

## Comparative Evaluation of Sustained Release Collagen Device Containing 5% Metronidazole (Metrogene) along With and Without Scaling and Root Planing at Regular Intervals with Treatment of Chronic Periodontitis: A Case Control Study

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### Abstract:

**Background:** A short-term study was undertaken with an objective to demonstrate the therapeutic benefit resulting from the use of Metronidazole sponges combined with and without mechanical debridement to mechanical treatment alone in the treatment of periodontal pockets in chronic periodontitis.

**Materials and Methods:** The study compared the plaque index, gingival index, sulcus bleeding index and probing pocket depth in twenty control sites that received superficial scaling and root planing without the local drug delivery with experimental site A (20 sites that received local drug delivery (5% metronidazole) without superficial scaling and root planing) and experimental site B (20 sites received superficial scaling, root planing and local drug delivery (5% metronidazole) at "0" day, 15<sup>th</sup> day and 30<sup>th</sup> day.

**Results:** There was a significant reduction in plaque index, gingival index, sulcus bleeding index and probing pocket depth in both experimental sites A and B at different intervals from the baseline.

**Conclusion:** From the above conclusions, it can be suggested that a single subgingival application of 5% metronidazole in a collagen carrier can be effective, when associated with debridement in the treatment of adult periodontitis.

**Key Words:** Chronic periodontitis, collagen, drug delivery system, metronidazole, periodontal pocket

### Introduction

Periodontal diseases can be treated by both non-surgical and surgical therapy. With the evidence of the bacterial specificity in periodontal diseases,<sup>1</sup> the non-surgical therapy alone may fail to eliminate the pathogenic bacteria completely because of their location within gingival tissues or in deeper areas inaccessible to periodontal inflammation. To overcome this problem, nowadays a treatment protocol that include the usage of host modulation agents and antimicrobial agents is being tried as an adjunct to mechanical therapy in the treatment of periodontal diseases.

By the introduction of metronidazole, a nitromidazole compound developed in France to treat protozoal infections, started the new era of antimicrobial which has highly effective antibacterial spectrum covering most of the strict anaerobic and certain facultative anaerobic bacteria. It appears to be one of the most useful antimicrobials for the treatment of periodontitis.

Numerous controlled studies<sup>2-7</sup> have demonstrated that metronidazole applied locally or administered orally alone or in combination with mechanical debridement induces a significant reduction in the depth of the periodontal pockets. These positive results are also supported by systematic reviews.<sup>8-10</sup> This clinical improvement is often accompanied by a reduction in the number of anaerobic micro-organisms in the subgingival flora of the dental plaque.

Systemic administration of Metronidazole has shown to have several undesirable effects. Its usage in periodontal lesions has been today limited to local delivery. Several materials have been developed such as bioabsorbable films,<sup>11</sup> electrospun poly (l-lactide-co-d/l-lactide) fibers,<sup>12</sup> hollow fibres gels and dialysis tubes,<sup>13</sup> acrylic strips,<sup>2</sup> ethyl cellulose strips<sup>14</sup> and subgingival irrigations<sup>15</sup> to act as a device for the local administration of the antibacterial agent in order to avoid the need for systemic administration which is responsible for adverse effects, failure to comply with treatment and resistance.

5% metronidazole using natural bovine collagen<sup>6</sup> when in contact with human gingival crevicular fluid, rapidly forms unresorbable gel that is nonirritant as it is virtually devoid of

any immunogenicity. This preparation in the form of collagen sponges containing 5% Metronidazole with the trade name "metrogene" is intended to be inserted into the periodontal pocket.

Here, an attempt has been made to evaluate the efficacy of 5% metronidazole in collagen device on periodontal status with and without scaling and root planing in chronic periodontitis patients.

### Materials and Methods

Twenty volunteers complying to the inclusion criteria were selected from the Department of Periodontics, Royal Dental College, Chalissery, Kerala. Three sites having moderate periodontitis with more than 5 mm periodontal pocket were identified in them.

#### Criteria for patient selection

1. Both the sexes were included in the age range of 35-70 years
2. All the volunteers were free from any systemic disease
3. The volunteers had not received surgical or non-surgical therapy for the past 6 months
4. All the volunteers were asked to abstain from smoking or drinking alcohol during the study period
5. Pregnant women or nursing mothers were not included in the study.

Selected sites had periodontal pockets measuring equal to or >5 mm in different quadrants of the mouth. In each patient, three sites were selected.

