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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The study compared the plaque index, gingival index, sulcus bleeding index and probing pocket depth in both experimental sites A and B at different intervals from the baseline.

Results: There was a significant reduction in plaque index, gingival index, sulcus bleeding index and probing pocket depth at “0” day, 15th day and 30th day.

There was a significant reduction in the depth of the periodontal pockets. These positive results are also supported by systematic reviews. 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, electrospun poly (l-lactide-co-d/l-lactide) fibers, hollow fibres gels and dialysis tubes, acrylic strips, ethyl cellulose strips and subgingival irrigations 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 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 planning 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,16 gingival index,17 bleeding index18 and measurement of probing pocket depth using William’s graduated probe at 0, 15th and 30th day (pockets were probed on 0 and 30th 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 administrated 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, 15th day and 30th day (Figures 1-6). However, the pocket depth was recorded on ‘0’ day and 30th day. The results were statistically analyzed.
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).

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

| Reduction in plaque score | Particulars | 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                |
|                          | $t$ 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                |
|                          | $t$ 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                |
|                          | $t$ 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

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\textsuperscript{th} day which is similar to the observations of Leeper et al.\textsuperscript{20} who observed Metronidazole therapy was no more effective than root planing alone, whereas as it contradicts the findings of Aziz Gandour et al.\textsuperscript{19} and Lindhen et al.\textsuperscript{14}

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.\textsuperscript{19} and Lindhen et al.\textsuperscript{14}

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.\textsuperscript{19} and Hitzig et al.,\textsuperscript{6} who observed a dramatic...
reduction in probing pocket depth after Metronidazole therapy along with mechanical debridement from 0th 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 2: Comparison of change in gingival index in different groups. |
|---------------------------------------------------------------|
| **Particulars** | Control site A | Experimental site A | Control site B | Experimental site A | Control site B | 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 |
| \( t \) value | 4.35 | 1.40 | 4.35 | 5.54 | 1.40 | 5.54 |
| Significance | HS | NS | HS | NS | HS | NS |
| 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 |
| \( t \) value | 2.13 | 2.14 | 2.13 | 0.57 | 2.14 | 0.57 |
| Significance | S | S | S | S | NS | 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 |
| \( t \) value | 2.39 | 3.86 | 2.39 | 5.2 | 3.86 | 5.2 |
| Significance | S | HS | S | HS | 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. |
|---------------------------------------------------------------|
| **Particulars** | Control site A | Experimental site A | Control site B | Experimental site A | Control site B | Experimental site A |
|----------------|----------------|---------------------|----------------|---------------------|----------------|---------------------|
| 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 |
| \( t \) value | 4.2 | 1.98 | 4.2 | 7.0 | 1.98 | 7.0 |
| Significance | HS | NS | HS | HS | NS | HS |
| 15-30 D Mean | 0.55 | 0.80 | 0.55 | 0.45 | 0.55 | 0.45 |
| SD | 0.76 | 0.95 | 0.76 | 0.6 | 0.95 | 0.6 |
| \( t \) value | 0.92 | 0.46 | 0.92 | 1.40 | 0.46 | 1.40 |
| Significance | NS | NS | NS | 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 |
| \( t \) value | 2.46 | 1.58 | 2.46 | 4.3 | 1.58 | 4.3 |
| Significance | S | NS | S | NS | 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 (%) |
| Control | Mean | 5.95 | 5.05 | 0.90 | 15.1 |
| SD | 0.89 | 0.90 | 0.72 |
| \( t \) 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 |
| \( t \) 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 |
| \( t \) value | 19.0 |
| \( P \) value | <0.001 |

\( P<0.001: \) Highly significant, **D:** Day, **SD:** Standard deviation
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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