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## A CLINICAL STUDY ON THE IMPACT OF DIFFERENT TREATMENT MODALITIES ON IMPROVING THE CLINICAL OUTCOMES IN CHRONIC PERIODONTITIS PATIENTS

DK Abou El-Fadl <sup>\*1</sup>, NA Sabri <sup>2</sup> and HA Abuel-Ela <sup>3</sup>

Department of Pharmacy Practice and Clinical Pharmacy<sup>1</sup>, Faculty of Pharmaceutical Sciences and Pharmaceutical Industries, Future University in Egypt, Cairo, Egypt.

Head of Clinical Pharmacy Department <sup>2</sup>, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt.

Department of Oral Medicine <sup>3</sup>, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Ain Shams University and Misr International University, Cairo, Egypt.

### Keywords:

Periodontal Disease,  
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### Correspondence to Author:

**DK Abou El-Fadl**

Department of Pharmacy Practice and Clinical Pharmacy, Faculty of Pharmaceutical Sciences and Pharmaceutical Industries, Future University in Egypt, Cairo, Egypt


**E-mail:** bizo\_151@yahoo.com

**ABSTRACT: Background:** Periodontal disease is one of the two main and most prevalent oral diseases all over the world. Treatment strategies are diverse. To date, scaling and root planing (SRP) is still the gold standard non-surgical therapy for periodontitis. Systemically administered antibiotics can be used as an adjunct to SRP to improve the treatment outcome of periodontitis. **Purpose:** To compare clinical outcome of systemically administered doxycycline versus combination of amoxicillin and metronidazole as an adjunct to SRP in the management of chronic periodontitis patients. **Methods:** This study was conducted on forty-two moderate to severe generalized chronic periodontitis patients who received non-surgical periodontal therapy. Following SRP, patients were randomly allocated to one of the following groups; group (I) received Doxycycline (loading dose 200 mg and maintenance dose 100 mg/day) for fifteen days, group (II) received a combination therapy of amoxicillin and metronidazole (750 mg/day) for eight days and group III (control group) which was treated by SRP without administration of systemic antibiotic therapy. The periodontal parameters; Plaque index (PI), Gingival index (GI), Probing depth (PD) and Clinical attachment level (CAL) were examined for the assessment of the clinical outcome. **Results:** This study revealed that combination of amoxicillin and metronidazole resulted in significant reduction in PD and significant gain in CAL. **Conclusion:** The combination of Amoxicillin and Metronidazole at a dose of 750 mg/day for eight days had a significant effect on enhancing the clinical outcome of chronic periodontitis patients.

**INTRODUCTION:** Oral health is integral to general health. There are important associations and interactions between oral diseases, particularly periodontal diseases and a variety of systemic conditions. There is also growing evidence that periodontal infections can have an influence on several systemic diseases and conditions.<sup>1</sup>

Periodontal diseases result from an inflammatory response to bacteria present in dental biofilms. The host response to the dental plaque biofilm may be confined to the gingival tissues or may progress to deeper periodontal structures, leading to clinical attachment loss.<sup>2</sup>

Periodontal diseases are classified according to the severity of the disease into two major stages; Gingivitis, an early stage of periodontal disease, if left untreated can advance to Periodontitis (progression of gingivitis, causing destruction of supporting tissues). It has been well documented that the oral bacteria present in periodontitis can reach the bloodstream and develop systemic

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disease such as cardiovascular disease<sup>3</sup> and preterm birth incidence<sup>4</sup>. Systemic effects are believed to arise from some combination of disseminated toxins, bacterial insult, and the actions of both innate and adaptive immunity. The exact connections between oral and systemic disease, however, remain complex and obscure. It is most probable that the causal agents and mechanisms differ among and within oral-systemic disease pairs.<sup>5</sup>

However, the periodontal etiology is complex and multifactorial, the main etiological factor of this infectious disease are the periodontal pathogens present in dental plaque biofilm. Thus, the destruction of periodontal tissues is associated with the activation of periodontal pathogen factors such as toxins, enzymes and products of metabolism, as well as host factors.<sup>6</sup> Nevertheless, the extent and severity of the disease depend on the nature of specific and individual host-microbial interactions.<sup>7</sup> Previous studies have demonstrated that long-term stability of the clinical benefits obtained via periodontal therapy can be maintained only when cause related treatment is followed by effective supportive periodontal care (SPC).<sup>8</sup> Within this SPC program, self-performed plaque control is crucial in attaining the best long-term results after periodontal therapy.<sup>9</sup> As patient compliances with mechanical oral hygiene practices are not always as good as desired, chemical agents have been used to improve plaque control and to reduce gingivitis.<sup>10</sup> The use of mouth-rinse containing antiseptic agents is an effective and feasible way to reduce viable bacteria in the oral cavity<sup>11-13</sup>

Treatment strategies are diverse; the leading method of non-surgical eradication of the periodontal pathogens is professional scaling and root planing (SRP). It has proven to be the gold standard of periodontal therapy. Its efficacy is well documented in systematic<sup>14-16</sup> and narrative reviews.<sup>17-19</sup> In the case of deep pockets<sup>20</sup> non-surgical therapy is supported with adjunctive antibiotic therapy. In this perspective, antibiotics used adjunctively to SRP can improve the outcome of periodontal therapy.

