

# Prescription of Antibiotics for Periodontal Disease among Dentists in the Region of Tirana

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## Abstract

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**BACKGROUND:** Periodontal disease has been and will be a challenge for dentists in the entirety of oral pathologies. To date, there is no data regarding the prescription of antibiotics for periodontitis in the district of Tirana.

**AIM:** Evaluate aspects related to the pattern of prescription of antibiotics among dentists in Tirana region for periodontitis.

**METHODS:** Prescriptions from dental practitioners were collected from 25 pharmacies, randomly selected. The only prescription containing a diagnosis of periodontitis, with at least one antibiotic given, was included in the study. Data analysis was done with SPSS 20.

**RESULTS:** Out of 1159 initial prescriptions, only 314 met the selection criteria. The average age of patients was  $39.91 \pm 15.21$  years. Mean duration of therapies was  $5.57 \pm 1.5$  days. The most common form of prescription was one broad-spectrum antibiotic (74.5%), combined antibiotics therapy (22.3%) and narrow-spectrum antibiotic (3.2%). Combined antibiotics involved the use of Metronidazole with Amoxicillin (12.1%) and Metronidazole with Spiramycin (10.2%). Significant differences in the patterns of prescription were identified in relation with patient age and therapy duration ( $P < 0.05$ ). No statistical difference was found in the patient's gender and the typology of the therapy ( $P > 0.05$ ).

**CONCLUSIONS:** Our study shows prescription characteristics of antibiotics for periodontal disease by dentists in Tirana for the first time. Amoxicillin is the most prescribed antibiotic, followed by amoxicillin with clavulanic acid. We found variation in dosage, frequency and duration for all antibiotics used, and perceptible discrepancies between observed and recommended practice. Guidelines on rational antibiotic use are needed for dental practitioners in Tirana and the Republic of Albania for better management of periodontitis and resistance prevention.

## Introduction

Periodontitis is an inflammatory disease which affects the supporting tissues of the tooth. It constitutes one of the most frequent bacterial infection in adults. There are hundreds of bacterial species associated with this disease, thus making it difficult to achieve a successful specific therapy for periodontitis [1]. Among these the most relevant are *Aggregatibacter actinomycetemcomitans* (A.a.), *Porphyromonas gingivalis* (*P. gingivalis*), *Treponema denticola* (*T. denticola*), *Fusobacterium nucleatum* (*F.*

*nucleatum*) and *Prevotella intermedia* (*P. intermedia*), [2] [3] [4]. *P. gingivalis* is considered as the main cause of chronic periodontitis, though no less important is the A.a., which is recognised as the leading cause of aggressive periodontitis [2] [5] [6]. Difficulties faced by periodontists lie in the fact that the restoration of normality for the periodontal tissues becomes difficult with time. If left untreated, it can progress into an irreversible situation [7]. There are some procedures and protocols aimed to prevent the progression of the lesion, maintain current levels of periodontal tissues and restore periodontal health. To succeed in these procedures, in addition to manual curettage and periodontal surgery, systemic antibiotic

therapy is a key factor [8] [9] [10] [11]. Strong evidence exists to support benefits of manual curettage to remove supra and subgingival plaque. Hence, without the use of antibiotics, this procedure is unable to eradicate pathogenic bacterial species and thus to maintain gingival levels of adhesion [8] [12] [13]. To support such procedures, except monotherapy with antibiotics, dental practitioners use a combination of antibiotics known as a combined therapy or dual antibiotic therapy [14] [15] [16].

To the best of our knowledge, to date, there is no data regarding the prescription of antibiotics for periodontitis in the region of Tirana.

## Materials and Methods

This retrospective drug utilisation study was conducted over a period of 3 months, March-June 2016. It involved prescriptions collected from 25 randomly selected pharmacies in the region of Tirana. We collected prescriptions dispensed by dentists and selection criteria included prescriptions: (a) limited and only for periodontitis in patients  $\geq 18$  years old; and (b) with at least one antibiotic prescribed. Prescriptions with other systemic drugs or local medications were excluded from the study.

Collected data were analysed using the statistical software SPSS 20 (IBM, USA). Differences between patterns of prescription, patient's age, gender and treatment duration were compared using One-way ANOVA and Chi-square tests. *P*-values  $< 0.05$  were considered statistically significant.

