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EFFECT OF 1% ORNIDAZOLE AND 0.25% CHLORHEXIDINE GLUCONATE (ORNIGREAT™ GEL) IN THE TREATMENT OF CHRONIC PERIODONTITIS: A CLINICAL EVALUATION
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S. P Gautami, M. Anudeep, P. Arunbhupathi and G. Ramyateja

ABSTRACT

Objectives: **To evaluate the efficacy of sub-gingivally delivered combination of 1% Ornidazole and 0.25% chlorhexidine gluconate gel in the treatment of chronic periodontitis.**
Design: **A split mouth randomized controlled clinical trial**
Subjects: **25 patients diagnosed with moderate to severe periodontitis.**
Interventions: **The selected patients underwent non-surgical periodontal therapy i.e., scaling and root planing and the sites with probing depth ≥5mm were randomly divided into any of the two parallel treatment arms according to split mouth design by flip of a coin.**
Group A: **Scaling and Root planing followed by placement of Ornigreat gel and**
Group B: **Scaling and Root planing alone.**
Periodontal examination at baseline and at 4 weeks after non-surgical periodontal therapy included the assessment of Plaque index (Loe and Silness for plaque index), Gingival index (Silness and Loe for gingival index), Probing depth and Clinical attachment level.
Results: **Intergroup comparison of plaque index at baseline and 4 weeks revealed the p value 0.88 for test sites and control sites which was statistically non-significant.**
Intergroup comparison of gingival index at baseline and 4 weeks revealed the p value 0.05 for test sites and control sites which was statistically non-significant
Probing depths at baseline and 4 weeks during intergroup comparison revealed the p-value < 0.05 for test sites and control sites which was statistically significant.
Conclusion: **Within the limitations of the study, it can be concluded that the local application of combination of 1% ornidazole and 0.25% chlorhexidine (Ornigreat) gel as an adjunct to SRP reduces the periodontal inflammation compared to Phase-I therapy alone.**

INTRODUCTION

Periodontitis is one of the most common infection which is polymicrobial in nature due to its complex interaction with a variety of microorganisms and its host defense mechanisms involving the progressive destruction of gingiva, periodontal ligament, cementum and alveolar bone happens to be the major cause of tooth loss.

Although conventional mechanical therapy which includes traditional treatment modality of scaling and root planning remains the 'gold standard' for the management of periodontitis it however failed in reduction or elimination of anaerobic infection at the base of the pocket (1).

This is because of the reason that microorganisms travel into lacunar defects in the cementum, which further extend into space dentin can act as bacterial reservoirs from which re-colonization of mechanically treated root surfaces can occur. Such bacterial reservoirs that are not eliminated by conventional periodontal therapy can be further suppressed with the use of chemotherapeutic agents (2). Antibiotics can be used locally or systemically. Systemic antibiotics reach all the oral surfaces and fluids, in addition to having the potential to reach periodontal pathogens that eventually invade the host's tissues.

The disadvantages of systemic antibiotics over locally applied antibiotics include adverse drug reactions, uncertain patient compliance and lower concentration of the drug at sub-gingivalsites (3). However, the severest criticism of the indiscriminate use of systemic antibiotics is the development of bacterial resistance. Localized antimicrobial therapy, in particular, has evoked growing interest because of the site-specific nature of periodontal infections, the higher concentration of anti-microbial agent sub- gingivally and reduced side effects of systemic antibiotic use (3).

Various locally delivered chemotherapeutic agents available are: tetracycline fibres, metronidazole gel, minocycline ointment and minocycline microspheres, chlorhexidine chip, doxycycline hyclate, etc. (4-8). Nitroimidazole compound is one such agent that acts by inhibiting DNA synthesis. It works on the principle that inactive form passively diffuses into cell where it is activated by chemical reduction. The nitro group gets reduced to anion radicals which causes oxidation of DNA leading to strand breakage and cell death (9). Hence, it has both antimicrobial and mutagenic effect. This effect is primarily seen on obligate gram negative anaerobes like p. gingivalis, p. intermedia, Fusobacterium, selenomonassputig in a, Bacteroides for sythus and the gram-positive anaerobes like peptosteptococcus, c. rectus which are implicated in periodontal disease (10).