Antibiotics can be administered locally (immediate or controlled release) or systemically as single or

combination therapy. Combination therapy or Polytherapy is the use of more than one medication for the treatment of one disease either as separate or combination drugs; dosage forms that contain more than one active ingredient. Metronidazole is a nitroimidazole compound with a broad spectrum of activity against protozoa and anaerobic bacteria.<sup>21</sup> The antibacterial activity against anaerobic cocci, anaerobic Gram - negative bacilli, and anaerobic Gram – positive bacilli had led to its use in the treatment of periodontal diseases.<sup>22</sup>

In periodontal treatment, metronidazole has been used both in tablet forms, and less commonly, as a topical application. The drug is well-absorbed after oral administration and the peak plasma level is usually reached in about one hour.<sup>23</sup> The half-life of metronidazole is about 8 hours and the principal site of metabolism is the liver. Metronidazole is excreted in the urine.

Tetracyclines are a group of closely related, bacteriostatic antibiotics that provide a “broad spectrum” of activity against both Gram-positive and Gram negative species, although more suitable antibiotics are usually preferred for Gram-positive infections. Tetracyclines are usually given orally, although topical application has been used in periodontal treatment regimens.<sup>24, 25</sup> All tetracyclines are distributed widely in the tissues and are localized in developing dental structures and bone. Tetracycline, minocycline and doxycycline are detectable in gingival crevicular fluid after oral dosing and their respective concentrations can reach levels 10 times and five times in the serum.<sup>26, 27</sup>

### **Role of Clinical Pharmacist in Dental Patients Care:**

The Clinical Pharmacist is one of the most visible and accessible members of the primary healthcare team for the general public.<sup>28</sup> The pharmacist's role has expanded significantly in recent decades from dispenser of medications to recognized member of the healthcare team. Rather than consult a dentist or physician, many individuals with oral problems seek help from their pharmacists.<sup>28</sup>

There are a variety of ways that the pharmacist can take a frontline approach to oral disease prevention,

identification, assessment, management, and referral. These include promoting the use of topical fluorides, especially fluoride toothpastes; the use of end rounded soft-bristle toothbrushes; encouraging effective oral hygiene practices; promoting healthy eating; encouraging use of dental services and preventative therapies; and giving parents and other family caregivers information, motivation, confidence, and skills to prevent oral disease.<sup>28</sup>

The pharmacist can also enhance patient care by communicating with other healthcare providers about oral health concerns. The pharmacist is in a good position to recognize patients who are at risk for developing periodontal disease, as well as recognize the medical conditions that might be affected by preexisting periodontal disease.<sup>28</sup>

#### **Aim of the study:**

To compare the clinical outcome of the administration of Doxycycline compared to a combination of Amoxicillin and Metronidazole in the treatment of generalized moderate to severe chronic periodontitis and to investigate the impact of patient education as a contribution of the clinical pharmacist in oral health enhancement.

#### **MATERIALS AND METHODS:**

##### **Patients and setting:**

The study is a Prospective, Randomized, Controlled clinical trial conducted on Egyptian Chronic Periodontitis patients. A total of forty-two chronic periodontitis patients were enrolled in the study throughout a period of 12 months (from October 2013 to September 2014 with age range from 30 to 55 years. Patients presenting to the outpatient clinic of Oral Medicine and Periodontology Department, Faculty of Dentistry, Ain Shams University and Faculty of Dentistry, Future University in Egypt were assessed for eligibility and only those meeting the inclusion criteria were recruited.

Patients included in the study were adult chronic periodontitis patients of both sexes who were able to return for the follow up visits. The excluded patients were those suffering from any systemic disease, compromised renal function, hepatic impairment, patients with history of periodontal surgery or history of antimicrobial therapy for at

least 4 months prior to the initiation of the study, patients with Known hypersensitivity to penicillin, tetracyclines, metronidazole (or other nitroimidazole derivatives), pregnant and/or nursing females and smokers.

The study protocol was assessed and approved by the Ethical Committee of faculty of pharmacy Ain Shams University. According to the Declaration of Helsinki, participants were informed about the study and their written informed consent was obtained directly before enrollment. Baseline data (age, gender, weight), medical and medication history were recorded.

