms, and perspectives. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics*, **94**:281-93.

Siqueira JF Jr, Rôças IN (2004) Exploiting molecular methods to explore endodontic Infections: Part 2 - Redefining the endodontic microbiota. *Journal of Endodontics*, **31**:488-496.

Slaus G, Bottenberg P (2002) A survey of endodontic practice amongst Flemish dentists. *International Endodontic Journal*, **35**:759-67.

Tulip DE, Palmer NO (2008) A retrospective investigation of the clinical management of patients attending an out of hours dental clinic in Merseyside under the new NHS dental contract. *British Dental Journal*, **205**:659-64; discussion 648.

Stein GE, Schooley S, Tyrrell KL, Citron DM, Goldstein EJ (2007) Human serum activity of telithromycin, azithromycin and amoxicillin/clavulanate against common aerobic and anaerobic respiratory pathogens. *International Journal of Antimicrobial Agents*, **29**:39-43.

Whitten BH, Gardiner DL, Jeannsonne BG, Lemon RR (1996) Current trends in endodontic treatment: report of a national survey. *Journal of the American Dental Association*, **127**:1333–41.

Wynn RL, Meiller TF, Crossley HL. (2001) Drug information handbook for dentistry. 6th ed. Hudson: Lexi-Comp, Inc.

Yingling NM, Byrne BE, Hartwell GR (2002) Antibiotic use by members of the American Association of Endodontists in the year 2000: report of a national survey. *Journal of Endodontics*, **28**:396-404.

FIGURE LEGENDS

Figure 1. Antibiotic survey.

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

Figure 3. Distribution of respondents by treatment duration.

FIGURE 1

ANTIBIOTIC SURVEY

PROVINCE:_____

GENDER: Male ☐   Female ☐

AGE (ys):   25-35 ☐   36-45 ☐   46-55 ☐   56-65 ☐

ACADEMIC DEGREE: MD (Stomatologist) ☐   DDS ☐   MD & DDS ☐

POSTGRADUATE FORMATION: Master in Endodontics ☐   Master in Oral Surgery ☐   ☐
Other

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?:**

- Clindamycin (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 ☐
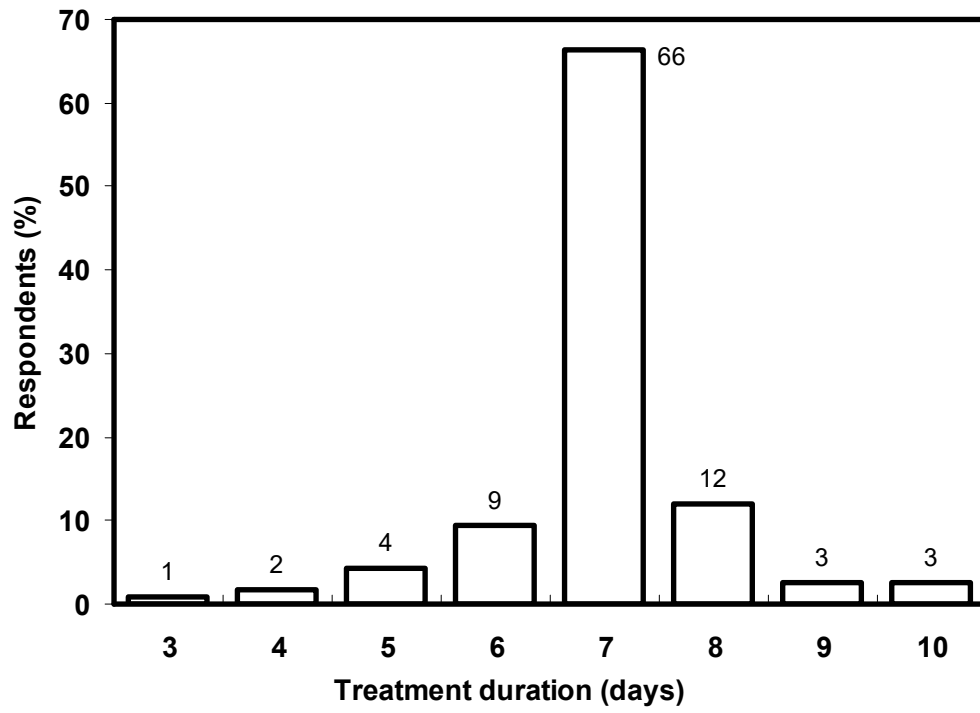
Thank you for your collaboration.