On the other hand, antiseptic agents like chlorhexidine have shown prolonged antiplaque action because of its wide spectrum of action against gram positive, gram negative bacteria and fungi, its substantivity (11), its ability to adsorb onto dental surfaces and desorb there from gradually (12), providing in effect, a timed release of the antimicrobial agent. It can be delivered in various forms such as mouth rinses, gels, sprays, toothpaste, varnish, chewing gum etc. (13).

Though many comparisons have been made to evaluate the efficacy of various locally delivered chemotherapeutic agents as an adjunct to scaling and root planning (srp) in the treatment of chronic periodontitis, there is dearth of literature available to evaluate the efficacy of sub-gingivally delivered combination 1% ornidazole and 0.25% chlorhexidine gluconate gel in the treatment of chronic periodontitis.

MATERIALS AND METHODS

A total of 25 patients, aged between 25 to 65years, who reported to the department of periodontics, Vishnu dental college and diagnosed with chronic generalized periodontitis were recruited for the study. Ethical clearance was obtained from the concerned Ethical committee of the institution. All patients received a detailed description of the proposed treatment and were asked to sign informed written consent. In this clinical trial 25 patients (10 females, 15 males) with chronic periodontitis were enrolled in the study. A total of 50 sites among the enrolled subjects were selected for the study. Each patient had at least three teeth with probing pocket depth of 5 to 8 mm that bled on probing at the initial visit. The selected patients should not have received local and/or systemic antibiotic therapy within the last 6 months prior to the baseline examination of the study.

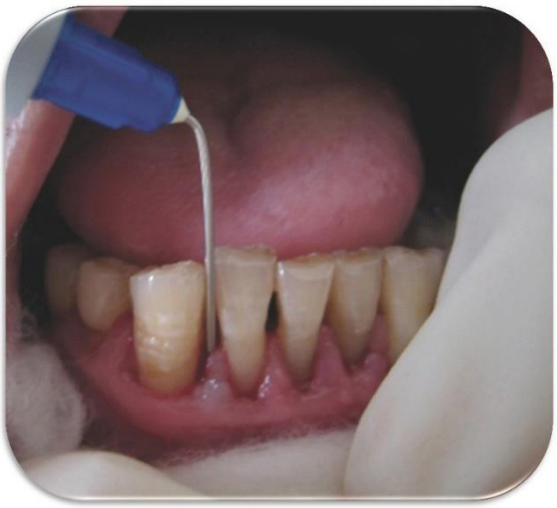
Before starting the trial all the patients underwent full mouth supra and sub-gingival srp using an ultrasonic scaler and curettes. They were given careful instructions for self-performed oral hygiene measures. The study was explained to patients and all patients signed informed consent at enrolment. The exclusion

criteria were history of any immunocompromised condition or chronic illness like diabetes, HIV infection, or those receiving radiotherapy or chemotherapy, pregnant, lactating females having overt hormonal disturbances, indication of periodontal disease that require surgical intervention. The selected qualifying sites were randomly divided into any of the two parallel treatment arms according to split mouth design by flip of a coin. Group A: Scaling and Root planing followed by placement of combination of 1% ornidazole and 0.25% chlorhexidine gluconate gel and Group B: Scaling and Root planing alone.

In group A, after isolating and drying the sites, the combination of 1% ornidazole and 0.25% chlorhexidine gluconate gel was injected into the periodontal pocket with a blunt needle without traumatizing or damaging the periodontal tissues and periodontal dressing was placed. (Figure-1)

Figure 1

Injecting Ornigreat gel into the periodontal pocket with a blunt needle



Periodontal examination at baseline and at 4 weeks after non-surgical periodontal therapy includes the assessment of Plaque index (Loe and Silness, 1964), Gingival index (Silness and Loe, 1963)

Bleeding index (Muhelmann h.r and son, 1971)

Probing pocket depth using graduated manual probe (HuFriedy UNC 15)

STATISTICAL ANALYSIS

Data collected were uploaded to a database. Mean & SD were calculated on each side. Intra and intergroup comparisons were conducted using the unpaired t-test and paired t-test respectively. Values of $p< 0.05$ were regarded as statistically significant.