##### **Grouping and Treatment protocol:**

Patients were randomly allocated to one of the three study groups. All patients received non-surgical periodontal therapy including Full mouth scaling and root planing and the use of Chlorohexidine mouthwash (Antiseptol Mouthwash, Kahira Pharma & Chem. Ind. co., Cairo-Egypt.). SRP was performed using ultrasonic Piezo-electric scaler (Electro Medical Systems EMS Piezon-Master 400, Switzerland) equipped with supragingival and fine subgingival tips and hand instruments under local anaesthesia to minimize patient discomfort.

Following SRP, group (I) patients received Doxycycline (loading dose 200 mg and maintenance dose 100 mg/day) for 15 days, group (II) patients were given a combination therapy of amoxicillin and metronidazole (750 mg/day) for 8 days while Group III patients (control group) didn't receive antibiotic therapy.

For the assessment of the impact of patient education on the clinical outcome, each group was divided into two subgroups: A and B. Subgroups IA, IIA and IIIA attended patient education sessions concerning oral health care in periodontal patients and received a patient education handout which included information about the disease, its signs and symptoms, complications, the non-pharmacological methods which help to prevent or reduce the incidence of periodontal disease as well as advices regarding the importance of oral hygiene measures and the proper use of oral hygiene products.

### **Clinical Outcomes:**

Patients were evaluated clinically by measuring Plaque index (PI)<sup>29</sup>, Gingival index (GI)<sup>30</sup>, Pocket depth (PD)<sup>31</sup> and Clinical attachment level (CAL)<sup>32</sup> at baseline, then at one, two and three months after the initiation of non surgical periodontal therapy.

**Plaque index (PI):** The PI as developed by Silness and Loe (1964) assesses the thickness of plaque at the cervical margin of the tooth. Four areas, distal, facial, mesial, and lingual were examined.

### **PI has four scores:**

- 0:** No plaque in gingival area.
- 1:** No plaque visible by the unaided eye, but plaque is made visible on the point of the probe after it has been moved across surface at entrance of gingival crevice.
- 2:** Gingival area is covered with a thin to moderately thick layer of plaque; deposit is visible to the naked eye.
- 3:** Heavy accumulation of plaque, the thickness of which fills out the niche produced by gingival margin and tooth surface; interdental area is stuffed with plaque.

**Gingival index (GI):** Also attributed to Loe and Silness (1967), the GI assesses the severity of gingivitis based on color, consistency, and bleeding on probing. Each tooth was examined at the mesial, lingual, distal, and facial surface.

### **GI has four scores:**

- 0:** Normal gingiva.
- 1:** Mild inflammation: slight change in color and slight edema; no bleeding on probing.
- 2:** Moderate inflammation: redness, edema, and glazing; bleeding on probing.
- 3:** Severe inflammation: marked redness and edema; ulceration; tendency to spontaneous bleeding.

### **Probing depth (PD):**

Probing depth (pocket depth) was measured from the gingival margin to the base of the periodontal pocket to the nearest mm (Caton, 1989). Six readings were recorded for each tooth: Mesiobuccal, Mesiolingual, Distobuccal, Distolingual, Midbuccal, Midlingual.

**Clinical attachment level (CAL):** The CAL provides an estimate of a tooth's stability and the loss of bone support. Clinical attachment level was measured with a graduated periodontal probe from the cemento-enamel junction to the base of the pocket to the nearest mm. (Glavind and Loe, 1967). These measurements were done using the University of Michigan O' probe with William's graduation (William's graduation probe, Hu Friedy Mfg.co., Inc. 3232 N. Rockwell Street/Chicago, IL 60618/U.S .A.)

### **Statistical analysis:**

Data were statistically described in terms of mean and standard deviation (SD), frequency and percentage when appropriate. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Age showed a parametric distribution, One way ANOVA has been used to study the effect of different tested groups on mean values. Tukey's post-hoc test was used for pair-wise comparison between the means when ANOVA test is significant. Independent t-test has been used to compare between different subgroups within different follow-up periods.

All the clinical parameters (PI, GI, PD and CAL) and the change after different follow-up periods showed non-parametric distribution; Kruskal Wallis test was used to compare between different tested groups followed by Mann-Whitney U test if the data were significant. Mann-Whitney U-test was used to compare between different Subgroups within different follow-up periods. Significance level was set at  $p < 0.05$ . Statistical analysis was performed with IBM® SPSS® (SPSS Inc., IBM Corporation, NY, USA) Statistics Version 22 for Windows.

