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Review Article

Evaluation of Different Local Drug Delivery Systems in Treatment of Periodontitis: An Institutional Study

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ABSTRACT

Periodontal disease can be treated in both non-surgical and surgical therapy. There could be a possible reason why non-surgical therapy causes failure due to bacteria virulent factors and also the depth of periodontal pocket is greater than the instrumentation available, drug concentration is low in GCF as well as in saliva. To overcome this problem a treatment protocol that would include short-term usage of systemic and or local antimicrobial agents is being tried as an adjunct to mechanical therapy in treatment of periodontal diseases. A total of 540 sites, from 72 patients in different quadrants of the mouth received these treatment modalities in assigned quadrants such as scaling and root planning using both hand and ultrasonic instruments under local anesthesia (if required), combination therapy and local drug delivery alone. Patients with periodontal diseased sites were divided into five groups, based on the local drug delivery system, as Group I: Elyzol (25% Metronidazole), Group II: Dentomycin (2% Minocycline hydrochloride), Group III: Metrogene (5% Metronidazole), Group IV: Periochip (2.5mg of Chlorhexidine gluconate) and Group V: Atridox (10% Doxycycline hyclate). In the present study, the bleeding index score showed better reduction, for all LDD systems. The results showed that SRP alone, and LDD alone had shown no significance in overall reduction of pocket depth where clinical parameters (Plaque Index, Gingival Bleeding Index and Gingival Index). Although the combined treatment of scaling and root planing plus the local drug therapy reported to have a significant benefit over SRP alone in the treatment of periodontal lesions.

Keywords: Anti-Bacterial Agents; Metronidazole; Minocycline; Doxycycline; Chlorhexidine; Local Drug Delivery Systems; Humans; Periodontitis; Periodontal Pocket; Root Planing

1 INTRODUCTION

Periodontal disease can be treated by both non-surgical and surgical therapy. With the evidence of bacterial specificity in periodontal disease, the non-surgical therapy alone may fail to eliminate the pathogenic bacteria completely because of their location within gingival tissues or in deeper areas, impossible to periodontal instrumentation, leading to recurrence of periodontal inflammation. To overcome this problem a treatment protocol that would include short-term usage of systemic and or local antimicrobial agents is being tried as an adjunct to mechanical therapy in treatment of periodontal diseases.

A number of materials have been created to serve as a device for the local antimicrobial drug adversities in order to prevent the need for systemic delivery, which is accountable for unfavorable effects, failure to respond to therapy, and resistance. To overcome the considerable disadvantages of systemic antibiotic therapy, local delivery of antimicrobial agents into periodontal pockets has been extensively developed and interrogated since late 1970s. In 1979, Dr. Max Goodson was the main proponent and developer of the idea of medicinal agents that could be discharged under control, such as antimicrobials or anti-inflammatory agents. Most of the issues with systemic treatment are avoided with local drug administration. By keeping the medication at its intended location and preventing or greatly reducing systemic absorption. In comparison to what is attainable via the systemic route, the local concentration that is obtained can be significantly greater.

Studies undertaken by Van Stenberge et al 1993[1] and Graca et al 1997[2] reported that adjunctive Minocycline gel provides a more advantageous outcome for non-surgical periodontal treatment in terms of probing attachment level and probing depth reduction. Ainamo J et al 1992[3] and Klinge et al 1992[4] with Metronidazole 25% dental gel when compared to SRP indicated that it resulted in a significant reduction in probing depth and other clinical parameters. Soskolne WA et al 1997[5] and Jeffcoat et al 2000[6] showed 205 mg CHX gelatin chip when compared with mechanical therapy, better reduction in probing depth and CAL. Hitzig et al 1994[7] reported high clinical efficacy of 5% metronidazole in a collagen device in the treatment of periodontal diseases. Poslon et al 1997[8] when compared to sanguinarine indicated that 10% doxycycline hyclate is an effective means of reducing the clinical signs of adult periodontitis and exhibited a benign safety profile. Garret et al 1999[9] when compared to SRP indicated that 10% doxycycline is equally effective as SRP in reducing the clinical sign of adult periodontitis.