1. Control site (these sites were treated by scaling and root planing without local drug delivery (5% metronidazole)
2. Experimental site A (these sites were treated by local drug delivery (5% metronidazole) without scaling and root planing)
3. Experimental site B (these sites were treated by scaling, root planing and local drug delivery (5% metronidazole).

Selected sites were subjected to baseline clinical examination which includes plaque index,<sup>16</sup> gingival index,<sup>17</sup> bleeding index<sup>18</sup> and measurement of probing pocket depth using William's graduated probe at 0, 15<sup>th</sup> and 30<sup>th</sup> day (pockets were probed on 0 and 30<sup>th</sup> day only).

At baseline after variable assessment, each patient received scaling and root planing. Metronidazole sponges on a collagen device were supplied in the form of square pieces. These sponges were administered to the apical limit of the pocket using a plastic spatula.

#### Observation with Discussion

Controlled delivery devices with solid supports have been used in resorbable or non-resorbable forms. However, the resorbable type has several advantages over non-resorbable

supports. Metronidazole sponges, the subject of the present application, therefore, appears to be a superior choice for the clinician over the other non-surgical modalities currently recommended for the treatment of periodontal diseases.

The clinical parameters like plaque index, gingival index and bleeding index were recorded at '0' day, 15<sup>th</sup> day and 30<sup>th</sup> day (Figures 1-6). However, the pocket depth was recorded on '0' day and 30<sup>th</sup> day. The results were statistically analyzed.



Figure 1: Control site: Clinical parameters – 15<sup>th</sup> day.



Figure 2: Control site: Pocket depth – 30<sup>th</sup> day.



Figure 3: Experimental site A: Clinical parameters – 15<sup>th</sup> day.

**Plaque index**

The mean reduction in plaque score between the control site, an experimental site A and experimental site B showed a significant reduction ( $P < 0.01$ ) overall (Table 1).

**Gingival index**

The mean reduction in gingival inflammation between the control site and experimental site A and experimental site B, showed a significant reduction ( $P < 0.001$ ) (Table 2).



**Figure 4:** Experimental site A: Pocket depth – 30<sup>th</sup> day.



**Figure 5:** Experimental site B: Clinical parameters – 15<sup>th</sup> day.

**Bleeding index**

The mean reduction in bleeding index between control and experimental site A and experimental site B showed a significant reduction ( $P < 0.001$ ) (Table 3).

**Probing pocket depth**

Comparison of probing pocket depth between control and experimental site A, did not show statistically significant differences in pocket depth on 0-30<sup>th</sup> day which is similar to the observations of Leeper *et al.*<sup>20</sup> who observed Metronidazole therapy was no more effective than root planing alone, where as it contradicts the findings the findings of Aziz Gandour *et al.*<sup>19</sup> and Lindhen *et al.*<sup>14</sup>

When it is compared between control and experiment site B, the difference was statistically highly significant, which is consistent with the findings of Aziz Gandour *et al.*<sup>19</sup> and Lindhen *et al.*<sup>14</sup>

The mean reduction in pocket depth between experimental site A and experimental site B shows a statistically highly significant difference which strongly supports the findings of Aziz Gandour *et al.*<sup>19</sup> and Hitzig *et al.*,<sup>6</sup> who observed a dramatic



**Figure 6:** Experimental site B: Pocket depth – 30<sup>th</sup> day.

**Table 1: Comparison of change in plaque score in different groups.**

Reduction in plaque score	Particulars	Reduction in plaque score					
		Control site A	Experimental site A	Control site B	Experimental site B	Experimental site A	Experimental site B
0-15 D	Mean	0.98	0.44	0.98	1.04	0.44	1.04
	SD	0.38	0.57	0.38	0.34	0.57	0.34
	i value	3.12		0.53		4.04	
	Significance	VS		NS		HS	
15-30 D	Mean	0.0	0.23	0.0	0.15	0.23	0.15
	SD	0.26	0.35	0.26	0.21	0.35	0.21
	i value	2.35		1.98			0.87
	Significance	S		NS		NS	
0-30 D	Mean	0.98	0.56	0.98	1.19	0.56	1.19
	SD	0.31	0.54	0.31	0.42	0.54	0.42
	i value	3.02		1.80		4.15	
	Significance	VS		NS		HS	

D: Day, HS: Highly significant ( $P < 0.001$ ), VS: Very significant ( $P < 0.01$ ), NS: Not significant, SD: Standard deviation

Table 2: Comparison of change in gingival index in different groups.