## **RESULTS:**

### **I. Demographic data:**

**Age:**

**TABLE 1: MEAN AND STANDARD DEVIATION (SD) OF AGE FOR THE DIFFERENCE TESTED GROUPS.**

		Subgroup				p-value
		A(With Pt Education)		B (Without Pt Education)		
		Mean	SD	Mean	SD	
Age	Group I	40.71	8.34	39.57	8.77	0.807 NS
	Group II	39.14	8.51	40.43	8.58	0.783 NS
	Group III	39.43	8.94	39.00	9.22	0.931 NS
	p-value	0.936 NS		0.955 NS		

\*= Significant, NS=Non-significant

**Gender distribution:**

**TABLE 2: FREQUENCY (n) AND PERCENTAGE (%) AND RESULTS OF CHI-SQUARE (x<sup>2</sup>) TEST FOR COMPARISON OF THE GENDER DISTRIBUTION BETWEEN THE TESTED GROUPS.**

			Subgroup				p-value
			A( With Pt Education)		B (Without Pt Education)		
			Count	%	Count	%	
Group	Group I	Male	4	57.1%	3	42.9%	0.593 NS
		Female	3	42.9%	4	57.1%	
	Group II	Male	3	42.9%	4	57.1%	0.593 NS
		Female	4	57.1%	3	42.9%	
	Group III	Male	4	57.1%	4	57.1%	1.00 NS
		Female	3	42.9%	3	42.9%	
p-value			0.826 NS		0.826 NS		

\*= Significant, NS=Non-significant

**II. Clinical periodontal parameters:**

**1. Plaque Index (PI):**

**A. Difference between tested groups in the mean change in Plaque Index (PI)**

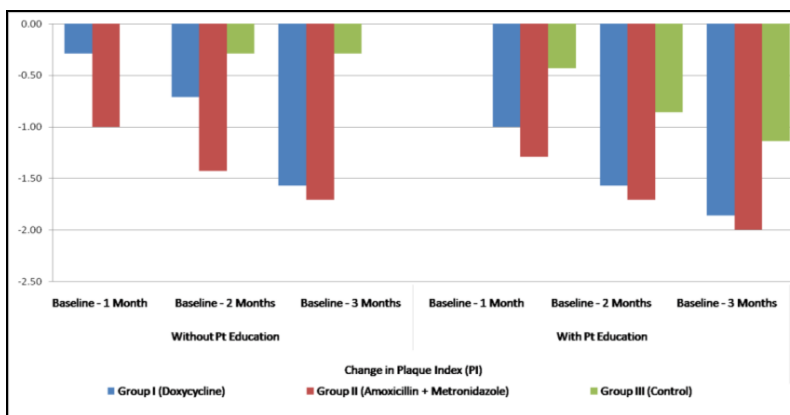
**Without Patient Education (B)**

After 1 month Group II produced the highest mean change in Plaque Index (PI) followed by Group I followed by Group III with a significant difference between the three groups. After 2 months and after

3 months Group II and Group I produced a significantly higher mean change in Plaque Index (PI) compared to Group III with an insignificant difference between group I and II.

**With Patient Education (A):**

After 1 month; Group II and Group I produced significantly higher mean change in Plaque Index (PI) compared to Group III with an insignificant difference between group I and II.



**FIG. 1: HISTOGRAM OF THE MEAN CHANGE IN PLAQUE INDEX FOR THE DIFFERENT TESTED GROUPS**

**B. Difference between tested Subgroups in the mean change in Plaque Index (PI):** After 1 month; Subgroup IIA produced a significantly

higher mean change in Plaque Index (PI) compared to Subgroup IIB. After 2 months; Subgroup IIA produced a significantly higher mean change in

Plaque Index (PI) compared to Subgroup IIB. Subgroup IIIA produced a significantly higher mean change in Plaque Index (PI) compared to Subgroup IIB after 3 months. (**Table 3**)

**TABLE 3: MEAN AND STANDARD DEVIATION (SD) OF CHANGE IN PLAQUE INDEX FOR THE DIFFERENT TESTED SUBGROUPS.**

Change in Plaque Index (PI)	Group	Time Point	Subgroup				p-value
			B (Without Pt Education)		A (With Pt Education)		
			Mean	SD	Mean	SD	
	Group I	Baseline - 1 Month	-1.00	0.00	-1.00	0.58	1.00 NS
		Baseline - 2 Months	-1.43	0.53	-1.57	0.53	0.710 NS
		Baseline - 3 Months	-1.71	0.76	-1.86	0.69	0.710 NS
	Group II	Baseline - 1 Month	-0.29 <sup>b</sup>	0.49	-1.29 <sup>a</sup>	0.49	0.011*
		Baseline - 2 Months	-0.71 <sup>b</sup>	0.49	-1.71 <sup>a</sup>	0.76	0.026*
		Baseline - 3 Months	-1.57	0.53	-2.00	0.82	0.383 NS
	Group III	Baseline - 1 Month	0.00	0.00	-0.43	0.53	0.209 NS
		Baseline - 2 Months	-0.29	0.49	-0.86	0.69	0.165 NS
		Baseline - 3 Months	-0.29 <sup>b</sup>	0.49	-1.14 <sup>a</sup>	0.69	0.038*

