Pattern of antibiotic prescription in the management of endodontic infections amongst Spanish oral surgeons

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Abstract


Aim To identify antibiotic prescription practices in the treatment of endodontic infections amongst Spanish oral surgeons.

Methodology 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 with 127 returned (64%).

Results The average duration of antibiotic therapy was 7.0 ± 1.0 days. Ninety five percent of respondents selected amoxicillin as the first choice antibiotic in patients with no medical allergies, alone (34%) or associated to clavulanate (61%). The first drug of choice for patients with an allergy to penicillins was clindamycin 300 mg (65%), followed by azithromycin (15%) and metronidazole-spiramycin (13%). For cases of irreversible pulpitis, 86% of respondents prescribed antibiotics. For the scenario of a necrotic pulp, acute apical periodontitis and no swelling, 71% prescribed antibiotics. Almost 60% of respondents prescribed antibiotics for necrotic pulps with chronic apical periodontitis and a sinus tract in this clinical situation, odontologists prescribed more frequently antibiotics compared to stomatologists (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.

Keywords: apical periodontitis, endodontic infections, irreversible pulpitis, orofacial infections, pharmacology.

Received 2 November 2009; accepted 15 December 2009

Introduction

Odontogenic infections, especially endodontic infections, are prevalent in Spain (Jiménez-Pinzón et al. 2004, Segura-Egea et al. 2005, 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 & Roças 2004). Thus, antibiotics, with analgesics, account for the vast majority of medicines prescribed by dentists. Al-Haroni & Skaug (2007) analysed 268 834 prescriptions issued by 4765 dentists and showed that the dentists’ prescriptions of antibiotics contributed 8% of the total national consumption in Norway. In 2004, a survey of over 6000 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 analysed the antibiotics prescribing habits of dentists showing that over prescription can occurs. 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. Amongst 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. 2001). 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 Martinez et al. 2004).

Recently, Rodriguez-Núñez et al. (2009) have reported that, with regards to irreversible pulpits and necrotic pulps with no systemic involvement, Spanish endodontists were overprescribing antibiotics. Odontogenic infections must be treated not only by endodontists but also by general dentists and oral surgeons. In Spain, oral surgery is not a specialty. However, some dentists have preferential, even exclusive, dedication to oral surgery in their professional practice. The majority of these dentists are the members of the Spanish Oral Surgery Society (SECIB). The purpose of this study was to identify the pattern of antibiotic prescription in the treatment of endodontic infections amongst Spanish oral surgeons.

Methodology

During the VII Congress of the Spanish Oral Surgery Society held in 2009, members were randomly selected and requested to answer a one-page questionnaire (Fig. 1) surveying about antibiotic use in the treatment of endodontic infections. The questions were based on those asked in previous surveys developed in the USA (Whitten et al. 1996, Yingling et al. 2002) and Spain (Rodriguez-Núñez et al. 2009). Two hundred questionnaires were delivered to the members of the Spanish Oral Surgery Society. Only 127 questionnaires were returned completed (64%).

In Spain, from 1948 to 1986, dentist status was obtained after complete training in Medicine and then in the speciality of Stomatology. Stomatologists were (are) medical doctors (MD) with the speciality of Stomatology. Actually, both stomatologists (MD), odontologists (DDS), and medical doctor trained in odontology (MD + DDS) are dentists in Spain. So, in the survey (Fig. 1), ‘academic degree’ was classified in three categories: DDS (odontologist), MD (stomatologist), and medical doctor and odontologist (MD + DDS).

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 analysed 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 <36 years old and 11% more than 45 years old. The mean age of the respondents was 34 years. The most frequent academic degree was DDS 88.2%. Stomatologist, medical doctor specialized in stomatology, represented 8% of total. Only 4% of the
respondents were both MD and DDS. In relation to post-graduate formation, 47% of the respondents had completed post-graduate 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 amongst respondents in relation with age, gender, academic degree, post-graduate formation, nor region (\( P > 0.05 \)).