RESULTS

PLAQUE INDEX:

Intragroup comparison of plaque index at different time periods revealed that the mean difference in gingival index score at baseline was 1.15±0.46 and 0.58±0.25 at 4 weeks for the test sites, which was statistically significant. The mean difference in plaque index score at baseline was 1.13±0.46 and 0.68±0.30 at 4 weeks for the control sites, which was statistically non-significant. (Table- 1).

Table 1

Intragroup comparison of periodontal parameters from baseline to 4 weeks

GROUPS	PARAMETERS	INTERVAL	MEAN±SD	P VALUE	S/NS
GROUP A (SRP+ORDINAZOLE)	GINGIVAL INDEX	BASELINE	1.13±0.48	<0.05	S*
		4 WEEKS	0.68±0.26		
	PLAQUE INDEX	BASELINE	1.15±0.46	<0.05	S*
		4 WEEKS	0.58±0.25		
	PROBING DEPTH	BASELINE	5.56±0.82	<0.05	S*
		4 WEEKS	3.20±0.76		
GROUP B (SRP ALONE)	GINGIVAL INDEX	BASELINE	0.91±0.30	<0.05	S*
		4 WEEKS	0.58±0.23		
	PLAQUE INDEX	BASELINE	1.13±0.46	<0.05	S*
		4 WEEKS	0.68±0.30		
	PROBING DEPTH	BASELINE	5.24±0.43	<0.05	S*
		4 WEEKS	4.08±0.81		

Intergroup comparison of plaque index at baseline and 4 weeks revealed the p value 0.88 for test sites and control sites which was statistically non-significant. (Table-2 & Figure- 2)

GINGIVAL INDEX

The mean difference in gingival index score, in intragroup comparison of gingival index at different time periods, at baseline was 1.13±0.48 and 0.68±0.26 at 4 weeks for the test sites, which was statistically significant whereas for control sites at baseline was 0.91±0.30 and 0.58±0.23 at 4 weeks, which was statistically non-significant (Table- 1). Intergroup comparison of gingival index at baseline and 4 weeks revealed the p value 0.05 for test sites and control sites which was statistically non-significant. (Table-2 & Figure-3)

Table 2

Intergroup comparison of periodontal parameters from baseline to 4 weeks

INTERVAL	PARAMETERS	GROUPS	MEAN±SD	P VALUE	S/NS
BASELINE	GINGIVAL INDEX	GROUP A	1.13±0.48	0.05	
		GROUP B	0.91±0.30		
	PLAQUE INDEX	GROUP A	1.15±0.46	0.88	NS
		GROUP B	1.13±0.46		
	PROBING DEPTH	GROUP A	5.56±0.82	0.09	NS
		GROUP B	5.24±0.43		

4 WEEKS	GINGIVAL INDEX	GROUP A	0.68±0.26	0.15	NS
		GROUP B	0.58±0.23		
	PLAQUE INDEX	GROUP A	0.58±0.25	0.23	NS
		GROUP B	0.68±0.30		
	PROBING DEPTH	GROUP A	3.20±0.76	<0.05	S*
		GROUP B	4.08±0.81		