In this compilation of single center study, Scaling and Root Planing, Local Drug delivery and combination of SRP with LDD have been presented. The use of local drug delivery with and without SRP included Elyzol (25% Metronidazole), Dentomycin (2% Minocycline hydrochloride), Metrogene (5% Metronidazole), Periochip (2.5mg of Chlorhexidine gluconate) and Atridox (10% Doxycycline hyclate).

However, to date there has been no report assessing the comparative efficacy of a number of currently marketed systems using the distributors recommended protocol on periodontal diseased sites. We report here the baseline to 6 months results of an investigation into the effect of five commercially available local antimicrobial delivery systems on the clinical parameters of sites with periodontal lesions.

The various LDD materials available in the market makes the clinician question the selection of LDD for the periodontal treatment. Usually, there are studies related to each LDD or combination of two materials. There are no studies to compare more than two LDD materials.

Considering this paucity of literature, we have the current review paper which provides insight on {Elyzol (25% Metronidazole), Dentomycin (2% Minocycline hydrochloride), Metrogene (5% Metronidazole), Periochip (2.5mg of Chlorhexidine gluconate) and Atridox (10% Doxycycline hyclate)} LDD materials clinical efficacy in simple terms to assist the decision making of clinician. And, the main benefit of this review is being evaluated by the experienced clinician using similar methodology along with the parameters under one roof. Hence, this compilation project would provide relevant information for various LDD materials in the treatment of furcation.

1.1 Procedural Steps for Methods of Five LDD Agents

The subjects for this study were chosen from the single center, College of Dental Sciences, Davanagere outpatient periodontics department. A total of 72 patients both males and females in the age group of 30-70 years were considered.

1.1.1. Criteria for Patient Selection

- Inclusion criteria
  - Patients who were diagnosed as suffering from periodontitis
  - Patients selected should have periodontal pockets measuring $\geq$ 5 mm and $\leq$ 7 mm

In different quadrants of the mouth on clinical examination and with radiographic evidence of bone loss.

- Exclusion Criteria
- Patient who had the history of taking antibiotics or using antibacterial mouthwashes.
- Patients who have previously abused alcohol.
- Patient's known to be hypersensitive metronidazole, doxycycline, minocycline, tetracycline or chlorhexidine.
- Pregnant women or nursing mothers.
- Patients on drugs such as anticoagulants, lithium disulfiram, and anticonvulsants.
- Sites with furcation lesions.

A total of 540 sites from 72 individuals with periodontal disease measuring between $\geq$ 5 and $\leq$ 7 mm in different mouth quadrants were chosen.

1.2 Study Design

Patients with periodontal diseased sites were divided into five groups based on the local drug delivery system as Group I: Elyzol (25% Metronidazole) [Figure 1 a,b], Group II: Dentomycin (2% Minocycline hydrochloride) [Figure 2 a,b], Group III: Metrogene (5% Metronidazole) [Figure 3 a,b], Group IV: Periochip (2.5mg Chlorhexidine gluconate) [Figure 4 a,b] and Group V: Atridox (10% Doxycycline hyclate) [Figure 5 a,b].

