# Antibiotic prescribing for endodontic infections: a survey of dental students in Italy

## M. Salvadori<sup>1</sup> (1), E. Audino<sup>1</sup>, G. Venturi<sup>1</sup>, M. L. Garo<sup>2</sup> & S. Salgarello<sup>1</sup>

<sup>1</sup>Department of Medical and Surgery Specialties, Radiological Sciences and Public Health, School of Dentistry, Brescia University, Brescia, Italy; and <sup>2</sup>Independent researcher, Brescia, Italy

### Abstract

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**Aim** To determine the knowledge of final year undergraduate students attending Italian universities on the appropriate use of systemic antibiotics for endodontic infections.

**Methodology** Final year dental students from twenty Italian universities completed a one-page questionnaire on antibiotic use for the treatment of endodontic infections. Data were analysed using descriptive statistics and chi-square tests.

**Results** A total of three hundred and three students completed the questionnaire. The average duration of antibiotic prescription proposed by respondents was  $5.48 \pm 1.06$  days. Amoxicillin with clavulanic acid was the first-choice antibiotic (85.2%) followed by amoxicillin alone (13.5%), azithromycin (1.0%) and clarithromycin (0.3%), for patients not allergic to

penicillin. Clarithromycin was the first-choice drug for patients with a penicillin allergy (56.1%), followed from azithromycin (31.7%), clindamycin (11.9%) and levofloxacin (0.3%). Alveolar abscess with systemic manifestations was reported as the principal reason to prescribe antibiotics (97.7%) followed by the same condition without systemic manifestations (85.5%). For the scenario of irreversible pulpitis, 5% of students considered antibiotics necessary. Almost 52% of students would prescribe antibiotics for apical acute periodontitis; 29.7% would prescribe antibiotics for chronic apical periodontitis with sinus tract, and 13.5% indicated these drugs for chronic apical periodontitis without sinus tract.

**Conclusions** The results demonstrate that it is necessary to improve the knowledge of Italian students on antibiotics and indications for their use in endodontics.

**Keywords:** antibiotics, dental students survey, endodontic infections.

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## Introduction

Although antimicrobial resistance (AMR), one of the principal threats to global public health, is a natural phenomenon, the inappropriate use of antibiotics in humans and animals has accelerated the process with widespread and devastating consequences (WHO 2014). AMR increases mortality and morbidity with substantial socioeconomic consequences. In 2007 within Europe alone, there were an estimated 400 000 infections and 25 000 deaths due to the most frequent multidrug-resistant bacteria (Prestinaci *et al.* 2015). If no action is taken, it is estimated that drug-resistant infections will kill 10 million people a year by 2050. AMR threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi that are no longer susceptible to the common medicines used to treat them. As healthcare professionals, it is our duty to reassess use of antibiotics in our daily practice.

Correspondence: Matteo Salvadori, Department of Medical and Surgery Specialties, Radiological Sciences and Public Health, School of Dentistry, Brescia University, Via Cerreto Basso 2, Bagolino (25072), Brescia, Italy (Tel.: 3388516676; e-mail: salvaz.dori@gmail.com).

A significant proportion of antibiotics are prescribed by dentistry for treatment of minor infections: this practice plays a noteworthy contributing factor in selection of resistance (Pallasch 2000, AAE 2012, Ajantha & Hegde 2012, Oberoi et al. 2015). Although dental undergraduates are taught that most oral infections may be treated by surgical or chemo-mechanical means without the use of antibiotics, there is growing concern about AMR in dental practice. The inappropriate or misuse of antibiotics in endodontics is the subject of much debate not only in Europe but also in the global scientific community (Mainjot et al. 2009, Rodriguez-Núñez et al. 2009, Segura-Egea et al. 2010, 2017a,b, Perić et al. 2015, AlRahabi & Abuong 2017, Germack et al. 2017, Bolfoni et al. 2018). The general consensus worldwide is that the widespread prescription of antimicrobials in the treatment of certain endodontic diseases is not appropriate. Evidence to date demonstrates that the routine prescription of antibiotics to prevent infection/pain is to be discouraged unless the patient is symptomatic/ immunocompromised (Cope et al. 2014, Aminoshariae & Kulild 2016, Segura-Egea et al. 2017a), whilst in certain conditions such as pulpits, periodontitis, and acute local apical abscesses, the use of the antibiotic is positively discouraged. (Fouad et al. 1996, Nagle et al. 2000, Agnihotry et al. 2016). The ESE position statement (ESE 2018) provide dentists with evidence-based criteria for when to use antibiotics in the treatment of endodontic infections, traumatic injuries of the teeth, revascularization procedures in immature teeth with pulp necrosis, and in prophylaxis for medically compromised patient. Dentists have a range of local procedures they can employ to control pain including pulpotomy, pulpectomy, root canal treatment, surgical incision and orthograde drainage or extraction as well as prescription of analgesics. ESE guidelines (ESE 2013) recommend that dental undergraduates should receive training in microbiology and about the mechanisms involved in AMR, as well as in immunology and pain management. They should also receive training in effective infection control in root canal interventions and how to tackle endodontic emergencies such as reversible/irreversible symptomatic pulpitis, symptomatic apical periodontitis and acute apical abscess.

