

## **HYBENX oral tissue decontaminant efficacy as an adjunctive treatment for periodontal disease (Clinical and Microbiological Study)**

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### **Abstract**

**Background:** This study evaluates the microbiological and clinical effect of HYBENX gel as adjunct to mechanical therapy in moderate Periodontitis patients and comparing this effect with scaling and root planning (SRP) only.

**Materials and Methods:** Forty moderate periodontitis patients (16 females, 24 males, age: from 30 to 60 years old) were involved in the study. They were divided into 2 groups randomly. First group composed of 20 patients who received SRP associated with the subgingival application of HYBENX (EPIEN Medical, Inc. St. Paul, MN, USA) and second group composed of 20 patients who received SRP only. Local drug delivery was applied once weekly for six weeks. All patients were evaluated clinically by measuring periodontal parameters (plaque index, gingival index, probing pocket depth and clinical attachment level), and microbiologically by culturing plaque samples anaerobically for detection of total bacterial count, *p.gingivalis* and *p.intermedia* counts at baseline and six weeks after periodontal treatment.

**Results:** Both groups showed a significant improvement in tested clinical and microbiological parameters as compared to baseline. However there was significant difference in clinical measures (PI, GI, and PPD) and the microbiological parameters (total bacterial count, *Porphyromonas gingivalis* and *Prevotella intermedia* count) when comparing between groups.

**Conclusion:** HYBENX gel in addition to SRP showed significant improvement clinically and microbiologically when compared to SRP alone.

**Keywords:** Chronic periodontitis. HYBENX gel. Local delivery. Conventional periodontal therapy.

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### **I. Introduction**

Periodontitis is a chronic inflammatory condition of the supporting tissues of the teeth, characterized by alveolar bone resorption and soft tissue attachment loss. Dental plaque, which contains pathogenic bacteria is considered to be the main etiologic factor.(1)

For the treatment of chronic periodontitis, non-surgical periodontal therapy is regarded the gold standard. It mainly consist of dental hygiene recommendations as well as mechanical supra/subgingival debridement (scaling and root planing).(2)

However, scaling and root planning (SRP) alone does not always induce pocket closure, particularly in deep pockets or inaccessible regions as sites related to multi-rooted teeth.(3)

Adjunctive therapies such as antibiotics, antiseptics, anti-inflammatory drugs, non-pharmacological agents as propolis, herbal products as *Moringa oleifera*, in addition, photodynamic therapy have been proposed to improve the efficacy of non-surgical periodontal treatment.(4, 5)

The focus of new pharmacological research on the treatment of diseases caused by biofilms has turned away from directly attacking the microorganisms with antibiotics or antiseptics toward destroying the biofilm's structure, resulting in the death of the bacteria it contains.(6)

A few years ago, HYBENX gel was introduced as an oral tissue decontaminant, which contains sulfonic/sulfuric acid solution. It has showed a characteristic of contact desiccant because it has a strong affinity for water.(7)

Its chemical action occurs as a result of interaction between water molecules and the sulphate group. The surface charge of a sulphate group is strongly negative, whereas the surface charge of water molecules is positively charged on one side. The large negative surface of a sulphate group tends to link with the many positive surfaces of water molecules and become reversibly bound, forming hydrogen bonds, and thus acting as a strong desiccant.(8)

However, desiccation of water in the plaque biofilm matrix causes the matrix and microbes to coagulate and shrink. The biofilm material precipitates, contracts together and separates from the root surface, allowing eradication of plaque microbes.(9)

## **II. Patients and Methods**

### **Patient selection**

The present study included 40 patients of both genders (24 men and 16 females) ranging in age from 30 to 60 years old. According to the International Workshop for Classification of Periodontal Diseases and Conditions in 1999, they were diagnosed with chronic periodontitis. They were chosen from Mansoura University Faculty of Dentistry's Department of Oral Medicine, Periodontology, Diagnosis, and Oral Radiology. All patients' medical and dental histories, as well as periodontal charting, were obtained. Informed consent was obtained from each patient after explaining the steps, method, benefits and potential risks of the treatment and accepted to be enrolled as a participants in the study.

### **Inclusion and Exclusion criteria**

The inclusion criteria were age 30 -60 years, probing pocket depth (PPD)  $\geq$  4 mm with no previous antibiotic or periodontal treatment in the last 3months. Smoking, pregnancy and systemic diseases that potentially influence periodontitis progression or treatment response (e.g. Diabetes Mellitus) were all excluded from the study.