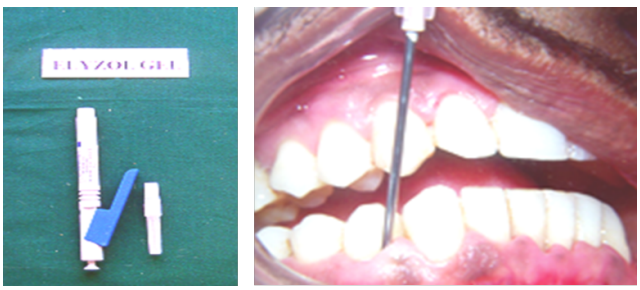

Fig. 1: a: Elyzol , b: Placement of 25% Metronidazole

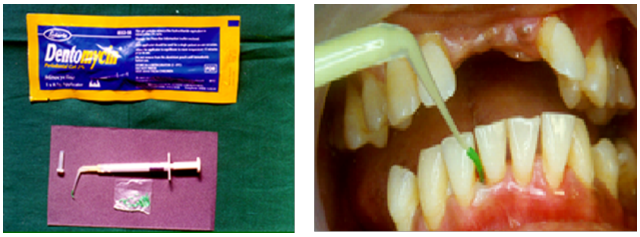

Fig. 2: a: Dentomycin , b: Placement of 2% Minocycline Hydrochloride

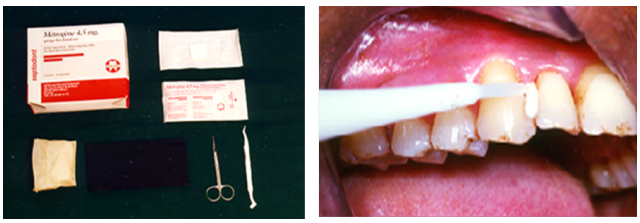

Fig. 3: a: Metrogene, b: Placement of 5% Metronidazole

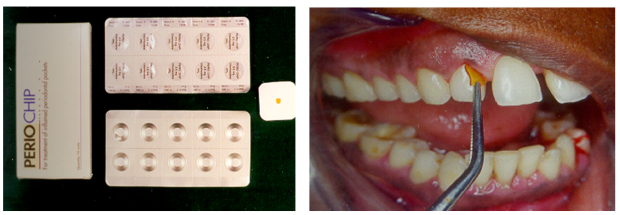

Fig. 4: a: Periochip, b: Placement of 2.5mg of Chlorhexidine gluconate

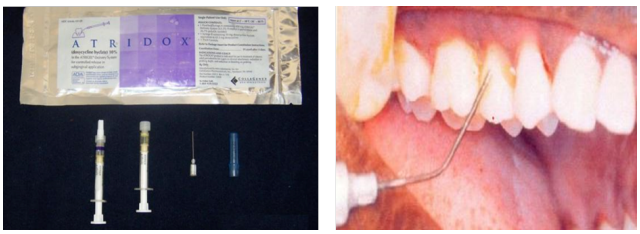

Fig. 5: a: Atridox, b: Placement of 10% Doxycycline hyclate

1.3 Subjects and Sites

All the 72 patients included in the study, completed the course of study. Patients fulfilling the inclusion criteria were informed of the study and gave informed consent. The selected sites received three different treatment modalities as SRP alone, SRP+ LDD and LDD alone.

1.4 Clinical Measurements

At the baseline visit and 6 months later following clinical parameters were measured by a single examiner. Customized acrylic stents were fabricated for the measurements of attachment levels. The plaque index (Silness & Loe 1964),[10] gingival index (Loe & Silness 1963),[11] Bleeding index (Ainamo and Bay 1975),[12] probing depth using UNC-15 manual probe and occlusal stents. The examiner was blind with respect to the antimicrobial system used in the study.

1.5 Treatment

A total of 540 sites, from 72 patients in different quadrants of the mouth received these treatment modalities in assigned quadrants such as scaling and root planning using both hand and ultrasonic instruments under local anesthesia (if required), combination therapy and local drug delivery alone. For each antimicrobial treatment the manufacturers or distributor recommendations were rigidly adhered to.

1.6 Statistical Analysis

For each treatment group, the 6 months probing depth and other parameters were subjected to unpaired 't' test.

2 RESULTS

Comparing the results between each treatment modalities for all local drug delivery system combination therapy was better for all parameters recorded as shown in Tables 1, 2 and 3.

The comparison of post-treatment plaque index changes for SRP alone, the Elyzol group had significant reduction compared to all the other groups. There was no significant difference between Dentomycine and Metrogene, Dentomycine and Atridox, Metrogene and Atridox groups in plaque score reduction from baseline to end of the study.

In the combination therapy (SRP + LDD) treatment group, Elyzol had significant plaque reduction compared to other groups. There was no significant difference in reduction of plaque scores, between Elyzol and Dentomycine, Metrogene and Atridox, and Metrogene and Atridox.

In the LDD alone group, Elyzol had significant plaque reduction, compared to other groups. There was no significant difference in plaque score reduction between Dentomycine and Atridox and Metrogene and Atridox.

For comparison of post treatment changes for bleeding index in SRP alone, the treatment group showed no significant difference between Elyzol, Atridox, Dentomycine and Periochip. The Metrogene group was found to show greater reduction from baseline to end of the study.

For combination therapy, the changes were not significant between Elyzol and Atridox. The Metrogene group showed better reduction compared to other groups.