A study conducted in four universities in Spain (Barcelona, Seville, Santiago de Compostela and Zaragoza) (Martín-Jiménez *et al.* 2018) concluded that whilst the majority of students were aware of the correct management of endodontic infections, others still displayed an inappropriate use of antibiotics. Of particular note was the proposed use of antibiotics in certain situations such as irreversible pulpitis, apical periodontitis, and use of antibiotic therapy for longer than 7 days. The authors concluded that the undergraduate curriculum should provide more focus on good prescribing practices, in particular on the identification and treatment of dental conditions that can be managed without antibiotics. Similarly, Al Masan et al. (2018) evaluated the views of final year dental surgery students at Cardiff University and general dental practitioners within the geographical area of Cardiff, Wales, UK. Results showed that final year dental undergraduates were aware of the antibiotic resistance crisis but around a third of respondents were not aware of guidelines for use of antibiotics in endodontic conditions. Dental undergraduates were more likely than general dental practitioners to prescribe antibiotics for cases of necrotic pulp with symptomatic apical periodontitis without systemic complications and less likely for other clinical scenarios such as necrotic pulp and asymptomatic apical periodontitis for patients with a history of rheumatic fever, symptomatic irreversible/reversible pulpitis, failure to achieve anaesthesia, chronic apical abscess for patients with diabetes.

To date, there are no corresponding data from Italian universities. In Italy, dental students, by the end of the fifth year of their undergraduate course, have already addressed the problem of AMR caused by inappropriate/over use of antibiotics and how to effectively manage endodontic infections. Therefore, the present study was designed to determine the knowledge of undergraduate students in the final year of their dentistry course (sixth year) on the use of systemic antibiotics in endodontic infections.

## **Materials and methods**

The first stage in the study was to translate and adapt the one-page questionnaire used in the Spanish study to the Italian clinical situation (Table 1) (Martín-Jiménez *et al.* 2018). The questionnaire was administered to dental students in the sixth and final year of their undergraduate course in a range of universities throughout Italy. To better determine the knowledge of dentistry students in Italy on the appropriate use of antibiotics and given the historical geographical differences that typify the Italian peninsula, respondents were identified both in relation to their university campus and the geographical area (North, Centre and Mezzogiorno). A professor/tutor from each university

Table	<b>1</b> Antibiotic	use in	endodontic	infections question-	
naire	administered	to final	year denta	l undergraduates in	
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Gender:	Male 🗆	Female 🗆
Age:		
Dental school:		

1) When systemic antibiotics are indicated, which antibiotic would you choose for the treatment of an endodontic infection in an adult, healthy patient with no medical allergies? (only one answer): Amoxicillin 500 mg □ 1 g 🗆 Amoxicillin + Clavulanic Acid 1 g 🗆 \_\_ 🗆 \_\_ 🗆 Azithromycin 500 mg 🗆 500 mg 🗆 \_\_ 🗆 Clarithromycin Clindamycin 300 mg □ \_\_ 🗆

2) For how many days would you prescribe antibiotics?:

3) When systemic antibiotics are indicated, which antibiotic would you choose for the treatment of an endodontic infection in an adult, healthy patient with allergy to parisilling (only one approximate)

penicillin? (only one answer):		
Azithromycin	500 mg 🗆	🗆
Clarithromycin	500 mg 🗆	🗆
Clindamycin	300 mg 🗆	🗆
Other:		

4) In which of the following situations do you consider that antibiotics are indicated? Check all that apply:

Irreversible pulpitis	
Apical acute periodontitis	
Chronic apical periodontitis without sinus	
Chronic apical periodontitis with sinus tract $\Box$	
Acute apical abscess without systemic involvement	
Acute apical abscess with systemic involvement (body temperature >38°, malaise, localized fluctuant swellings, lymphadenopathy)	

dental school administered the questionnaire to students attending regular classes during one specific day and students who were absent from class that day were not included in the study. The respondents' participation was voluntary, anonymous and without any form of remuneration. Administration of the survey and collection of completed questionnaires was carried out over a period of 3 months (from November 2017 to January 2018). Questionnaires received after these dates were not included in the statistical analysis.