### **Study groups and treatment phase**

Forty patients with moderate periodontitis were divided into two groups: the first, consisting of twenty patients, was treated with HYBENX gel after scaling and root planning (SRP), and the second, consisting of twenty patients, was treated with SRP alone. The subgingival plaque sample and clinical parameters were taken from all patients before and after six weeks of treatment by the same periodontist. All patients in both groups received phase 1 therapy including scaling and root planning and oral hygiene instructions as basic treatment at first day. Full mouth SRP was completed within 15 days from the first day in two subsequent visits to confirm the complete removal of calculus that was not removed from the first session, using ultrasonic and hand instruments under local anesthesia if needed. After that HYBENX gel was injected into the selected periodontal pocket of all patients in group 1 once weekly for six weeks. Scaling and root planning was repeated for all patients in groups 2 once weekly with reinforced to maintain good oral hygiene in form of regular tooth brushing.

### **Application of HYBENX gel**

Gel was applied subgingival into the selected periodontal pocket by the use of the cannula attached to the delivery syringes of 1 ml each, the selected sites were isolated with cotton rolls and air dried then gel was applied slowly starting from the base of the pocket top ward until it reached the gingival margin, it was left in place to act for 45-60 seconds, and rinsed away by abundant water or saline irrigation to visualize white dehydrated superficial tissues. Gel application was performed once a week for six weeks. Patients were questioned about their experience after the gel application if there was any adverse effect or abnormal sensation.

### **Microbiological assessment**

Plaque samples were obtained at the beginning of this study and six weeks following therapy. Three different bacterial media were used to culture the samples quantitatively: first, brain heart infusion agar (Oxoid). Second, *Porphyromonas gingivalis* was detected using 5.0 ug/ml hemin added to brain heart infusion agar. Third, *Prevotella intermedia* was detected using 10 mg sulphamethoxazole and 0.5 mg trimethoprim per liter of blood agar. Inoculated plates were incubated at 37° C for 5 days under anaerobic conditions using an anaerobic jar and anaerobic gas packs (Oxoid) with catalyst.

### **Clinical assessment**

At baseline and after 6 weeks of therapy, the plaque index (PI), gingival index (GI), pocket probing depth (PPD), and clinical attachment level (CAL) were all measured.

### Statistical analysis

The statistical software IBM SPSS version 20.0 was used to analyze the data. After testing normality with the Shapiro- Wilk test, the mean and standard deviation were calculated for quantitative analysis. All tests were two-tailed, and the statistical significance of the obtained results is defined as a value at the 0.05 level. To compare two studied groups, a student t-test was utilized for parametric quantitative variables. To compare parametric continuous variables before and after treatment within the same group, use a paired t-test. Between clinical indices and laboratory data, Pearson correlation was used to correlate continuous parametric variables, with  $r$  more than 0.6 considered strong correlation.

## III. Results

### Clinical result

**Plaque index:** pre-treatment; there was no statistically significant difference between both studied groups with mean PI value was  $2.355\pm 0.23$  &  $2.51\pm 0.26$  for groups 1 & 2, respectively. Post-treatment PI showed statistically significant lower mean value among group 1 than group 2 ( $p=0.015$ ). Higher percent of improvement was detected among group 1 than group 2 (72.1% & 69.5%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (1) & Figure (1)

**Gingival index:** pre-treatment; there was no statistically significant difference between both studied groups with mean GI value was  $1.797\pm 0.164$  &  $1.759\pm 0.15$  for groups 1 & 2, respectively. Post-treatment GI showed statistically significant lower mean value among group 1 than group 2 ( $0.336\pm 0.064$  &  $0.583\pm 0.141$ , respectively) ( $p<0.001$ ). Higher percent of improvement was detected among group 1 than group 2 (81.3% & 66.9%, respectively) with statistically significant change between pre and post treatment values ( $p<0.001$ ). Table (1) & Figure (1)

**Pocket probing depth:** pre-treatment; there was no statistically significant difference between both studied groups with mean periodontal probing depth value was  $3.275\pm 0.313$  &  $3.250\pm 0.352$  for groups 1 & 2, respectively. Post-treatment periodontal probing showed statistically significant lower mean value among group 1 than group 2 ( $2.12\pm 0.416$  &  $2.560\pm 0.29$ , respectively) ( $p<0.001$ ). Higher percent of improvement was detected among group 1 than group 2 (35.3% & 21.2%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (1) & Figure (1)

**Clinical attachment level:** pre-treatment; there was no statistically significant difference in mean CAL values between the two groups tested, which were  $2.695\pm 0.339$  and  $2.69\pm 0.354$  for groups 1 and 2, respectively. There was no statistically significant difference in mean CAL values between the examined groups after treatment ( $p=0.788$ ). Higher percent of improvement was detected among group 1 than group 2 (29.7% & 28.3%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (1) & Figure (1)