Reduction in plaque score	Particulars	Reduction in plaque score					
		Control site A	Experimental site A	Control site B	Experimental site A	Experimental site A	Experimental site A
0-15 D	Mean	0.95	0.40	0.95	1.10	0.40	1.10
	SD	0.31	0.42	0.31	0.37	0.42	0.37
	i value	4.35		1.40		5.54	
	Significance	HS		NS		HS	
15-30 D	Mean	0.09	0.36	0.09	0.30	0.36	0.30
	SD	0.38	0.42	0.38	0.21	0.42	0.21
	i value	2.13		2.14		0.57	
	Significance	S		S		NS	
0-30 D	Mean	1.04	0.76	1.04	1.43	0.76	1.43
	SD	0.29	0.44	0.29	0.35	0.46	0.35
	i value	2.39		3.86		5.2	
	Significance	S		HS		HS	

D: Day, HS: Highly significant, S: Significant, NS: Not significant, SD: Standard deviation

Table 3: Comparison of change in bleeding index in different groups.

Reduction in plaque score	Particulars	Reduction in plaque score					
		Control site A	Experimental site A	Control site B	Experimental site B	Experimental site A	Experimental site B
0-15 D	Mean	1.80	0.90	1.8	2.25	0.90	2.25
	SD	0.77	0.55	0.77	0.66	0.55	0.66
	i value	4.2		1.98		7.0	
	Significance	HS		NS		HS	
15-30 D	Mean	0.55	0.80	0.55	0.45	0.80	0.45
	SD	0.76	0.95	0.76	0.6	0.95	0.60
	i value	0.92		0.46		1.40	
	Significance	NS		NS		NS	
0-30 D	Mean	2.35	1.70	2.35	2.70	1.70	2.70
	SD	0.81	0.86	0.81	0.57	0.86	0.57
	i value	2.46		1.58		4.3	
	Significance	S		NS		HS	

D: Day, HS: Highly significant, S: Significant, NS: Not significant, SD: Standard deviation

Table 4: Pocket depth (mm) (within group comparison).

Sites	Particulars	0 D	30 D	Difference	% reduction
Control	Mean	5.95	5.05	0.90	15.1
	SD	0.89	0.90	0.72	
	i value			5.6	
	P value			<0.001	
Experimental site A	Mean	5.85	5.00	0.85	14.5
	SD	1.09	0.97	0.67	
	i value			5.7	
	P value			<0.001	
Experimental site B	Mean	6.45	3.90	2.55	39.5
	SD	1.00	0.97	0.60	
	i value			19.0	
	P value			<0.001	

P<0.001: Highly significant, D: Day, SD: Standard deviation

reduction in probing pocket depth after Metronidazole therapy along with mechanical debridement from 0<sup>th</sup> day to the end of the study.

Local administration of metronidazole along with root planing and no plaque control reinforcement in case of experimental site B appeared to be more effective in reducing pocket

depth than oral administration of metronidazole along with root planing and no plaque control. This can be attributed to a greater effectiveness of local delivery of metronidazole rather than its systemic administration in periodontal therapy (Tables 4 and 5).

### Conclusion

The major advantage of local application of antibacterial agents as a control release device form is to limit the drug to its target site and thus achieving maximum local concentration. Collagen appears to be a good resorbable support for the immobilization of various drug substances.

From the above study, it can be concluded that the subgingival application of 5% metronidazole in a collagen carrier can be more effective when associated with mechanical debridement in the treatment of chronic periodontitis. This observation is widely supported by several other previous studies done in this regard.

The local tolerance of the sponges, a rapidly resorbable and virtually non-immunogenic material, was excellent, and the

Table 5: Comparison of change in pocket depth in different groups.

Reduction in pocket depth from Day 0 to 30						
	Control site A	Experimental site A	Control site B	Experimental site B	Experimental site A	Experimental site B
Mean	0.90	0.85	0.90	2.55	0.85	2.55
D	0.72	0.67	0.72	0.60	0.67	0.66
i value	0.23		7.87		8.46	
P value	NS		HS		HS	

NS: Not significant, HS: Highly significant

risk of developing systemic adverse effects is very unlikely in view of the very small quantity of Metronidazole administered.

However, further studies with larger sample size and microbiological assays would be helpful in establishing a concrete inference of these results.

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