Data were collected in an Excel file (Microsoft Corp., Redmond, WA, USA) and analysed using STATA15 software (Stat Corp., College Station, TX, USA). Descriptive statistics were first performed to identify the correct sample composition in relation to gender and age. Frequency distributions were created to describe percentages of responds regarding the use of antibiotics and the cases where respondents considered that the use of antibiotic(s) was appropriate. Statistical significances of these frequency distributions were also analysed using chi-square tests, whilst quantitative data were analysed using *U*-Mann-Whitney test, given the non-normal distribution of the data. The statistical significance was set at 5% (P < 0.05), and the power sample was examined using the chi-square likelihood-ratio.

#### Results

In total, 399 students from 20 universities were enrolled and 303 (76%) completed the questionnaire and were eligible for analysis. Overall, 51.7% of respondents were male (n = 154) and 48.3% female (n = 144). The respondents' mean age was 25.02 years (SD  $\pm$  2.65 years, median = 24 years) (Table 2). The largest number of respondents were from the University of Turin (13.86%, n = 42), followed by the University of Catania (7.6%, n = 23) (Fig. 1).

Considering the three geographical areas, 46.5% of respondents attended a university in northern Italy (n = 141), 31% a university in the Mezzogiorno (n = 94), and 22.4% a university in central Italy (n = 68).

#### Prescription and duration of antibiotics

The average duration of antibiotic prescriptions proposed by respondents was  $5.48 \pm 1.06$  days and about half (50.5%) indicated a duration of 6 days. Students in northern Italy indicated a longer period of medication (6 days) compared to their counterparts in the South (5 days). This comparison was characterized by a statistical significance at the 5% level (P = 0.001). To better measure the appropriate use of antibiotics by Italian students, a qualitative variable

Table 2	Description	of respondents	(n =	303)
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$\mathbf{C}$ and $\mathbf{r}$ (0())			
Gender (%)			
Male	154 (51.7)		
Female	144 (48.3)		
Mean age $\pm$ SD (years)	$25.02\pm2.65$		
Geographical area			
North	141 (46.5)		
Centre	68 (22.4)		
Mezzogiorno	94 (31.0)		

Other:

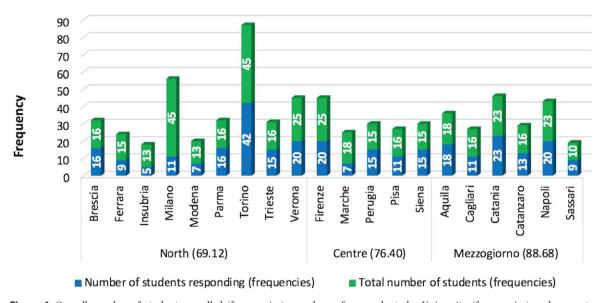


Figure 1 Overall number of students enrolled (frequencies), numbers of respondents by University (frequencies) and percentages of respondents by geographical area in relation to students enrolled.

was created using previous data, called 'range days'. From this analysis 99% of students indicated a treatment duration of 3–7 days. No significant differences were detected for this variable in relation to the three geographical areas: the majority of students indicated the range of 3–7 days (Table 3).

#### Indications for use of antibiotics

Overall 97.7% (n = 296) and 85.5% (n = 259) of students would prescribe antibiotics in cases of alveolar abscess with or without systemic manifestations, respectively (Table 3). In patients with chronic apical periodontitis with sinus tract, 29.7% of students indicated the possible use of antibiotics, whilst a smaller percentage (13.5%) of respondents considered

antibiotic treatment was appropriate to treat chronic apical periodontitis without sinus tract. In cases of pulpitis, only 5% of students indicated the appropriateness of an antibiotic prescription. Observing these values in light of the three geographical areas, alveolar abscess without systemic manifestation was indicated mainly from the northern students (93.6%, n = 132), and to a lesser extent from the southern students (78.7%) and the respondents in the Centre (77.9%) (P = 0.001).