Most of respondents (95%) chose amoxicillin in non-allergic-patients (Table 2), alone (40%) or associated to clavulanic acid (61%). Amoxicillin/Clavulanic acid 875/125 mg was prescribed as first choice antibiotic by 42% of respondents, whereas 18%, 9%, 3% and 1% 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%), followed by azithromycyn (15%) and metronidazole-spiramycin (13%) (Table 3).

Table 4 lists the percentage of respondents who prescribed antibiotics for various pulpal and periapical diagnoses. For cases of irreversible pulps with moderate/severe symptoms and irreversible pulps with acute apical periodontitis and moderate/severe symptoms, 32% and 54% of respondents, respectively, prescribed antibiotics. In cases of a necrotic pulp, chronic apical periodontitis, no swelling and no other symptoms, antibiotics were prescribed by 31%. In the scenario of necrotic pulp, acute apical periodontitis, moderate/severe symptoms but no swelling, 71%
prescribed antibiotics. For a case of necrotic pulp, chronic apical periodontitis, asymptomatic but with a sinus tract, 60% prescribe antibiotics. In the case of a necrotic pulp, acute apical periodontitis, swelling and other moderate/severe symptoms, 95% of respondents prescribed antibiotics.

There were no significant differences amongst 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, multivariate logistic regression analyses were carried out 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 or explanatory factors.
dichotomized variables and the dependent variable ‘antibiotics prescription in the fifth clinical situation’ (i.e. Necrotic Pulp (NP) with Chronic Apical Periodontitis (CAP); sinus tract present; no/mild pre-op symptoms) with the values 0 = absent, 1 = present (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 clinical situation compared to MD ($P = 0.0080$; odds ratio $= 8.0$; C. I. 95% $= 1.7–37.1$).

**Discussion**

In our study, the questions and the six endodontic treatment situations proposed were based on those asked in previous surveys developed in the USA (Whitten et al. 1996, Yingling et al. 2002) and Spain (Rodriguez-Núñez et al. 2009). The overall response rate of 64% can be considered to be an acceptable rate of return for surveys.

In relation with antibiotic therapy, an endodontic 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). Endodontic infections typically have a rapid onset and short duration, 2–7 days or less, particularly if the cause is treated or eliminated (Pallasch 1993). The average length of antibiotic prescriptions in this study was $7.0 \pm 1.0$ days, in accordance with the result (6.8 days) reported previously by Rodríguez-Núñez et al. (2009) amongst Spanish endodontists. The proper dose and duration of an antibiotic are 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 3–7 days (Epstein et al. 2000); thus, the 18.0% of respondents who routinely prescribe antibiotics for more than 7 days should reassess how they prescribe antibiotics.

Traditionally, $\beta$-lactam antibiotics have been used as first-line therapy in odontogenic infections (Abu Fanas et al. 1991). In our survey, amoxicillin, alone (34%) or associated to clavulanic acid (61%), was the most prescribed antibiotic for patients who were not allergic to penicillin, being used by 95% of respondents. Amoxicillin is a moderate-spectrum, bacteriolytic, $\beta$-lactam antibiotic that represents a synthetic improvement upon the original penicillin molecule. Amoxicillin

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

IP, irreversible pulpitis; NP, necrotic pulp; AAP, acute apical periodontitis; CAP, chronic apical periodontitis.

Table 4 Clinical situations in which antibiotics were prescribed

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>B</th>
<th>P</th>
<th>Odds Ratio</th>
<th>C. I. 95% Inf. Limit</th>
<th>C. I. 95% Sup. Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>-0.2447</td>
<td>0.5285</td>
<td>0.7830</td>
<td>0.3659</td>
<td>1.6756</td>
</tr>
<tr>
<td>Age</td>
<td>-0.2360</td>
<td>0.6618</td>
<td>0.7998</td>
<td>0.2744</td>
<td>2.2736</td>
</tr>
<tr>
<td>Post-graduate formation</td>
<td>0.3768</td>
<td>0.3259</td>
<td>1.4576</td>
<td>0.6874</td>
<td>3.0910</td>
</tr>
<tr>
<td>Academic degree</td>
<td>2.0772</td>
<td>0.0080</td>
<td>7.9820</td>
<td>1.7191</td>
<td>37.0618</td>
</tr>
</tbody>
</table>

