# CLINICAL EFFICACY OF LOCALLY DELIVERED MINOCYCLINE IN PERIODONTITIS – A SYSTEMATIC REVIEW:

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**Abstract:** Chronic periodontitis (CP), the most common periodontal disease, is an inflammatory disease leading to the destruction of connective tissue and loss of the adjacent supporting bone and is multifactorial in etiology. Periodontal therapy including either surgical and/or non-surgical methods usually results in improvements in periodontal health. In some cases, scaling and root planing (SRP) is insufficient to solve periodontal infection. SRP combined with local antibiotics has been shown to yield better results than SRP only. Recently, minocycline, a broad spectrum antibiotic is found to be effective against periodontal pathogenic micro-organisms.

The aim of this systematic review is to evaluate the clinical efficacy of locally delivered minocycline in the treatment of periodontitis.an electronic search was carried out using the keywords, "minocycline". "periodontal" and "periodontitis" via the PubMed/Medline, ISI Web of Science and Google Scholar databases for relevant articles published from 1949 to February 2019. The addressed focused question was: To review current literature, to analyse

the efficacy of minocycline as a local adjunct to SRP in the treatment of periodontitis. Following the removal of duplicate results, the primary search resulted in articles and articles were excluded based on title and abstract. Hence, articles were read completely for eligibility. After exclusion of irrelevant studies,6 articles were included. All of them were RCT's, all of them were human studies, were clinical and were microbial analysis.

**Key Words:** Minocycline , local adjunct, periodontal, periodontitis.

## 1. INTRODUCTION:

Periodontitis is a complex, multifactorial disease characterized by the loss of connective tissue attachment with destruction of periodontium. Chronic Periodontitis is caused by pathogens called the red complex, which includes Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola. The RCBs are Gram-negative, anaerobic, and asacharolytic, with virulence factors that include an array of proteolytic enzymes. Porphyromonas gingivalis and Tannerella forsythia are rod-shaped bacteria, whereas Treponema denticola is a spirochete. Together, these three species have been strongly associated with chronic periodontal disease and recognized as periodontal pathogens.

These pathogens dominate the subgingival layers and are recognized as the most important pathogens in adult periodontal disease, currently thought to be closely associated with CP. Several risk and susceptibility factors have been proposed to explain the onset and progression of the disease (Page et al. 1997). Periodontal treatment involves mechanical cleaning of tooth surfaces to remove calculus and dental biofilm, and strict control of biofilm prevents recolonization of the subgingival area. Periodontal therapy usually results in improvements in periodontal health if good plaque control is obtained (Lindhe & Nyman 1975). Adjunctive antimicrobial regimens are designed to aid the mechanical methods of dealing with subgingival plaque. Local application of antibiotic directly at the subgingival area (into the periodontal pocket) has become an alternative.) One of the advantages of local drug delivery system is that the drug can be placed at a higher concentration, sub-gingivally, for 24hrs with sustained release. The drug concentration decreases exponentially following a first order kinetics. Local administration can avoid many of the side effects associated with systemic antibiotic therapy by limiting the agent to the periodontal pocket, minimizing systemic absorption. As a local drug delivery system, tetracycline is used widely in periodontal treatment as it is active against periodonto-pathogenic microorganism.

Minocycline is a broad-spectrum tetracycline antibiotic compared to the other members of the group. Minocycline is an antimicrobial tetracycline derivative which is active against a broad spectrum of Gram -negative and Gram-positive anaerobes including pathogens associated with adult periodontitis. It is one of the most active antibiotics against most of the microorganisms associated with periodontal disease. A stable, sustained-action formulation of minocycline gel has been developed for subgingival use. It has the most marked substantivity and shows greater solubility in lipids. It is classified as long acting drug and is commercially available as "Periofeel" which is a bio-absorbable sustained local drug delivery system consisting of 2% minocycline hydrochloride in a matrix of hydroxyethyl-cellulose, aminoalkylmethacrylate, triacetine and glycerine.