With reference to chronic apical periodontitis with sinus tract, there was a significant difference (P = 0.000) between students from the Mezzogiorno, who were more inclined to prescribe antibiotics (45.7%), and other students (19.9% of northern students, and 27.9% of students from the Centre), less

**Table 3** Duration of antibiotic prescription and therapeutic conditions where use of antibiotics was indicated (results expressed in % of geographical area, likelihood chi-square ratio)

Duration of therapy (days)	North, <i>n</i> = 141	Centre, $n = 68$	Mezzogiorno, $n = 94$	Total	Ρ
<3	0	0	1.1	0.3	-
3–7	100.0	100.0	96.8	99.0	-
>7	0	0	2.2	0.7	-
Therapeutic conditions where use of antibiotics india	cated				
Alveolar abscess with systemic manifestations	97.9	97.1	97.9	97.7	0.926
Alveolar abscess without systemic manifestations	93.6	77.9	78.7	85.5	0.001
Chronic apical periodontitis with sinus tract	19.9	27.9	45.7	29.7	0.000
Chronic apical periodontitis without sinus tract	23.4	5.9	4.3	13.5	0.000
Acute apical periodontitis	56.7	23.5	64.9	51.8	0.000
Pulpitis	2.1	7.4	7.5	5.0	0.107

inclined to use antibiotics. Considering chronic apical periodontitis without sinus tract, there was a decisive decrease in percentages for all three Italian areas: antibiotic treatment was considered suitable by 23.4% of students in the North, 5.9% of students in the Centre, and for 4.3% of southern students (P = 0.000). Finally, there were significant differences (P = 0.000) amongst students in relation to acute apical periodontitis 64.9% of students in the South indicated the correctness of the antibiotic use in these cases, followed by 56.7% of northern students. Only students in the Centre did not indicate antibiotics as a suitable treatment (23.5%).

#### First-choice antibiotic

Amoxicillin in combination with clavulanic acid was the first and most indicated choice for patients without penicillin allergy (85.2%, n = 258). Amoxicillin alone represented the first-choice antibiotic for 13.5% (n = 41) of students, whilst azithromycin and clarithromycin were first-choice antibiotics for 1% (n = 3) and 0.3% (n = 1), respectively.

Amoxicillin/clavulanic acid 1 g was selected by 98.8% (n = 255) of respondents, whilst amoxicillin 1 g alone was indicated by 70.7% of students. Furthermore, 29.3% of respondents indicated they would prescribe amoxicillin 500 mg alone, whilst 1.2% (n = 3) would prescribe amoxicillin 500 mg combined with clavulanic acid. Amoxicillin 500 mg was indicated by 75% of students from the South, whilst 91.3% of northern students and 83.3% of students from the Centre recommended amoxicillin 1 g

 Table 4
 Antibiotic preferences (%)

(Table 4). In addition, amoxicillin 1 g combined with clavulanic acid was the most selected option and only a small percentage of students (4.8%) chose amoxicillin/clavulanic acid 500 mg.

#### Second-choice antibiotic

When the data on the second-choice antibiotic (suitable for allergic patients) was analysed, there was a greater heterogeneity compared to that noted with the first-choice antibiotic: 56.1% (n = 170) of respondents stated they would prescribe clarithromycin, 31.7% (*n* = 96) of students considered that azithromycin was appropriate, and 11.9% considered clindamycin as an appropriate treatment for patients allergic to penicillin. Combining data on the secondchoice antibiotics and recommended dosages, clarithromycin 500 mg and azithromycin 500 mg were the most indicated: 98.8% of respondents would prescribe clarithromycin as a second-choice antibiotic and 99% (n = 95) azithromycin (Table 4), whilst 62.9% and 37.1% of students would prescribe clindamycin 300 mg and 600 mg, respectively. These percentages were characterized by a significant difference at level of 1% (P = 0.000) and the sample had an excellent representativeness of population as emerged from the power test (power = 1.000).