### Microbiological results

**Total bacterial count:** pre-treatment; no statistically significant difference between both studied groups with mean value of total bacterial count was  $1226.05\pm 177.50$  &  $1240.5\pm 148.87$  for groups 1 & 2, respectively. Post-treatment total bacterial count showed statistically significant lower mean value count among group 1 than group 2 ( $495.26\pm 79.47$  &  $560.5\pm 90.35$ , respectively) ( $p=0.02$ ). Higher percent of improvement was detected among group 1 than group 2 (59.6% & 54.8%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (2) & Figure (2)

**Prevotella intermedia:** pre-treatment; no statistically significant difference between both studied groups with mean value of *P.intermedia* count was  $31.58\pm 6.75$  &  $30.20\pm 6.01$  for groups 1 & 2, respectively. Post-treatment *P.intermedia* count showed statistically significant lower mean value count among group 1 than group 2 ( $4.84\pm 4.48$  &  $12.30\pm 2.45$ , respectively) ( $p<0.001$ ). Higher percent of improvement was detected among group 1 than group 2 (84.7% & 59.3%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (2) & Figure (2)

**Porphyromonas gingivalis:** pre-treatment; no statistically significant difference between both studied groups with mean value of *P.gingivalis* count was  $27.63\pm 6.91$  &  $27.70\pm 4.21$  for groups 1 & 2, respectively. Post-treatment *P.gingivalis* count showed statistically significant lower mean value count among group 1 than group 2 ( $2.63\pm 2.34$  &  $10.20\pm 2.75$ , respectively) ( $p<0.001$ ). Higher percent of improvement was detected among group 1 than group 2 (90.5% & 63.2%, respectively) with statistically significant change between pre and post treatment mean values ( $p<0.001$ ). Table (2) & Figure (2)

## IV. Discussion

HYBENX gel was utilized as an adjuvant to SRP in this study to treat patients with moderate periodontitis. It's a combination of sulfonic and sulfuric acids that dehydrates and denaturizes biofilms.(10)

A statistically significant improvement of both clinically and microbiologically tested parameters were noted in **group 1** (test group) when compared to their baseline values. This may be attributed to the fact that HYBENX

has a desiccating effect due to its acidic components rapidly extracting water from biofilm matrix. This may cause the biofilm matrices and microorganisms to coagulate and shrink, resulting in the death of bacterial cells. These findings were supported by **Isola et al.**, who evaluated the effect of HYBENX oral tissue decontaminant as an adjuvant therapy to SRP in patients with chronic periodontitis in a randomized controlled clinical trial. Clinical, microbiological and inflammatory mediators assessments were repeated at 15, 30, 60, 180, and 365 days after therapy and they found that the gel improved clinical parameters (PI, GI, PPD, and CAL) associated with decrease the levels of different bacteria from the orange and red complexes, including *T. forsythia*, *P. intermedia*, and *P. gingivalis*. When compared to SRP alone, the levels of pro-inflammatory cytokines such as TNF- $\alpha$  were lower.(11)

In a randomised clinical and microbiological study by **Lombardo et al.** They found that when HYBENX was used as an adjuvant to SRP in the periodontal pocket, the bacterial load in patients with moderate to severe chronic periodontitis decreased after three months, which is consistent with our findings. Furthering, they noted reduction of the gingival inflammation parameters including (PI, GI, and PPD) while the clinical attachment level (CAL) only minimal changes were found after 3 months of treatment.(12)

Additionally, the results of this study completely agree with the results described by **Lauritano et al.** who tested the effect of HYBENX gel on the microbiological parameters of 11 moderate periodontitis patients. They found a highly statistically significant reduction in red complex bacteria and overall bacteria loading, and concluded that HYBENX is an efficient adjuvant for eradicating bacterial loading in pockets of periodontitis patients.(10)

Concerning **group 2** (control group) the patients were treated by SRP only, clinically and microbiologically showed statistically significant improvement compared to the pre-treatment values. This may be due to SRP disrupt the subgingival plaque biofilm, allowing reduction of microorganisms and inflammatory mediators, then leading to resolution of gingival inflammation.(13)

The results were in agreement with **Predin et al.** who evaluated the effect of SRP both clinically and microbiologically in chronic periodontitis patients. After 3 months of therapy, they saw significant improvements in PI, GI, PPD, and CAL, as well as a slight drop in the levels of *P. gingivalis* and *P. intermedia*. However, the authors used Polymerase chain reaction (PCR) for microbial analysis.(14)