NS= non- significant result, S = significant result.*

Figure 2

Graphical representation of comparison of plaque index at baseline and 4 weeks

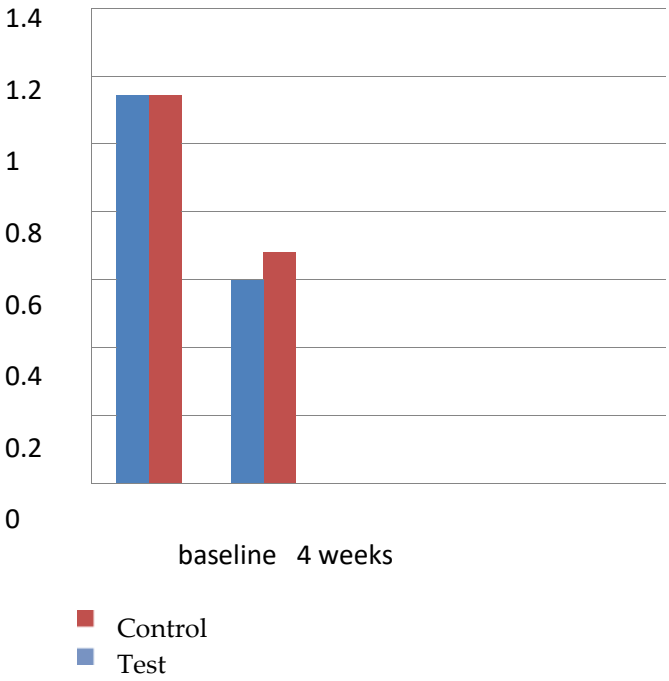
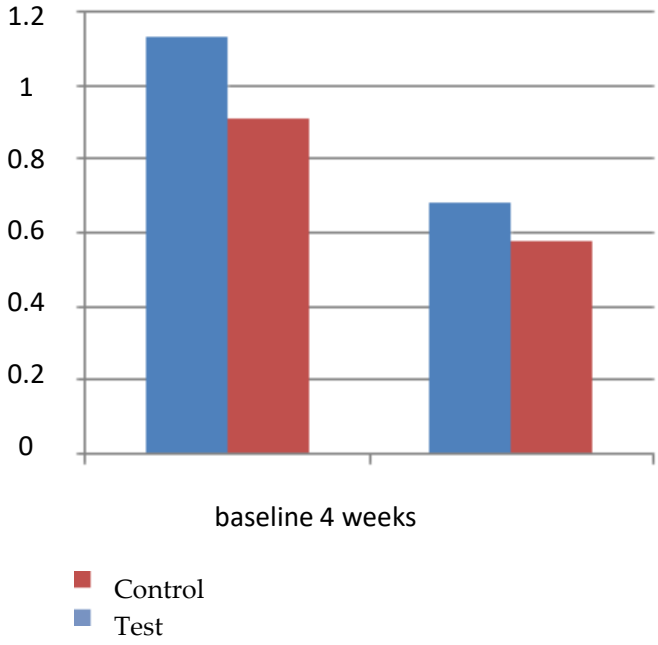


Figure 3

Graphical representation of comparison of gingival index at baseline and 4 weeks



PROBING DEPTHS

Probing depths at different time periods during intragroup comparison revealed that the mean difference in gingival index score at baseline was 5.56±0.82 and 3.20±0.76 at 4 weeks for the test sites, which was statistically significant (Figure-5) and for the control sites, at baseline was 5.24±0.43 and 4.08±0.81at 4 weeks, which was statistically non-significant.(Figure-6) (Table- 1) probing depths at baseline and 4 weeks during intergroup comparison revealed the p-value < 0.05 for test sites and control sites which was statistically significant.(Table-2), (Figure- 4).