#### Discussion

The results of this study provide a wide range of data on the use of antibiotics in endodontic infections by dental students within Italy. The results also identify

	Antibiotic	Dose	Nord, <i>n</i> = 141	Centre, n = 68	Mezzogiorno, n = 94	Total	Ρ
Patients without penicillin	Amoxicillin	500 mg	8.7	16.7	75.0	29.3	0.000
allergy		1 g	91.3	83.3	25.0	70.7	
	Amoxicillin + Clavulanic	500 mg		4.8		1.2	0.008
	Acid	1 g	100.0	95.2	100.0	98.8	
	Azithromycin	500 mg			100.0	100.0	-
	Clarithromycin	500 mg	100.0			100.0	-
	Clindamycin	500 mg				0.0	-
Patients with penicillin	Azithromycin	500 mg	100.0	100.0	97.7	99.0	0.536
allergy	Clarithromycin	1 g			2.3	1.0	
		500 mg	97.9	100.0	100.0	98.8	0.810
		600 mg	0.6			0.6	
		1 g	1.1			0.6	
	Clindamycin	300 mg	40.0	80.0	80.0	62.9	0.053
		600 mg	60.0	20.0	20.0	37.1	
	Levofloxacin	500 mg		100.0		100.0	-

areas where interventions may be required to increase their knowledge base and skills, with the overall objective of reducing the percentage of students who still use antibiotic therapy inappropriately.

Overall, 399 students from 20 universities in Italy participated. Its main strengths were that the large cohort ensured results were representative of the overall population and that students surveyed were in regular attendance at classes. Data were analysed according to: gender, age, geographical area of university, first-choice antibiotic (beta-lactam antibiotic), duration of antibiotic therapy, second choice antibiotic (antibiotic not beta-lactam) and reasons for the use of antibiotics. The sample mean age was  $25.0 \pm 2.7$  years.

The average duration of antibiotic therapy proposed by Italian students was  $5.5 \pm 1.1$  days. Furthermore, 99% of Italian students indicated a treatment from 3– 7 days, with 0.1% selecting a duration of >7 days. In contrast, Martín-Jiménez *et al.* (2018) reported that 20% of Spanish students prescribed antibiotics > 7 days. In general, endodontic infections have a rapid and short onset and generally last from 3 to 7 days so treatment for less than 7 days is indicated, although both scenarios are broadly in line with literature recommendations (Segura-Egea *et al.* 2017a).

Amoxicillin was indicated as the first-choice antibiotic by 99% of Italian respondents with 29% of students indicating it should be administered alone, whilst the remaining 71% considered that it should be prescribed in combination with clavulanic acid. Regarding the use of Amoxicillin as a first-choice antibiotic, the results agree with those reported by Martín-Jiménez et al. (2018): in that study Amoxicillin was chosen by 100% of the respondents. Lower percentages are collected by Guzmán-Álvarez et al. (2012) and by Jain et al. (2015): however, the data obtained on the students of the respective universities confirm that Amoxicillin was indicated as the most prescribed molecule. Amoxicillin, a moderate-spectrum beta-lactam antibiotic, is suitable for endodontic infections (Skucaite et al. 2010, Segura-Egea et al. 2017a) as it provides coverage for gram-positive, gram-negative, anaerobic and strictly anaerobic bacteria. However, its effectiveness is reduced when the same infections are sustained by beta-lactamase-producing bacteria. Amoxicillin is therefore frequently administered in combination with clavulanic acid, which improves its bactericidal effect, despite the fact that in this case the risk of Clostridium Difficile infection increases (Gordon 2010, Chilton et al. 2012). Furthermore, although the combination of amoxicillin with clavulanic acid is characterized by a broader spectrum of action, it carries a higher risk of developing resistant bacteria (Barcelona *et al.* 2008, Montagner *et al.* 2014).

Data from the literature confirm that amoxicillin alone and in combination with clavulanic acid represents an optimal first-choice antibiotic in the treatment of endodontic infections, although care should be taken to ensure the correct dosage/duration is used (ESE 2018).

Clarithromycin was the second-choice antibiotic in patients allergic to  $\beta$ -lactam antibiotics with 56% of Italian students citing a preference for this drug, whilst Martín-Jiménez *et al.* (2018) reported that 99% of respondents would prescribe clindamycin 300 mg. Referring to odontogenic infections, Jain *et al.* (2015) and Guzmán-Álvarez *et al.* (2012) reported Clindamycin as the most prescribed antibiotic in case of penicillin allergy. These results are in line with protocols that recommend the use of clindamycin, clarithromycin or azithromycin in patients allergic to beta-lactam antibiotics (ESE 2018).