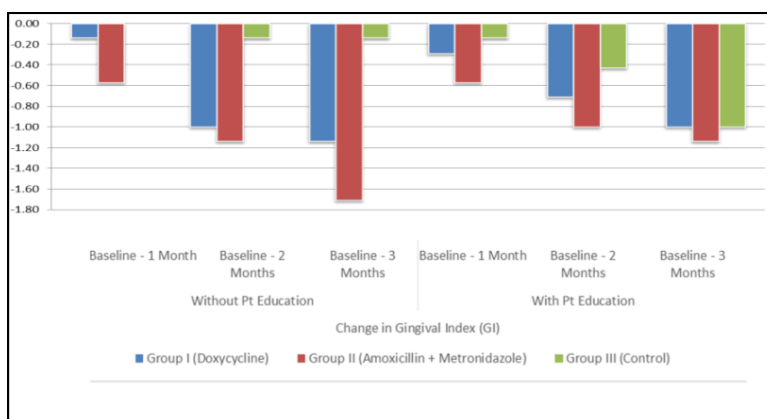
\*= Significant, NS=Non-significant

**2. Gingival Index (GI):**

A. Difference between tested groups in the mean change in Gingival Index (GI)

Group II and Group I produced a significantly higher mean change in Gingival Index (GI) compared to Group III after 1 month, 2 months and 3 months with an insignificant difference between group I and II.

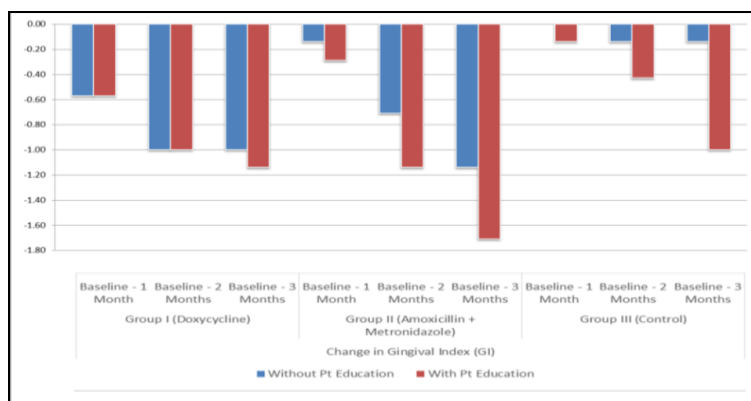
Without Patient Education (B)



**FIG.2: HISTOGRAM OF THE MEAN GINGIVAL INDEX FOR THE DIFFERENT TESTED GROUPS.**

B. Difference between tested Subgroups in the mean change in Gingival Index (GI) Subgroup IIIA produced significant higher change in Gingival

Index (GI) compared to Subgroup IIB after 3 months.



**FIG.3: HISTOGRAM OF THE MEAN CHANGE IN GINGIVAL INDEX FOR THE DIFFERENT TESTED SUBGROUPS.**

**3. Probing Pocket Depth (mm):**

**A. Difference between tested groups in the mean change in Probing Pocket Depth (mm)**

Without Patient Education (B)

Group I and Group II produced a significantly higher mean change in Probing Pocket Depth compared to Group III after 1 month, 2 months and

3 months with an insignificant difference between group I and II. **(Table 4)**

With Patient Education (A) Group I and Group II produced a significantly higher mean change in Probing Pocket Depth compared to Group III after 1 month, 2 months and 3 months with an insignificant difference between group I and II. **(Table 4)**

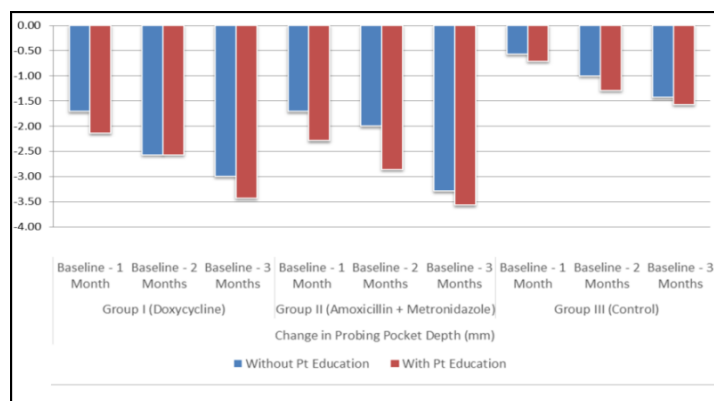
**TABLE 4: MEAN AND STANDARD DEVIATION (SD) OF CHANGE IN PROBING POCKET DEPTH FOR THE DIFFERENT TESTED GROUPS.**