Figure 4

Graphical representation of comparison of probing depths at baseline and 4 weeks

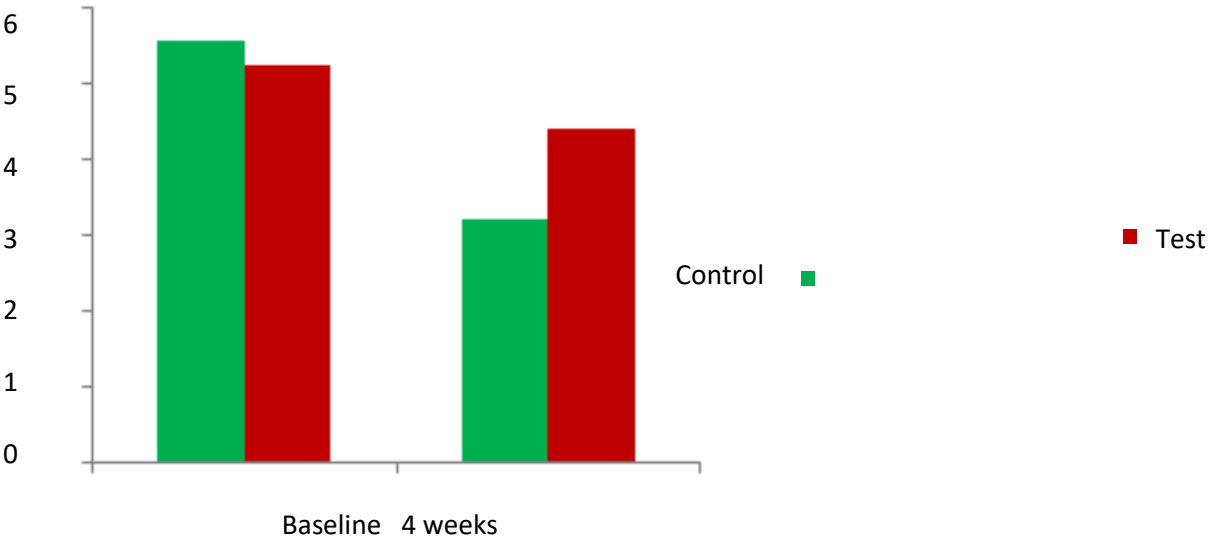


Figure 5

Comparison probing depths among SRP + Ornigreat gel introduced sites

a) Preoperative depth of about 6mm

b) Reduction of probing depth to 4mm after SRP + Ornigreat gel

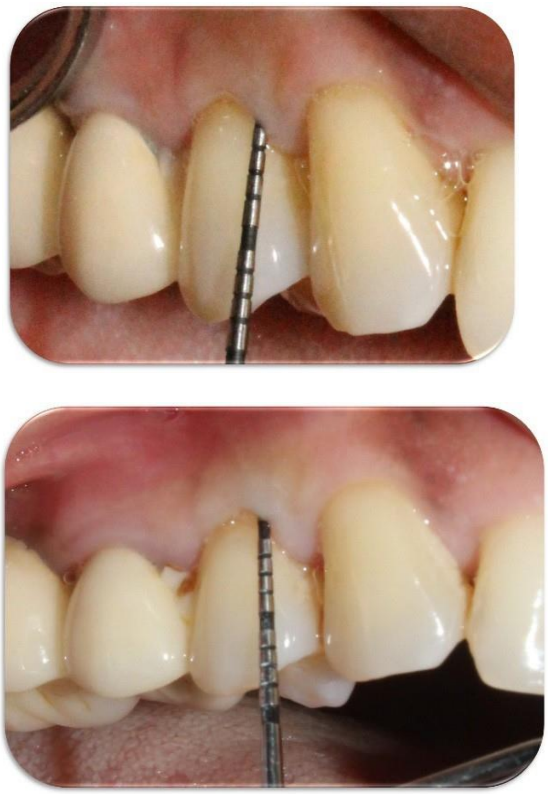
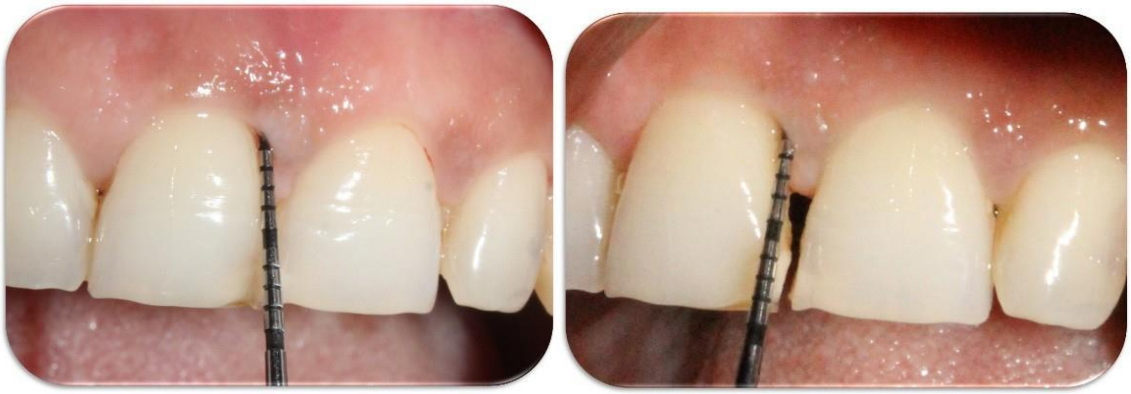


Figure 6

Comparison probing depths among SRP alone sites

a) Preoperative depth of about 6mm

b) Persistent probing depth of about 5mm after SRP



DISCUSSION

Successful periodontal therapy is dependent on procedures aimed at eliminating the pathogenic organisms that are found in dental plaque biofilm associated with tooth surface. The present study was conducted to evaluate the efficacy of the combination of 1% ornidazole and 0.25% chlorhexidine gluconate gel in the treatment of chronic periodontitis.