Our results came in agreement with **Doungudomdacha et al.** who reported a statistically significant improvement in clinical parameters (PD, PI and CAL) and the populations of all three species, *P.gingivalis*, *P.intermedia*, and *Actinobacillus actinomycetemcomitans*, decreased significantly after 3-6 months of SRP.(15)

In our study, there was a statistically significant difference between groups 1 and 2 in clinical parameters (PI, GI, and PPD). While regarding CAL, there was no statistically significant difference between both groups, but higher percent of CAL improvement was detected among group 1 than group 2. Concerning microbiological parameters (total bacterial count, *P.gingivalis* and *P.intermedia* count), there was a statistically significant difference between groups 1 and 2.

This could be explained by the role played by SRP in periodontal tissue improvement by removing subgingival plaque biofilm and calculus leading to reduction of the bacterial level without the ability to eradicate all the quantity. While in group 1 our results could be attributed to the additional anti-microbial (inhibitory and cidal) and cleaning properties provided by HYBENX that has high binding affinity for the water in the biofilm matrix and denaturing the bacteria's adhesion proteins that help them stick to the surface. So, destroys the biofilm attachment mechanisms to the underlying tissues and kills bacterial cells.(16, 17)

HYBENX gel could be a promising option as adjunctive therapy to SRP in treatment of moderate periodontitis patients and more research is needed to confirm its effect and potential benefits in treating other types of periodontal disease.

However, this study has some limitations like stinging sensation and local hypersensitivity following HYBENX application which may be due to response to sulfuric acid, which resulted in missing some of the participants during the study. In addition, it needs to be tested on a greater number of patients and for a longer period of time to derive final conclusions on the effectiveness of HYBENX as an adjunct in periodontal therapy.

## V. Conclusions

HYBENX gel in addition to SRP showed significant improvement clinically and microbiologically when compared to SRP alone, and could be considered as a promising adjunctive option to SRP in treatment of moderate periodontitis patients.

### Ethical consideration

The study methodology was authorised by the Mansoura Faculty of Dentistry's Ethics Committee under the number A09010720, and it was carried out in compliance with the 1975 Helsinki Declaration, as modified in 2013.

**Author’s contributions**

J.M.Y, U.M.S: designed the study, controlled all study procedures, wrote and edited the manuscript. M.A.D: wrote and analyzed the microbiological data. A.M.K: collected the clinical parameters and microbiological samples. All authors discussed the results and contributed to the final manuscript.

**Table (1): Clinical parameters before and after treatment among both studied groups**

		Group 1 n=20	Group 2 n=20	test of significance (Student t test)
<b>Plaque index (mean±SD)</b>	Before	2.355±0.23	2.51±0.26	t=1.89,p=0.07
	After	0.657±0.133	0.766±0.138	t=2.56,p=0.015*
	Paired t test	t=44.0 p<0.001*	t=36.97 p<0.001*	
	% of improvement	72.1%	69.5%	
<b>Gingival index (mean±SD)</b>	Before	1.797±0.164	1.759±0.15	t=0.742,p=0.463
	After	0.336±0.064	0.583±0.141	t=7.14,p<0.001*
	Paired t test	t=53.54,p<0.001*	t=54.29,p<0.001*	
	% of improvement	81.3%	66.9%	
<b>Periodontal probing depth (mean±SD)</b>	Before	3.275±0.313	3.250±0.352	t=0.238,p=0.813
	After	2.12±0.416	2.560±0.29	t=3.84,p<0.001*
	Paired t test	t=21.77,p<0.001*	t=11.63,p<0.001*	
	% of improvement	35.3%	21.2%	
<b>Clinical attachment level (mean±SD)</b>	Before	2.695±0.339	2.69±0.354	t=0.046,p=0.964
	After	1.895±0.393	1.93±0.424	t=0.271,p=0.788
	Paired t test	t=21.77,p<0.001*	t=11.63,p<0.001*	
	% of improvement	29.7%	28.3%	

t: Paired t-test p: p value for comparing between group 1 and 2 (Data was expressed using Mean ± SD)

Mean: mean value, SD: standard deviation, n: number of patients

\*: Statistically significant at p< 0.05

**Table (2): Total bacterial count, and counts of *P.intermedia* & *P. gingivalis* among study groups pre- and post-treatment**