			Group						p-value
			Group I		Group II		Group III		
			Mean	SD	Mean	SD	Mean	SD	
Change in Probing Pocket Depth (mm)	Without Pt Education (Subgroup B)	Baseline - 1 Month	-1.71 <sup>b</sup>	0.76	-1.71 <sup>b</sup>	0.49	-0.57 <sup>a</sup>	0.79	0.021*
		Baseline - 2 Months	-2.57 <sup>b</sup>	1.13	-2.00 <sup>b</sup>	0.58	-1.00 <sup>a</sup>	0.58	0.008*
		Baseline - 3 Months	-3.43 <sup>b</sup>	0.98	-3.29 <sup>b</sup>	0.49	-1.43 <sup>a</sup>	0.53	0.001*
	With Pt Education (Subgroup A)	Baseline - 1 Month	-2.14 <sup>b</sup>	0.69	-2.29 <sup>b</sup>	0.95	-0.71 <sup>a</sup>	0.76	0.007*
		Baseline - 2 Months	-2.57 <sup>b</sup>	0.53	-2.86 <sup>b</sup>	1.68	-1.29 <sup>a</sup>	0.95	0.046*
		Baseline - 3 Months	-3.00 <sup>b</sup>	0.58	-3.57 <sup>b</sup>	1.13	-1.57 <sup>a</sup>	0.79	0.005*

Means with the same letter within each row are not significantly different at p=0.05.

\*= Significant, NS=Non-significant

**B. Difference between tested Subgroups in the mean change in Probing Pocket Depth (mm)**



**FIG. 4: HISTOGRAM OF THE MEAN CHANGE IN PROBING POCKET DEPTH FOR THE DIFFERENT TESTED SUBGROUPS.**

**4. Clinical Attachment Level (mm):**

**B. Difference between tested Subgroups in the mean change in Clinical Attachment Level (mm)**

Without Patient Education (B)

Group II produced the highest mean change in Clinical Attachment Level (mm) followed by Group I followed by Group III after 1 month with a significant difference between the three groups. After 2 months; Group II and Group I produced a

significantly higher mean change in Clinical Attachment Level (mm) compared to Group III with an insignificant difference between group I and II. After 3 months; Group II produced the highest mean change in Clinical Attachment Level (mm) followed by Group I followed by Group III with a significant difference between the three groups. **(Table 5)**

**With Patient Education**

After 1 month and 2 months; Group II and Group I produced a significantly higher mean change in Clinical Attachment Level (mm) compared to

Group III with an insignificant difference between group I and II. After 3 months; Group II produced the highest mean change in Clinical Attachment

Level (mm) followed by Group I followed by Group III with a significant difference between the three groups. (Table 5)

TABLE 5: MEAN AND STANDARD DEVIATION (SD) OF CLINICAL ATTACHMENT LEVEL FOR THE DIFFERENT TESTED GROUPS.

Change in Clinical Attachment Level (mm)	Without Patient Education (Subgroup B)	With Patient Education (Subgroup A)	Group						p-value	
			Group I		Group II		Group III			
			Mean	SD	Mean	SD	Mean	SD		
	Baseline - 1 Month	Baseline - 2 Months	Baseline - 3 Months	-1.86 <sup>b</sup>	1.07	-2.14 <sup>c</sup>	0.38	-0.29 <sup>a</sup>	0.49	0.002*
				-2.43 <sup>b</sup>	0.79	-2.71 <sup>b</sup>	0.95	-0.57 <sup>a</sup>	0.53	0.001*
				-2.71 <sup>b</sup>	1.38	-3.43 <sup>c</sup>	0.79	-1.29 <sup>a</sup>	0.49	0.003*
	Baseline - 1 Month	Baseline - 2 Months	Baseline - 3 Months	-1.57 <sup>b</sup>	0.53	-2.14 <sup>b</sup>	0.90	-0.43 <sup>a</sup>	0.79	0.007*
				-2.71 <sup>b</sup>	1.11	-3.29 <sup>b</sup>	0.95	-1.14 <sup>a</sup>	0.38	0.003*
				-2.43 <sup>b</sup>	0.79	-4.43 <sup>c</sup>	1.51	-2.00 <sup>a</sup>	0.82	0.003*

Means with the same letter within each row are not significantly different at p=0.05.

\*= Significant, NS=Non-significant

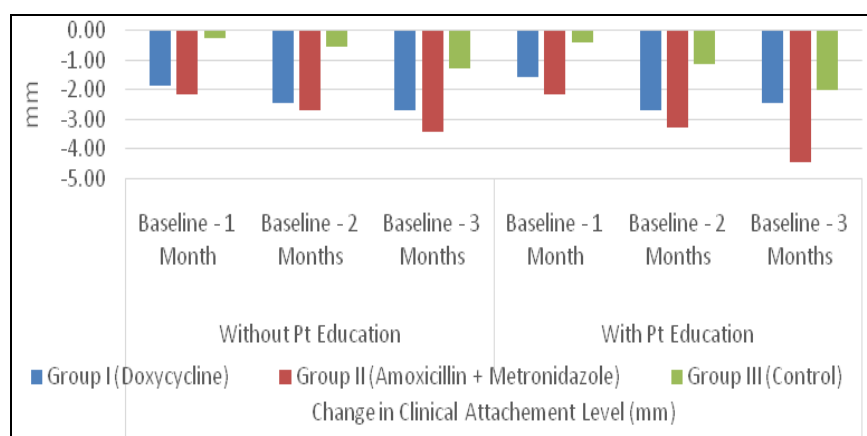


FIG.5: HISTOGRAM OF THE MEAN CLINICAL ATTACHMENT LEVEL FOR THE DIFFERENT TESTED GROUPS.