The subjects selected in this study presented with chronic generalized periodontitis and were randomly divided into test and control groups. Mechanical scaling and root planing (SRP) which is the traditional therapy for periodontal disease, eliminates the deposits from the tooth surface and shifts the pathogenic microbiota to one compatible with periodontal health (14-17). However, the pocket anatomy is a significant limiting factor in mechanical access, and sufficient reduction of the bacterial load is difficult to achieve (18). An increased interest in antibiotic therapy as an adjunct to standard periodontal treatment regime began in the late 1970's with the realization that certain bacteria are frequently associated with the disease process (10).

Thus, emerging evidence of bacterial specificity in certain types of periodontitis has led to treatment strategies, which are primarily aimed at suppression or elimination of specific periodontal pathogens (10). These therapeutic rationales rely heavily on systemic or local administration of anti-microbial agents. Since use of systemic antibiotics is associated with some disadvantages such as inability of systemic drugs to achieve high gingival crevicular fluid concentration (19), an increased risk of adverse drug reactions (20), increased selection of multiple antibiotic-resistant micro-organisms and uncertain patient compliance(21), the local administration of drugs is recommended (22).

Amongst the various antimicrobials used as local drug delivery agents, ornidazole is the most recent antimicrobial drug. Ornidazole specifically acts on gram negative anaerobic, facultative bacteria which are responsible for periodontal disease. Ornidazole requires a very low minimum inhibitory concentration to inhibit the growth of periodontal pathogens as compared to that of Metronidazole. The antimicrobial activity of ornidazole has been proposed due to the reduction of nitro group to a more reactive amine that attacks microbial DNA, inhibiting further synthesis and causing degradation of existing DNA (23-25).

On the other hand, combining ornidazole with chlorhexidine has shown prolonged antiplaque action, as chlorhexidine has a wide spectrum of action against gram positive, gram negative bacteria and fungi, its substantivity, its ability to adsorb onto dental surfaces and desorb there from gradually, providing in effect, a timed release of the antimicrobial agent. Although, the present study showed improvement in clinical parameters such as plaque index, gingival index and papillary bleeding index at test sites where combination of1% ornidazole and 0.25% chlorhexidine gel (Ornigreat) was used, the intergroup comparisons wherein Ornigreat gel at test sites and SRP alone at control sites were used was not statistically significant

. In the present study, there was no statistically significant difference in the mean plaque scores between two sites. These results correlate with the study done by Sato K et al (1993, 26), stating that scaling is effective in reducing gingival plaque. Also, in a study done by Patel B. 2014 in which ornidazole gel was used as an adjunct to scaling, there was no significant difference in mean plaque score between two sites (10).

On the other hand, in a study by Hungund S. (2010, 27), 1% metronidazole and 0.25% chlorhexidine gluconate (metrohex gel) was used as an adjunct to scaling in treatment of gingivitis and showed statistically significant difference in plaque index scores. In this study, there was no significant difference in gingival scores between two sites. These results correlate with the study done by Sato K. et al (1993, 26), stating that scaling is effective in reducing gingival plaque. The results concluded that scaling alone can improve the gingival status; however additional benefits can be obtained when antimicrobial gel is used as an adjunctive therapy as elicited by Hungund S. (2010, 27), wherein 1% metronidazole and 0.25% chlorhexidine gluconate (metrohex gel) was used as an adjunct to scaling in treatment of gingivitis and showed statistically significant difference in plaque index, gingival index and papillary bleeding index. Probing depths were significantly reduced in the test group compared to control group which correlates with the study by Radvar M. (1996, 28) and Kianan D. (1999, 29) wherein a six-month comparison of three periodontal local antimicrobial therapies in persistent periodontal pockets along with scaling was done and showed statistically significant improvement in gingival status compared to scaling alone. An adjunctive antimicrobial (Ornigreat gel™) treatment in this study produced greater improvement in clinical parameters than the other group without any adverse effects and was well tolerated by the

patients. The efficacy of this locally applied agent for the treatment of persistent periodontitis on long term basis needs further investigation.

CONCLUSION

Within the limitations of the study, it can be concluded that the local application of combination of 1% ornidazole and 0.25% chlorhexidine (Ornigreat™) gel as an adjunct to SRP reduces the periodontal inflammation compared to phase-i therapy alone. In certain periodontal inflammatory conditions where in standard scaling procedures don't give adequate results, the adjunctive use of Ornigreat™ gel can give desired beneficiary effect.

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