## Results

From 1159 collected prescriptions, only 314 met the selection criteria. The gender ratio was 1:1.12 consisting of 148 Males (47.1%) and 166 Females (52.9%). The average age was  $39.91 \pm 15.21$  years (18-81). Mean duration of therapies was  $5.57 \pm 1.5$  days (3-10) (Table 1).

**Table 1: Age and therapy duration variables parameters**

	Age of patients	Duration of therapy
Mean	39.91	5.57
Median	36.00	5.00
Mode	25	5
Standard deviation	15.21	1.50
Minimum	18	3
Maximum	81	10

Three patterns of antibiotic prescription were observed: (a) 74.5% single therapies with a broad-spectrum antibiotic (BSA), (b) 22.3% combined

therapies (CT) consisting in a broad-spectrum antibiotic and a narrow-spectrum antibiotic and (c) 3.2% narrow-spectrum antibiotic (NSA) (Table 2).

**Table 2: Frequency of type of antibiotic therapies**

The pattern of antibiotic prescription	Value	%
Broad spectrum	234	74.5
Broad and narrow spectrum combination	70	22.3
Narrow spectrum	10	3.2

Among 234 BSA prescriptions, Amoxicillin is the most prescribed drug (32.5%), followed by Amoxicillin-Clavulanic Acid (22%) and Spiramycin (12.7%). Instead, Erythromycin (4.1%), Azithromycin (1.6%) and Ciprofloxacin (1.6%) are less prescribed drugs. CT involved the use of Amoxicillin with Metronidazole (12.1%) and Spiramycin with Metronidazole (10.2%). Regarding the use of NSA, only Metronidazole was prescribed (Table 3).

**Table 3: Percentage of antibiotic prescription and characteristics of therapy duration**

Antibiotic	Therapy duration (days)				
	%	Mean	Maximum	Minimum	Mode
Broad spectrum					
Amoxicillin	32.5	5	7	3	5
Amoxicillin with Clavulanic Acid	22	5	7	3	5
Spiramycin	12.7	5	7	3	5
Erythromycin	4.1	5	6	3	5
Ciprofloxacin	1.6	5	7	4	4
Azithromycin	1.6	5	5	5	5
Mixed spectrum					
Metronidazole+Amoxicillin w/Clavulanic Acid	12.1	7	10	6	7
Metronidazole+Spiramycin	10.2	8	10	5	7
Narrow spectrum					
Metronidazole	3.2	6	7	6	6

One-way ANOVA test indicated the statistically significant difference between the three typologies of antibiotic therapy prescribed, patient's age and treatment duration (Table 4).

**Table 4: One Way ANOVA test results for patients age and treatment duration about the type of therapy**

	Sum of Squares	df	Mean Square	F	Sig.
Age	3106.280	2	1553.140	6.962	0.001
Treatment duration	399.900	2	199.950	201.206	0.000

Post Hoc test demonstrated that the single BSA therapy and CT do not show significant differences in mean patients age, while NS therapy presented significant difference compared with both therapies (Table 5).

**Table 5: Multiple comparisons where the dependent variable is patient age**

(I) Antibiotic type	(J) Antibiotic type	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Broad spectrum antibiotic	Combined therapy	1.469	2.035	.751	-3.32	6.26
	Metronidazole	17.912 <sup>*</sup>	4.823	.001	6.55	29.27
Combined therapy	Broad spectrum antibiotic	-1.469	2.035	.751	-6.26	3.32
	Metronidazole	16.443 <sup>*</sup>	5.049	.004	4.55	28.33
Narrow spectrum antibiotic	Broad spectrum antibiotic	-17.912 <sup>*</sup>	4.823	.001	-29.27	-6.55
	Combined therapy	-16.443 <sup>*</sup>	5.049	.004	-28.33	-4.55

Data shows that NSA like Metronidazole tends to be prescribed to younger patients with a mean age of 23 years (Figure 1).