For the LDD alone treatment group, there was no significant difference between Elyzol, Dentomycine, and Elyzol and Atricox. The Metrogene group showed better reduction compared to other groups.

The comparison of post-treatment changes in gingival index for SRP alone treatment group showed no difference

Table 1: SRP alone group

Plaque Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.83 ± 0.45	Between Dentomycine and Metronidazole, Dentomycine and Periochip, Metronidazole and Atridox	Between Elyzol and Periochip, Dentomycine and Periochip, Atridox and Periochip,
II	1.21 ± 0.57		
III	0.98 ± 0.31		
IV	0.38 ± 0.04		
V	1.14 ± 0.75		
Gingival Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.88 ± 0.36	Between Dentomycine and Metronidazole, Metronidazole and Atridox	Between Elyzol and Periochip, Atridox and Periochip, Metronidazole and Periochip
II	0.96 ± 0.56		
III	1.01 ± 0.29		
IV	0.35 ± 0.04		
V	1.32 ± 0.91		
Bleeding Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	0.95 ± 0.22	Between Elyzol and Atridox, Dentomycine and Periochip,	Between Metronidazole and Periochip, Metronidazole and Atridox, Atridox and Periochip
II	1.39 ± 0.89		
III	2.35 ± 0.81		
IV	0.49 ± 0.07		
V	0.84 ± 0.37		
Probing Depth			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.45 ± 0.74	Between Elyzol and Periochip, Metronidazole and Periochip,	Between Dentomycin and Atridox, Elyzol and Atridox, Metronidazole and Atridox, Periochip and Atridox
II	2.00 ± 0.37		
III	0.98 ± 0.72		
IV	1.15 ± 0.11		
V	0.06 ± 0.31		

between Dentomycine and Metrogene, Metrogene and Atridox. The Elyzol showed better reduction from baseline to 6 months.

For combination therapy, there was no significant difference between Elyzol and Dentomycine, Elyzol and Metrogene, Dentomycine and Atridox, Metrogene and Atridox. The Metrogene showed better reduction.

For the LDD alone treatment group, there was no significant difference between Dentomycine and Metrogene, Metrogene and Atridox. The Elyzol group showed better reduction.

The comparison of post treatment changes probing depth for SRP along the treatment group showed no difference between Elyzol and Periochip, Metrogene and Periochip. The Denotmycine group showed better reduction.

For combination therapy, there was no significant difference between Dentomycine and Metrogene. The Metrogene group showed better reduction.

For the LDD alone treatment group, there was no difference between Elyzol and Dentomycine, Dentomycine and Metrogene, Metreogene and Perochip, Elyzol and Metrogene. The Dentomycine group showed better reduction from baseline to 6 months.

3 DISCUSSION

The parallel design study evaluated the clinical response to five local drug systems of antimicrobials as adjunct SRP. The participants in this study were treated for chronic periodontal disease using quadrant SRP under local anesthesia except for the LDD alone group.

All treatment modalities used in this study including SRP alone resulted in a significant probing depth reduction and other parameters.

Table 2: SRP + LDD

Plaque Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.28 ± 0.47	Between Elyzol and Dentomycine, Dentomycine and Metronidazole, Metronidazole and Atridox, Elyzol and Metronidazole, Elyzol and Atridox	Between Elyzol and Periochip, Dentomycine and Periochip, Metronidazole and Periochip, Atridox and Periochip
II	1.24 ± 0.54		
III	1.19 ± 0.42		
IV	0.63 ± 0.06		
V	1.12 ± 0.68		
Gingival Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.36 ± 0.44	Between Elyzol and Dentomycine, Elyzol and Metronidazole, Dentomycine and Atridox, Metronidazole and Atridox	Between Metronidazole and Periochip, Elyzol and Periochip, Atridox and Periochip
II	1.19 ± 0.42		
III	1.93 ± 0.35		
IV	0.57 ± 0.84		
V	1.20 ± 0.94		
Bleeding Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	0.85 ± 0.36	Between Elyzol and Atridox	Between Metronidazole and Periochip, Metronidazole and Atridox, Metronidazole and Elyzol, Dentomycine and Periochip
II	1.48 ± 0.91		
III	2.70 ± 0.87		
IV	0.67 ± 0.05		
V	0.86 ± 0.35		
Probing Depth			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.40 ± 0.73	Between Dentomycine and Metronidazole	Between Elyzol and Atridox, Dentomycin and Atridox, Metronidazole and Atridox, Periochip and Atridox
II	2.41 ± 0.49		
III	2.55 ± 0.60		
IV	2.00 ± 0.11		
V	0..22 ± 0.42		