Periofeel contains 10mg of minocycline in 0.5gm of ointment in a disposable polypropylene applicator (2% minocycline HCl). Research has yielded promising results with the local application of minocycline in the treatment of periodontal disease, compared with other non-surgical therapies. The local application of minocycline in the treatment of periodontal disease has promising results compared with other nonsurgical therapies. By focusing on the therapeutic outcome of reducing the proportion of RCB, we seek to evaluate periodontal

treatments in their ability to shift microbial ecology from a pathogenic state to a condition of relative health. Changing concepts relative to the hypersensitivity potential of locally administered antibiotics and the rationale of targeting localized areas of periodontal destruction have led to great interest in controlled release, local delivery systems for antimicrobial/antibiotic therapy of Periodontitis.

**PRIMARY OBJECTIVE:**

To review current literature, to analyse efficacy of minocycline as an adjunct to non-surgical and surgical periodontal therapy on reducing probing depth, bleeding on probing and improving attachment level in periodontitis.

**CRITERIA FOR SELECTION OF STUDIES:**

The **inclusion criteria** for this study were:

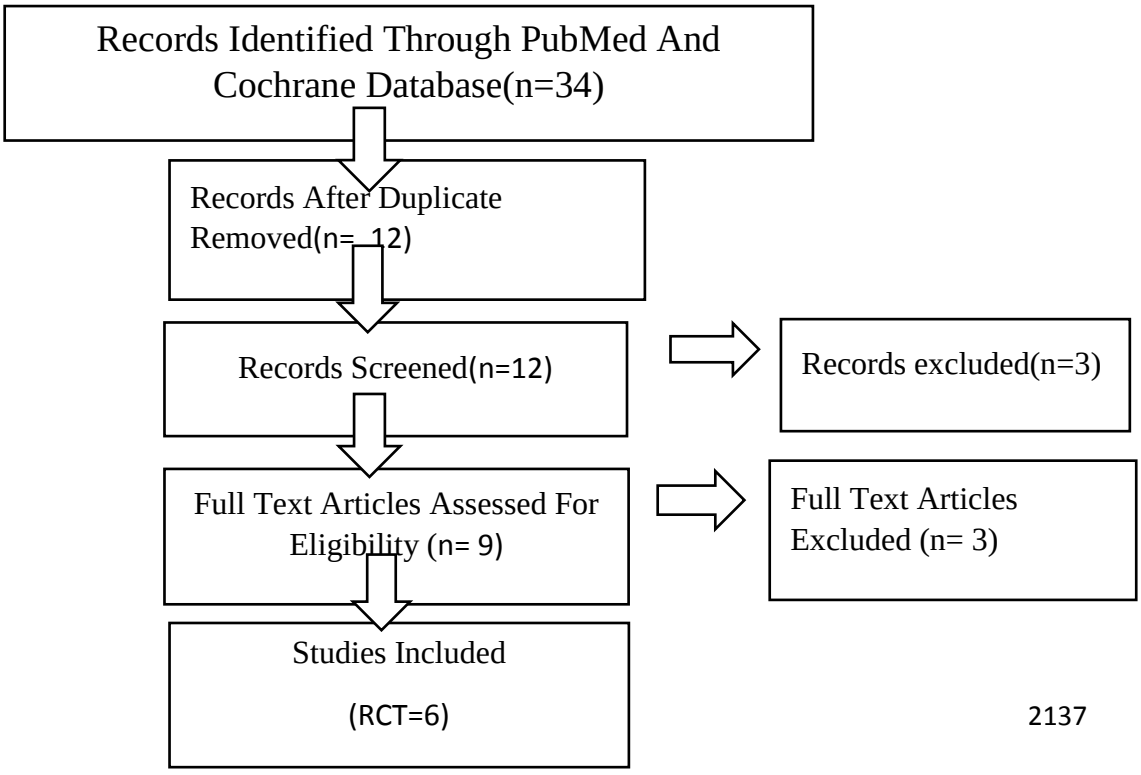
1. Articles published from 2000 to 2019,
2. Human studies,
3. Randomised controlled trails,
4. Original studies published in English language,
5. Locally delivered minocycline to treat periodontitis.