		Group 1 n=20	Group 2 n=20	test of significance (Student t test)
<b>Total bacterial count mean±SD</b>	Before	1226.05±177.50	1240.50±148.87	t=0.488 p=0.628
	After	495.26±79.47	560.50±90.35	t=2.39 p=0.02*
	Paired t test	t=18.23, p<0.001*	t=19.49, p<0.001*	
	% of improvement	59.6%	54.8%	
<b>Bacterial count (PI) mean±SD</b>	Before	31.58±6.75	30.20±6.01	t=0.674,p=0.504
	After	4.84±4.48	12.30±2.45	t=6.49,p<0.001*
	Paired t test	t=16.50, p<0.001*	t=11.90, p<0.001*	
	% of improvement	84.7%	59.3%	
<b>Bacterial count (PG) mean±SD</b>	Before	27.63±6.91	27.70±4.21	t=0.038, p=0.970
	After	2.63±2.34	10.20±2.75	t=9.25, p<0.001*
	Paired t test	t=14.68, p<0.001*	t=17.25, p<0.001*	
	% of improvement	90.5%	63.2%	

t: Paired t-test p: p value for comparing between group 1 and 2 (Data was expressed using Mean ± SD)

Mean: mean value, SD: standard deviation, n: number of patients

\*: Statistically significant at p< 0.05

PI: *Prevotella intermedia* PG: *Porphyromonas gingivalis*  
Colony Forming Units (CFU) X 10<sup>3</sup>

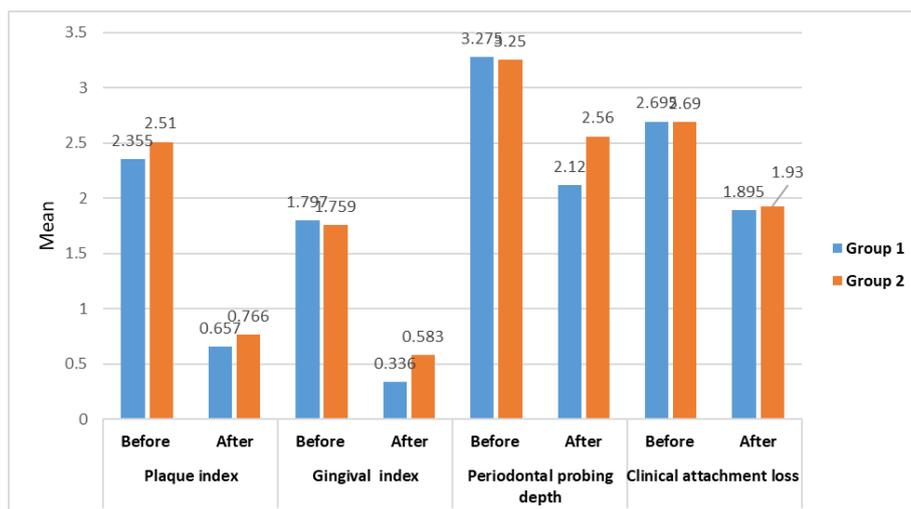


Figure (1): Clinical parameters before and after treatment among studied groups

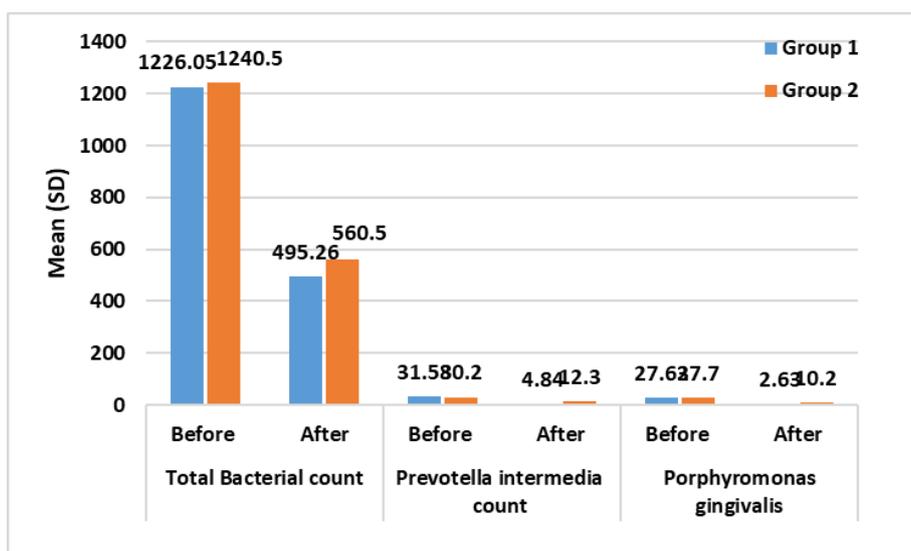


Figure (2): Bacterial count before and after treatment among studied groups

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