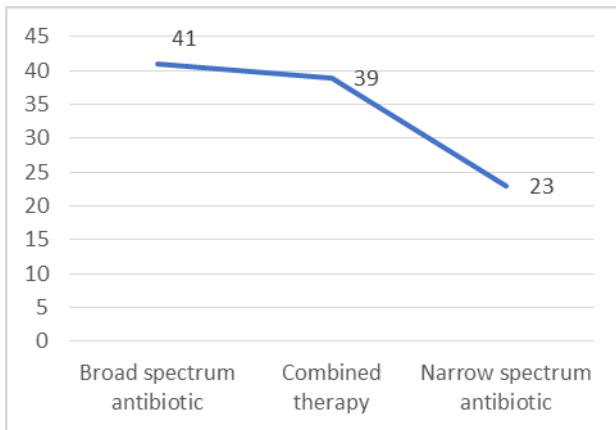


Figure 1: Mean patients age

Furthermore, Post Hoc test showed the statistically significant difference between all three types of antibiotic therapies regarding the duration of therapies (Table 6).

Table 6: Multiple comparisons where the dependent variable is therapy duration

(I) Antibiotic type	(J) Antibiotic type	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Broad spectrum antibiotic	Combined therapy	-2.705 <sup>*</sup>	0.136	0.000	-3.03	-2.39
	Metronidazole	-1.377 <sup>*</sup>	0.322	0.000	-2.14	-0.62
Combined therapy	Broad spectrum antibiotic	2.705 <sup>*</sup>	0.136	0.000	2.39	3.03
	Metronidazole	1.329 <sup>*</sup>	0.337	0.000	.53	2.12
Narrow spectrum antibiotic	Broad spectrum antibiotic	1.377 <sup>*</sup>	0.322	0.000	.62	2.14
	Combined therapy	-1.329 <sup>*</sup>	0.337	0.000	-2.12	-0.53

The single broad-spectrum antibiotic regime has a mean duration of 4.92 days while Metronidazole therapy for 5 days. Dual therapy has the longest regimen, with a mean of 7.63 days (Figure 2).

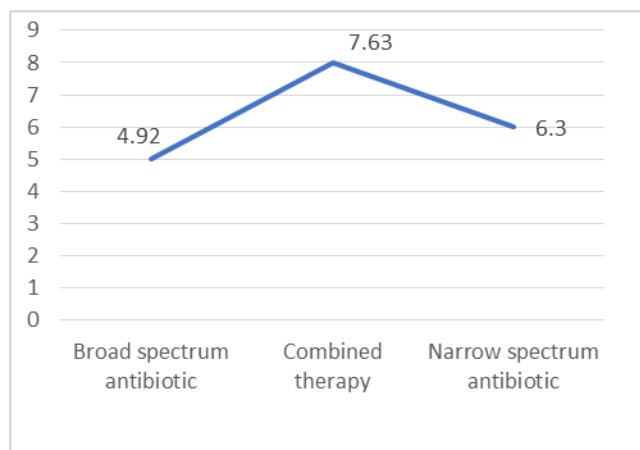


Figure 2: Mean therapy duration

No statistical difference was found in the patient's gender and the typology of the therapy ( $P > 0.05$ ).

## Discussion

This study shows that dentists in the Tirana region tend to prescribe BSA in 74.5% of cases. Amoxicillin alone and its combination with Clavulanic acid are prescribed in more than half of cases (54.5%). Amoxicillin is found to be useful in the management of patients with aggressive periodontitis, in both localised and generalised forms [17] [18]. Also, its combination with Clavulanate potassium shows to incline bacterial resistance. Also, Spiramycin is frequently used. In 12.7% of prescription, it is used alone for the management of periodontal disease. Spiramycin has shown promising results in the treatment of advanced forms of periodontitis, and as an adjunct to thorough scaling and root planning, provides a statistically significant improvement in probing depths for up to 24 weeks when compared with scaling and root planing alone. Furthermore, it produces a significant improvement in attachment level [18] [19] [20] [21].

On the other hand, NSA alone, such as Metronidazole remains a non-primary choice for the pharmacological treatment of periodontal disease, with only 3.2% of prescriptions. Although, the literature shows that Metronidazole has a prominent effect on periodontitis, yet there is scepticism among dentists who are reluctant to prescribe it. However, Metronidazole alone it's not the drug of choice for treating A.a. infections. Instead, it's a combination with other antibiotics shows to be effective against these bacteria [22] [23]. Also, it is effective against anaerobes such as *P. gingivalis* and *P. intermedia* [24]. Studies have suggested that Metronidazole combined with Amoxicillin or Amoxicillin-Clavulanate potassium, it may be with great impact in the management of patients with aggressive periodontitis [23] [25] [26] [27] [28]. In our study, Metronidazole was mostly used in combination with Amoxicillin 12.1% and with Spiramycin in 10.2%. Of the cases.