Following type of studies were **excluded**:

1.Animal studies,
2.Cell-culture studies,
3.Case series and case reports,
4.Historic reviews,
5.Letter to the editor.

**SEARCH METHODOLOGY**:

The systematic review was conducted following the guidelines of PRISMA. Systematically articles were searched the online PubMed, Cochrane, Embase from earliest records till 2019 by using key terms “minocycline and periodontitis”, “minocycline and periodontal disease”, “minocycline and periodontal treatment”, “minocycline and periodontal therapy.



## RESULTS:

### SEARCH RESULTS:

Following the removal of the duplicate search results, the primary search results resulted in 12 articles in total. 6 articles were excluded based on title and abstract. Hence remaining 6 articles were read completely for eligibility[1,2,3,4,5,&6] were included in this review.

### HUMAN STUDIES:

All human studies were randomized control trials (RCTs) trials [1,2,3,4,5&6]. The number of subjects ranged from 15 to 748. The age of the patients ranged from 25 to 80 years. In all the studies, minocycline microspheres were administered locally. Among these in the study[1] ,the test group 1 received SRP plus vehicle were given a unit dose of 3mg of polymer alone, Group 2 receives SRP plus minocycline microspheres were given a unit dose of 4mg of drug containing 1mg of minocycline and 3mg of polymer, and the control group received SRP only. In the study[2] the test group received SRP+ a single unit dose of minocycline microspheres containing 1mg of minocycline and 3mg of polyglycolic acid in a microsphere was administered and the control group received SRP alone. In the study[3] the test group received modified widmann flap surgery with minocycline microspheres and the control group receives modified widmann flap surgery alone. In the study[4] the test group were treated with open flap debridement followed by the application of minocycline ointment and the control group were treated with open flap debridement alone. In the study[5] the test group received SRP followed by four times of local application of minocycline HCl 2%gel and the control group received SRP alone. In the study[6] the test group received SRP along with locally delivered 2%minocycline gel, and the control group received SRP alone. The follow up period ranged from 21 days to 9 months in all the groups. The general characteristics of the human studies(RCT's)are provided in the Table 1.

### ASSESSMENT OF PARAMETERS:

In the human studies[1,2,3,4,5&6]. In the study[1] the Pocket probing depth, Vertical clinical attachment loss and Bleeding on probing was measured at baseline,1,3,6 and 9 months. In the study[2],the Pocket probing depth, Bleeding on probing, and Clinical attachment loss was measured at baseline and at 30 days. In the study[3]the primary clinical assessment of Probing depth reduction and the secondary clinical assessments of CAL,BOP and PI are assessed at baseline, week 13 and week 25. In the study[4] the Plaque Index, PPD,CAL and GI were recorded at 0 day, 3rd month and 6th month. In the study[5] the PPD,CAL and papilla bleeding index were examined at baseline,21 days,2,3 and 6months. In the study[6] PD,CAL and Plaque index were evaluated at baseline,3,6 and 9 months. The assessment of the parameters are provided in Table 2.