FIGURE 2
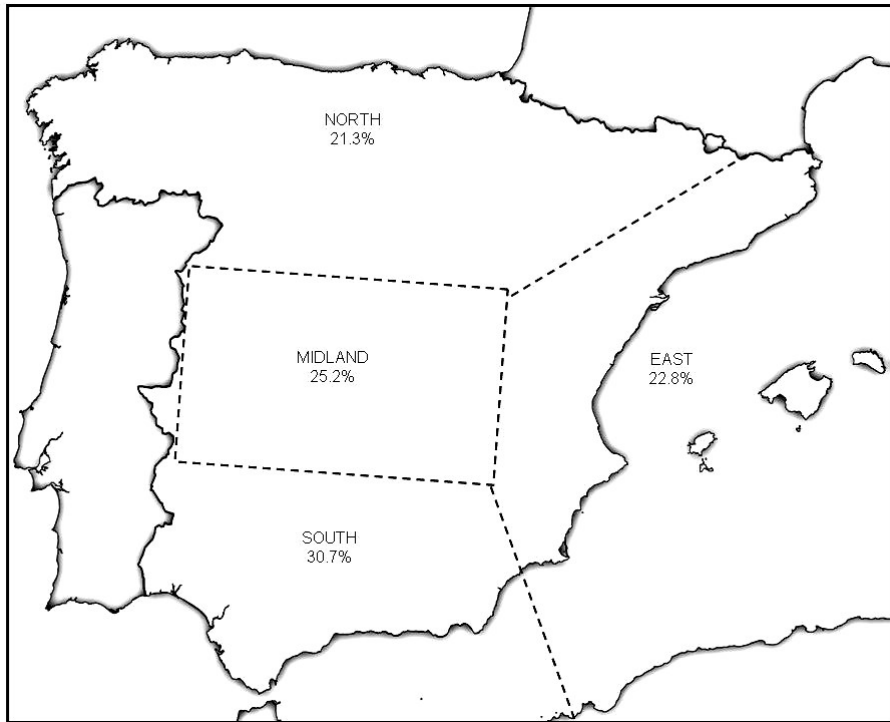
FIGURE 3

TABLES

Table 1. Description of respondents

Gender		
	Male	48.8 %
	Female	51.2 %
Age (yr)		
	25 - 35	75.6 %
	36 - 45	13.4 %
	46 - 55	9.4 %
	56 - 65	1.6 %
Mean age (yr)		33.7 $\pm$ 6.3
Academic degree		
	DDS	88.2%
	MD (stomatologist)	7.9%
	MD + DDS	3.9%
Postgraduate formation		
	In Oral Surgery	46.5%
	In Endodontics	3.1%
	Both Endodontics and Surgery	1.6%
	Other	13.4%
	No postgraduate formation	35.4%

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

Antibiotic		%
Amoxicillin	500 mg	8.7
	750 mg	18.1
	1000 mg	7.1
Amoxicillin / Clavulanic acid	250 / 62.5 mg	3.9
	500 / 125 mg	15.0
	875 / 125 mg	41.7
Metronidazole / Spiramicyn	125 mg / 750.000 UI	0.8
Clindamicyn	300 mg	3.1
Azithromicyn	500 mg	1.6
Other		1.3

Table 3. Antibiotic preference in patients with medical allergies.

Antibiotic		%
Clindamicyn	300 mg	65.4
Metronidazole / Spiramicyn	125 mg / 750.000 UI	13.4
Erythromicyn	500 mg	4.7
Lincomicyn	500 mg	1.6
Azithromicyn	250 mg	0.8
	500 mg	11.8
	1.000 mg	2.4

Table 4. Situation in which antibiotic were prescribed.

Situation	Prescribe antibiotics (%)
IP; mod/severe pre-op symptoms	31.5
IP with AAP; mod/severe pre-op symptoms	54.3
NP with CAP; no swelling, no/mild pre-op symptoms	30.7
NP with AAP; no swelling, mod/severe pre-op symptoms	70.9
NP with CAP; sinus tract present; no/mild pre-op symptoms	59.8
NP with AAP; swelling present; mod/severe pre-op symptoms	94.5

IP: Irreversible Pulpitis.
NP: Necrotic Pulp.
AAP: Acute Apical Periodontitis.
CAP: Chronic Apical Periodontitis.

Table 5. Multivariate logistic regression analysis of the influence of the independent variables gender (0 = female; 1 = male), age (0 ≥ 35 yrs; 1 = < 35 yrs), post-graduate formation (0 = no formation; 1 = training in oral surgery), and academic degree (0 = MD; 1 = DDS), on the dependent variable "antibiotics prescription in the fifth situation" (0 = no; 1 = yes).

Independent variables	B	*p*	Odds Ratio	C. I. 95% Inf. Limit	C. I. 95% Sup. Limit.
Gender	- 0.2447	0.5285	0.7830	0.3659	1.6756
Age	- 0.2360	0.6618	0.7898	0.2744	2.2736
Postgraduate formation	0.3768	0.3259	1.4576	0.6874	3.0910
Academic degree	2.0772	0.0080	7.9820	1.7191	37.0618