Table 5 Multivariate logistic regression analysis of the influence of the independent variables: gender (0 = female; 1 = male), age (0 $\geq$ 35 years; 1 $<$ 35 years), 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)
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 longer. However, studies suggest that amoxicillin antimicrobial activity against some bacteria involved in odontogenic infection is declining as a result of the increasing emergence of β-lactamase producing bacteria. Consequently, some 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 a first-line treatment option for odontogenic infections because of its wide spectrum, low incidence of resistance, pharmacokinetic profile, tolerance and dosage (Kuriyama et al. 2007, Stein et al. 2007). In Spain, the leading antibiotic prescribed in 2007 was amoxicillin plus clavulanic acid (5.15 DID) (DID: defined daily dose per 1000 inhabitants and day) followed by amoxicillin alone (2.95 DID) (LLor et al. 2009). In this survey, amoxicillin associated to clavulanic acid was prescribed by 61% of respondents.

In a previous report on prescribing antibiotic habits amongst Spanish endodontists, amoxicillin alone, followed by amoxicillin associated to clavulanic acid, was 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 (Salako 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 that study (Demirbas et al. 2006). In USA, a similar feature can be seen. Amoxicillin was prescribed only by 28% of members of the American Association of Endodontists (AAE) (Yingling et al. 2002) who selected mainly penicillin VK as the first choice antibiotic (69%). 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 because of the composition of and resistance to antibiotics in bacterial biofilms adhering to the root canal surface (Mohammadi & Abbott 2009).

In this study, the second prescribed antibiotic for non-penicillin-allergic patients was clindamycin 300 mg (34%), 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 150–450 mg, four times a day for orofacial infections (Wynn et al. 2001).

Other antibiotics prescribed for non-allergic patients were azithromycin 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%), in accordance with the result previously found amongst Spanish endodontists (63%) (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 the study carried out by Yingling et al. (2002) found a percentage (57.03%) similar to that reported in this study.

Other antibiotics prescribed for patients with an allergy to penicillins were metronidazole-spiramycin, erythromycin, lincomycin and azithromycin. 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? (Salako 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 and at the United States as Flagyl® (Sanofi Aventis, S.A., Alcorcón, Madrid, Spain), is an antibiotic that is effective against obligate anaerobes but not against facultative anaerobic bacteria. If amoxicillin is not effective after 2–3 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 of metronidazole-spiramycin is potentially synergic and appropriate for treatment of odontogenic abscesses (Roche & Yoshimori 1997). 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 our study, metronidazole-spiramycin was prescribed by 14% 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 & 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 the 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% 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). The 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. In a healthy patient, there is no indication for antibiotic use and treatment should be limited to nonsurgical root canal treatment, but, in this survey 31% of respondents prescribed antibiotics. On the contrary, only 14.3% of Spanish endodontists prescribed antibiotics in such situation (Rodríguez-Núñez et al. 2009).

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. This survey’s result was 71% that again is very high compared to all previous published studies. This again is over-usage of antibiotics.

Interestingly, 60% of respondents still prescribed antibiotics for asymptomatic cases of necrotic pulp, chronic apical periodontitis and cases with sinus tracts (the fifth scenario). Unless there is a systemic involvement, management of uncomplicated abscesses is effective drainage and removal of the cause. However, 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 (Dorn et al. 1977, Gatewood et al. 1990, Whitten et al. 1996, Yingling et al. 2002, Rodriguez-Núñez et al. 2009) ranged from 87% to 99%. The results of our survey were comparable at 95% 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 interesting point in this survey is that, with regards to irreversible pulpitis, necrotic pulps with no systemic involvement and sinus tracts, Spanish oral surgeons are over-prescribing. It is important that not only the dental profession but also 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


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