A. Difference between tested Subgroups in the mean change in Clinical Attachment Level (mm)

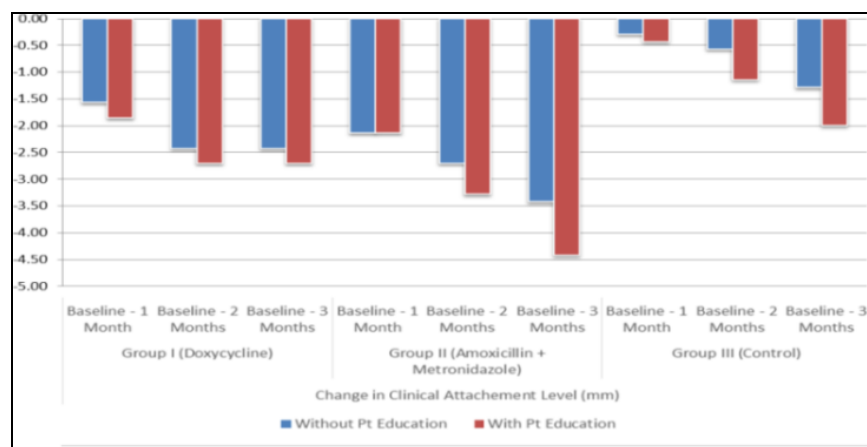


FIG. 6: HISTOGRAM OF THE MEAN CHANGE IN CLINICAL ATTACHMENT LEVEL FOR THE DIFFERENT TESTED SUBGROUPS.

**DISCUSSION:** WHO data show that periodontal diseases are common and comprise a serious health problem, for example, in many developing countries.<sup>33</sup> The prevalence of periodontitis in an adult population is 10–15%, independently of

ethnicity and geographic location.<sup>34</sup> Destructive periodontal disease is a concern because of the potential damage to the dentition and the financial burden of treatment.<sup>35</sup> Although the main established standard in periodontal therapy,



irrespective of the stage and severity of periodontal infection, is the mechanical debridement of the plaque and prevention of its accumulation, in some clinical cases professional SRP is not always successful.<sup>20, 36, 37</sup> This is because instrumentation inevitably leaves behind significant numbers of microorganisms, including putative pathogens.<sup>38</sup> The use of antibiotics as an adjunct to nonsurgical periodontal therapy may thus enhance the clinical outcome of treatment and may, in addition, reduce the need for subsequent surgical intervention.<sup>39</sup>

Periodontitis patients may benefit from systemic antibiotics, topical antibiotics and topical antiseptics. However, therapeutic success or failure depends not only on the intrinsic antimicrobial activity of chemotherapeutics but also on the clinical status of the patient (important with bacteriostatic drugs), the presence of foreign material (may include subgingival calculus) and the location of the infection (base of deep periodontal pockets and furcations that may be difficult to reach by topical therapy).<sup>40</sup>

Studies show that the adjunctive use of antibiotics is more cost effective when administered systemically versus local delivery at the periodontal defect.<sup>41</sup> Furthermore, in clinical cases where antibiotics are indicated, it is recommended that the agents be used as an adjunct to SRP rather than alone.<sup>42</sup>

Systemically administered antibiotics penetrate the periodontal tissues and the pocket via serum. There they can reach the microorganisms which are inaccessible to scaling instruments and local antibiotic therapy.<sup>43</sup> Systemic antibiotic therapy is therefore advantageous for the eradication and prevention of infections by periodontal pathogenic bacteria that invade the periodontal tissues.

Early approaches to systemic antibiotics in periodontal treatment included mainly single drug therapies with tetracyclines, penicillins, metronidazole or clindamycin. Tetracyclines, including doxycycline and minocycline, are active against important periodontal pathogens and they also have anti-collagenase properties and can reduce tissue destruction and bone resorption.<sup>44-46</sup> Since periodontitis lesions often harbor a mixture

of pathogenic bacteria, drug combination therapies have gained increasing importance.<sup>43</sup> In a combination treatment, antibiotics can be more effective displaying either an additive effect, i.e. an effect equal to the sum of the treatments, or a synergistic effect, i.e. an effect greater than the sum of the treatments. A combination of two antibiotics can also be antagonistic, with the effect of the combination treatment being less than the effect of the respective single-drug treatments.<sup>47</sup> One major benefit of combination therapies is that they reduce development of drug resistance, since a pathogen is less likely to have resistance to multiple drugs simultaneously administered. In addition, polytherapy causes lower treatment failure rate as well as lower case-fatality ratios.