Previous study comparing these local antibiotic therapies by Radvar M et al 1996 [13] which was a parallel design study stated significant improvement in clinical parameters in all these adjunctive treatment groups than the scaling and root planing alone group. In his study, the treatment regimen of SRP plus tetracycline fiber replacement gave the greatest advantage in the treatment of periodontal lesions during a 6 week period. The present study did not use the tetracycline fiber system.

In the present study, the bleeding index score showed better reduction, for all LDD systems. The scores in descending order are Metrogene, Dentomycine, Atridox, Elyzol and Periochip for combination therapy (SRP + drug). Similar results were shown by the SRP alone and LDD alone treatment modalities. For combination therapy (SRP and LDD), the reduction in gingival index are in the descending order such as Elyzol, Atridox, Metrogene, Dentomycine, and Periochip. The probing depth reduction was significantly greater in the Dentomycine group in case of SRP alone and LDD alone. The results were in descending order as Dentomycine, Elyzol, Periochip, Metrogene and Atridox. In case of combination therapy, the order was Metrogene, Dentomycine, Perochip, Elyzol and Atridox.

The Periochip and Atridox showed least reduction in all parameters for all treatment modalities from baseline to 6 months.

All adjunctive antimicrobial treatments in this comparative study showed greater mean improvements in all clinical parameters. No drug showed better improvement for all parameters, each drug showed different improvement for various parameters.

A meta-analysis of various LDD used from this single center is a valuable informative compilation for the clinicians [14].

Table 3: LDD alone group

Plaque Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	2.10 ± 0.67		
II	1.16 ± 0.58	Between Dentomycine and Atridox, Metronidazole and Atridox,	Between Elyzol and Periochip, Metronidazole and Periochip, Dentomycine and Periochip, Atridox and Periochip
III	0.56 ± 0.54		
IV	0.28 ± 0.05		
V	0.86 ± 0.98		
Gingival Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.96 ± 0.36		
II	0.62 ± 0.44	Between Dentomycine and Metronidazole, Metronidazole and Atridox	Between Elyzol and Metronidazole, Elyzol and Periochip, Elyzol and Dentomycine, Atridox and Periochip
III	0.76 ± 0.4		
IV	0.3 ± 0.05		
V	1.04 ± 0.85		
Bleeding Index:			
LDD system	Reduction	Significance	
		Non significant	Significant
I	0.90 ± 0.30		
II	1.16 ± 0.58	Between Dentomycine and Metronidazole, Metronidazole and Atridox	Between Metronidazole and Periochip, Metronidazole and Elyzol, Dentomycine and Periochip, Metronidazole and Atridox
III	1.70 ± 0.87		
IV	0.41 ± 0.06		
V	0.74 ± 0.45		
Probing Depth			
LDD system	Reduction	Significance	
		Non significant	Significant
I	1.20 ± 0.68		
II	1.30 ± 1.36	Between Dentomycine and Metronidazole, Metronidazole and Atridox	Between Elyzol and Atridox, Dentomycin and Atridox, Metronidazole and Atridox, Periochip and Atridox
III	0.85 ± 0.67		
IV	0.80 ± 0.09		
V	0.17 ± 0.83		

In the current paper, authors have presented only a few other comparative studies pertinent to individual LDD as a complete protocol without an elaborate approach to minimize the discussion. As such there are no studies to compare the concept of the current paper on LDD compilation of five agents. However, the published studies [15–20] from our single center served as the best support to formulate and provide a reckoner to clinicians. In the current digital world, an access to a query ′ which LDD to be used ′ is provided in this paper.

4 CONCLUSION

Various local drug systems have been used as an adjunct to scaling and root planning in the treatment of periodontal lesions. Each drug system has their own advantage. In the present study the combined treatment of scaling and root planing plus the local drug therapy reported to have a significant benefit over SRP alone in the treatment of periodontal lesions.

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