Antibiotic therapy is indicated in healthy patients with acute apical abscess with systemic involvement (localized swelling, body temperature >38 °C, lymphadenopathy, trismus), in progressive infections (severe infection with rapid onset, less than 24 h, cellulitis or diffuse infection, osteomyelitis) where onward referral to oral surgery is necessary, in the re-implantation of a permanent tooth following avulsion and in soft tissue trauma requiring treatment (ESE 2018). Acute apical abscess is characterized by rapid onset, spontaneous pain, pus formation and swelling associated with the soft tissues. Over 90% of Italian students considered the prescription of the antibiotics necessary in acute apical abscess with systemic manifestations. These results provide confirmation that they were able to correctly recognize the clinical scenario in which the adoption of systemic antibiotic therapy is necessary. Interestingly, 86% of Italian respondents indicated that antibiotic prescription is required in patients with acute apical abscess without systemic involvement. The general consensus is that treatment aimed at intracanal or surgical drainage is sufficient to control the infection and systemic antibiotic therapy is not necessary (Segura-Egea et al. 2017a). Similarly, the use of an antibiotic is considered ineffective in patients with symptomatic irreversible pulpitis because it does not stop the processes of necrosis and does not reduce symptomatology (George 2014, Hoskin & Veitz-Keenan 2016). In line with recommendations, only 5% of respondents in this study would prescribe an antibiotic for pulpitis. Higher percentages are reported by Martín-Jiménez et al. (2018) and Al Masan et al. (2018), respectively, 65% and 25% of respondents. It is probable that this difference can be attributed to the differences in the curriculum, and not to the methodology used to collect the answers. In fact, the present study used the same methodology described by Martín-Jiménez et al. (2018) providing students with the diagnosis so to help them in their decision-making process. On the contrary, Al Masan et al. (2018) provided Cardiff students with a series of clinical scenarios in which each student chose to use or not use of antibiotics in accordance with the specific scenario proposed. Because Italian universities share the same diagnostic terminology, Italian students are correctly focused on recognizing endodontic disorders and associating them with their respective clinical scenarios.

As regard acute apical periodontitis, 52% of Italian students would prescribe antibiotics. Similarly, Martín-Jiménez *et al.* (2018) and Al Masan *et al.* (2018) report that 44% and 75% of the students, respectively, indicated the antibiotic in the treatment of teeth with necrotic pulp and symptoms of apical periodontitis. Antibiotics are ineffective in controlling pain in endodontic infections (Fouad *et al.* 1996, Henry *et al.* 2001, Keenan *et al.* 2006, Cope *et al.* 2014). Instead, the recommended management of acute apical periodontitis is the prescription of analgesics and anti-inflammatories (Agnihotry *et al.* 2016), and / or with the treatment of the root canal (Paredes-Vieyra & Enriquez 2012).

Inappropriate use of antibiotics emerged in the management of chronic apical periodontitis with and without fistula, where 30% and 14%, respectively, of respondents from Italian universities and 38% and 16% from Spain (Martín-Jiménez et al. 2018) replied that they would prescribe antibiotics for these conditions. Moreover, the larger percentage of respondents who would use antibiotics for chronic apical periodontitis with fistula, suggests that students erroneously believe the presence of a fistula, in dental infections, is a symptomatic indication of worsening condition, whereas the fistula represents an orifice which connects a closed area of an infection with an epithelial surface-whereby internal pressure can be discharged, thus helping to prevent swelling, pain and spread of the infection in the anatomical spaces. The presence of fistula does not mean an exacerbated endodontic infection and chronic apical periodontitis associated with fistula should be treated with a canal treatment and intermediate medications but not with antibiotics (Mittal & Gupta 2004).

The results of this study provide useful data on the state of knowledge of final year undergraduate dental students and demonstrate where gaps in their knowledge exist. To deadline these deficiencies, it is necessary that students improve their knowledge of the biological and microbiological principles underlying inflammation and infection and now to best manage these conditions. One of the main messages to emerge is that the misuse/inappropriate use of antibiotics is effectively associated with a lack of knowledge on the part of those who prescribe them, combined with lack of awareness from patients who frequently expect to be treated with an antibiotic-erroneously associating the use of antibiotics with therapeutic advantages and the reduction of pain (Cope et al. 2014, Martín-Jiménez et al. 2018).

## Conclusions

The inappropriate use of systemic antibiotics in endodontic infections contributes to the growing public health problem of AMR. The results confirm that newly qualified dentists should receive training in line with international guidelines on the appropriate use of antibiotics in their daily practice. Results of the present study identified where gaps in knowledge and training existed, and it is vital that they are effectively incorporated into undergraduate dentistry courses to ensure dentists of the future have the necessary tools for the effective prevention and treatment of infections and to work towards addressing the devastating consequences of AMR.

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## **Conflict of interest**

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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