Clinical research suggests that Ciprofloxacin with Metronidazole is a powerful antibiotic combination against mixed infections. At present, Ciprofloxacin is the only antibiotic in periodontal therapy to which all strains of A.a. are susceptible [29] [30] [31] [32]. Metronidazole targets obligate anaerobes, and Ciprofloxacin targets facultative anaerobes. This type of therapy can be of great benefit for the patients since periodontal infections contain a wide diversity of bacteria, and this scenario makes it mandatory to use more than one antibiotic, either serially or in combination [33] [34] [35] [36] [37]. Nevertheless, data shows that dentists in Tirana

region do not use this combination.

The duration of the treatment shows to be a problem itself, with a mean of  $5.57 \pm 1.5$  days. Dentists who prescribe only one antibiotic, prefer a 5-days therapy. In contrast, dentists that have chosen a combination therapy have prescribed it for a longer time, and this can be the case of chronic resistant periodontitis. Only the CT has a mean duration of 7.63 days. None of the prescriptions had a prolonged therapy for more than ten days. Therapies with BSA, have a mean duration of 4.92 days and a therapy with NSA has a mean duration of 6.3 days. This is a short-term therapy which may pose a risk regarding antibiotic resistance rather than a successful treatment for the disease. This, especially in cases of chronic periodontitis where the presence of periodontal pathogens, specifically A.a., is known to endure in tissues after therapy and re-infect the pocket. Thus, the use of systemic antibiotics was thought to be necessary to eliminate pathogenic bacteria from the tissues [27].

Interpretation of the processed data, not only does show that NSA like Metronidazole have a limited number of prescriptions, but it is more used in young adults. Patients with a generalised form of the disease usually appear to be young, and they present generalised attachment loss and poor antibody response. Therefore, these patients often have a fair, poor, or questionable prognosis, and they need an effective systemic antibiotics therapy. This is in contrast with our findings of NSA use in younger adults.

Evidence shows that there is a lack of knowledge for antibiotic prescription patterns and duration of therapy in dentists in the region of Tirana. The increasing resistance problems of recent years are probably related to the over-or misuse of antibiotics. There is a clear need for the development of prescribing guidelines and educational initiatives to encourage the rational and appropriate use of antibiotics in dentistry, especially periodontal problems. These are issues we found to be present also in other countries [38] [39] [40] [41] [42] [43] [44].

While the use of antibiotics in periodontal treatment will probably always be controversial, the position paper of the American Academy of Periodontology contains valuable guidance for their use, and we would recommend their application in everyday practice by dentists. Following exhaustive literature searches, this paper determined that patients with aggressive periodontitis appear to benefit from the adjunctive use of systemic antibiotics during treatment. Systemic antibiotic therapy helps the manual curettage and improves immune response to eliminate subgingival bacteria, which are not affected by manual therapy [12]. The mechanical curettage without the addition of systemic antibiotics would probably be a failure considering the rapid bacterial colonisation of periodontal pockets [36].

Based on WHO latest report, antimicrobial resistance poses a "global health security threat" to public health [45]. Subsequently, to benefit the most from these therapies, we must limit their use and prescribe the right dosage and duration of therapy to prevent further resistance.

In conclusion, our study shows prescription characteristics of antibiotics for periodontal disease by dentists in Tirana for the first time. Most of the dentist in the district of Tirana, for periodontitis, prescribes only one broad-spectrum antibiotic. Amoxicillin was the most preferable, followed by amoxicillin with clavulanic acid. Metronidazole a narrow spectrum antibiotic is prescribed more in young adults, while combined therapies and broad-spectrum antibiotics tend to be prescribed with the increasing of patient's age. We found variations in dosage and frequency for all the antibiotics used, particularly concerning data exists regarding the short duration of therapies prescribed. Perceptible discrepancies were observed between recommendations and practice. Therefore, these observations highlight the need for dentists to improve antibiotic prescribing practices for periodontal problems. Guidelines on rational antibiotic use are needed for dental practitioners in Tirana and in the Republic of Albania for a better management of periodontitis and resistance prevention.

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