Metronidazole was found to be effective, when combined with *amoxicillin*, in patients suffering from aggressive periodontitis.<sup>48</sup> In a recent study, Guerrero et al.<sup>36</sup> clearly demonstrated that the systemic administration of a combination of metronidazole and amoxicillin, in conjunction with nonsurgical treatment of aggressive periodontitis, significantly improved clinical results for a period of six months.

The maintenance of optimum oral health is dependent on the efficacy of oral self-care. The goals of periodontal therapy couldn't be achieved without the implementation of proper oral hygiene measures. Patient's motivation and upholding a good oral regime is a fundamental step in the therapy. This emphasizes the importance of providing oral health education and promotion programs for periodontal disease patients.

Being a crucial member of healthcare team the clinical pharmacist can promote patient care by interacting with periodontists and patients. As clinical pharmacists have the precise knowledge about therapeutics and are regularly interacting with prescribers, they are ideally placed to bridge the gap between patients and periodontists.<sup>49</sup> Through knowledge of the dental health issues and providing oral and dental patient education the pharmacist is given another means of making a major contribution to improving quality of life for all those being served.<sup>28</sup>

This study was designed to assess the clinical outcome of the administration of Doxycycline compared to a combination of Amoxicillin and Metronidazole as an adjunct to SRP in chronic periodontitis treatment and to investigate the impact of patient education as a contribution of the clinical pharmacist in the treatment of chronic periodontitis.

In our study clinical periodontal parameters including PI, GI, PD and CAL were assessed to determine the clinical periodontal status in patients of the three groups. This was in accordance with Vernal et al. (2005)<sup>50</sup>; Pradeep et al. (2009)<sup>51</sup> and Schenkein et al. (2010)<sup>52</sup> who used these parameters to assess the periodontal status.

The results of our study showed that there was an obvious improvement in all clinical parameters at one, two and three months after therapy in the three groups. This may be related to the fact that the initial non-surgical mechanical therapy has proven to be effective in reducing the bacterial load, thus resulting in clinical improvement. Similarly, Chapple et al. in (2007)<sup>53</sup> obtained a significant reduction in PD and sites of BOP following nonsurgical therapy. Also the results of Perry and Beemsterboer (2007)<sup>54</sup> showed a reduction in both gingival inflammation and PD, leading to a gain of CAL following SRP in most periodontal patients. Moreover, Grant et al. in (2010)<sup>55</sup> confirmed the success of non-surgical periodontal therapy by observing reduction in PD.

When the clinical parameters of our groups were compared at baseline there were no significant differences. Randomized controlled trials by Guerrero et al. (2005)<sup>36</sup>, Matarazzo et al. (2008)<sup>48</sup> and Silva et al. (2011)<sup>56</sup> have used mean changes in PD or CAL in deep sites as the primary outcome variable in testing different periodontal treatments, similarly in our study the mean changes in the four clinical parameters from their baseline values were compared among the three groups at one, two and three months after the initiation of therapy.

Our results revealed that systemic antibiotics combined with SRP offer additional clinical improvements compared to SRP alone. Patients receiving doxycycline and patients who took the

combination therapy of amoxicillin and metronidazole as an adjunct to SRP had a statistically significant greater reduction in PD and gain in CAL than those receiving SRP only at most time points. When the two antibiotic treatments were directly compared, no statistically significant differences were detected at most points. However, a tendency towards overall greater benefits for the combination therapy of amoxicillin and metronidazole was observed. The clinical improvements in the combination therapy patients were more pronounced over those of doxycycline patients for all parameters evaluated.

The clinical superiority of metronidazole and amoxicillin for reducing pocket depth was also observed in previous studies.<sup>36, 48, 57-60</sup> The decrease in deep PD values is thought to be due to the effect of this combination on periodontal pathogens.<sup>36, 57, 58</sup> The decrease in PD prevents the progress of the disease and effectively protects and maintains periodontal health.<sup>36, 57, 58</sup> The findings of our study are thus consistent with those of these studies.

To the best of our knowledge, this is the first study to highlight the role of clinical pharmacist in improving oral and dental health. In order to do this the clinical parameters were compared between the subgroups of each group, where the patients received the same treatment and the presence or absence of patient education provided by the clinical pharmacist was the only variable. Our results showed better overall clinical outcomes for the subgroups who received patient education with significant difference at some points.

**CONCLUSION:** Within the limits of the current study, it can be concluded that the adjunctive use of antibiotics had a significant effect on enhancing the clinical outcomes of therapy in chronic periodontitis patients. The combination therapy of amoxicillin and metronidazole at a dose of 750 mg/day for eight days offered overall greater benefits for all clinical parameters evaluated. The clinical results for the patients who received patient education were more promising than those of patients who received periodontal treatment only.

**RECOMMENDATIONS:** Further longitudinal studies with larger sample size and with the

observation of both clinical and microbiological activities are recommended.

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