**Table 1: GENERAL CHARACTERISTIC FEATURES OF HUMAN STUDIES:**

| STUDY (AUTHOR &YEAR) | STUDY DESIGN | NUMBER OF SUBJECTS | TYPES OF PERIODONTAL LESIONS | AGE | INTERVENTION | | FOLLOW UP | OUTCOME |
|---|---|---|---|---|---|---|---|---|
| | | | | | TEST | CONTROL | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| RAY.C. WILLIAM Et al(2001) | RCT | 748 | MODERATE TO ADVANCE PERIODONTITIS | 30 AND M ORE | SRP PLUS VEHICLE(T1)<br><br>SRP PLUS MINOCYCLINE MICROSPHERES (T2) | SRP ALONE | BASELINE,1,3,6 AND 9 MONTHS | SCALING AND ROOT PLANING PLUS MINOCYCLINE MICROSPHERES IS MORE EFFECTIVE THAN SCALING AND ROOT PLANING ALONE IN REDUCING PROBING DEPTHS IN PERIODONTITIS PATIENTS. |
| J MAX GOODSON Et al(2007) | RCT | 130 | PD > OR EQUAL TO 5MM,> OR EQUAL IN 16 TEETH | 30-65 | MINOCYCLINE MICROSPHERES PLUS SRP | SRP ALONE | BASELINE TO 30 DAYS | TEST GROUP REVEALED REDUCED PROPORTION OF RCBS, BOP, PD AND CAL |
| HELLSTROM. M.K(2008) | RCT | 60 | MODERATE TO SEVERE, TO CHRONIC PERIOD | 25-80 | 2% MINOCYCLINE AFTER SURGERY | SURGERY ALONE. | BASELINE, WEEK 2, 3 AND WEEK 5. | APPLICATIONS OF LOCAL MINOCYCLINE AS AN |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | ONTITIS | | | | | ADJUNCT TO SURGERY IN ADULTS WITH MODERATE TO SEVERE, CHRONIC PERIODONTITIS WERE ASSOCIATED WITH STATISTICALLY SIGNIFICANT GREATER REDUCTIONS IN PROBING DEPTH THAN SURGERY ALONE. |
| SARA ABBAS Et al(2016) | A CLINICAL STUDY | 60 | PERIODONTITIS WITH POCKET DEPTH OF 6MM OR MORE IN 2 OR MORE TEETH. | 30-50 | OPEN FLAP DEBRIDEMENT PLUS 2 PERCENTAGE MINOCYCLINE | OPEN FLAP DEBRIDEMENT ALONE | BASELINE, 3MONTHS AND 6MONTHS | SIGNIFICANT REDUCTION IN BOP, PD, AND CAL IN SURGICAL PLUS MM AND ALSO PLAQUE INDEX |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Y SOEROSTO Et al(2017) | RCT | 81 | 4 TO 6MM OF PD | 30-55 | SRP PLUS 2 PERCENT MINOCYCLINE GEL | SRP ALONE | BASELINE 21 DAYS,2 MONTHS ,3 AND 6 MONTHS | TOTAL NO OF RCB IS REDUCED IN SRP PLUS MINOCYCLINE GROUP |
| RITU JAIN(2019) | RCT | 15 | CAL OF MORE THAN 5MM IN SEVERE CHRONIC PERIODONTITIS CASE | N/A | SRP PLUS GEL | SRP ALONE | BASELINE,3 6 AND 9 MONTHS | REDUCTION IN THE NO OF ORGANISMS AND ALSO THE CLINICAL PARAMETERS |

Table 2 : MEAN CHANGES AND CLINICAL PARAMETERS REPORTED BY SELECTED STUDIES:

| STUDY (AUTHOR AND YEAR) | FOLLOW UP | PPD | | | CAL | | | BOP | | | PI | | | GI | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | T/G1 | T/G2 | C/G1 | T/G1 | T/G2 | C/G1 | T/G1 | T/G2 | C/G1 | T/G1 | T/G2 | C/G1 | T/G1 | T/G2 | G/G1 |
| RAY.C.WILLIAMS Et al 2001 | BASELINE | 5.2-8.4 | 5-7.8 | 5.2-7.5 | 2.11-10.19 | 2.13-9.50 | 2.21-9.05 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| | 9MONTHS | 3.7-6.9 | 4-7.0 | 5.0-5.9 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| J.MAX.GOODSON Et al 2007 | | T | | C | T | | C | T | | C | T | | C | T | | C |
| | BASELINE | 3.87±0.45 | | 3.92±0.51 | 41.6±1.09 | | 4.14±1.09 | 60.9±24.77 | | 61.4±25.5 | N/A | | N/A | N/A | | N/A |
| | 30 DAYS | 1.38 | | 1.01 | 1.16 | | 0.80 | 25.2 | | 13.8 | N/A | | N/A | N/A | | N/A |
| HELLSTROIN.M.K Et al,2008 | BASELINE | 5.66±0.37 | | 5.75±0.33 | 6.71±1.16 | | 6.60±0.96 | 94±14 | | 97±21 | 43±30 | | 44±31 | N/A | | N/A |
| | WEEK 13 | 2.48±0.10 | | 2.29±0.09 | N/A | | N/A | 64±4 | | 62±4 | N/A | | N/A | N/A | | N/A |
| | WEEK 25 | 2.51±0.10 | | 2.18±0.10 | N/A | | N/A | 64±3 | | 56±3 | N/A | | N/A | N/A | | N/A |
| SARA ABBAS et al 2016 | BASELINE | 6.73±0.64 | | 6.45±1.37 | 7.30±0.64 | | 6.97±1.53 | N/A | | N/A | 1.84±0.36 | | 1.90±0.37 | 92.19±10.52 | | 94.37±8.98 |
| | 3RD MONTH | 4.22±0.65 | | 5.04±1.10 | 4.61±0.93 | | 5.51±1.39 | N/A | | N/A | 1.20±0.41 | | 1.41±0.42 | 57.78±10.95 | | 72.33±11.80 |
| | 6TH MONTH | 3.04±0.52 | | 3.99±0.96 | 3.41±0.96 | | 4.45±1.39 | N/A | | N/A | 0.91±0.28 | | 1.08±0.29 | 26.42±9.27 | | 55.11±10.27 |
| YSOEROSO et al 2018 | BASELINE TO 2 MONTHS | -1.58±0.57 | | -1.40±0.95 | -1.58±0.57 | | -0.76±0.99 | N/A | | N/A | N/A | | N/A | N/A | | N/A |
| | 2 TO 3 MONTHS | -0.01±0.58 | | -0.33±0.76 | -0.01±0.58 | | -0.26±0.78 | N/A | | N/A | N/A | | N/A | N/A | | N/A |
| | 2 TO 6 MONTHS | 0.01±0.68 | | -0.27±0.88 | 0.01±0.68 | | -0.13±0.98 | N/A | | N/A | N/A | | N/A | N/A | | N/A |
| | 3 TO 6 MONTHS | 0.02±0.60 | | 0.06±0.70 | 0.02±0.60 | | -0.13±0.82 | N/A | | N/A | N/A | | N/A | N/A | | N/A |
| RITU JAIN | BASELINE | 6.17 | | 6.02 | 13.03 | | 12.91 | 0.86 | | 0.72 | N/A | | N/A | N/A | | N/A |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| et al 2019 | 3MONTHS | 3.71 | 4.22 | 11.30 | 11.40 | 0.31 | 0.54 | N/A | N/A | N/A | N/A |
| | 6 MONTHS | 3.64 | 4.24 | 11.31 | 11.30 | 0.31 | 0.54 | N/A | N/A | N/A | N/A |
| | 9 MONTHS | 3.81 | 4.63 | 11.16 | 11.29 | 0.50 | 0.61 | N/A | N/A | N/A | N/A |

CAL-Clinical Attachment Level; PPD-Pocket Probing Depth; GI-Gingival index , BOP-Bleeding On Probing; PI-Plaque Index

TABLE 3: MEAN CHANGES AND MICROBIOLOGICAL PARAMETERS REPORTED BY SELECTED STUDIES:

| **STUDY (AUTHOR AND YEAR)** | **FOLLOW UP** | **PORPHYROMONAS GINGIVALIS** | | **TANNERELLA FORSYTHIA** | | **TREPONEMA DENTICOLA** | | **SPIROCHETES** | | **COCCI** | | **MOTILE BACILLI** | | **NON-MOTILE BACILLI** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **T** | **C** | **T** | **C** | **T** | **C** | **T** | **C** | **T** | **C** | **T** | **C** | **T** | **C** |
| J.MAX .GOODSON et al 2007 | BASE | 4.21 | 4.44 | 5.7 | 6.8 | 3.7 | 4.01 | N/A | N/A | N | N/A | N/A | N/A | N/A | N/A |
| | 30 DA | 2.51 | 1.68 | 2.6 | 2.4 | 1.4 | 0.77 | N/A | N/A | N | N/A | N/A | N/A | N/A | N/A |
| Y SOEROSO et al 2018 | BASE TO 2MO | -0.93±2 | -1.43±2 | -0.5 2.2 | -0.87 1.54 | -0.4 2.8 | -0.5 2.00 | N/A | N/A | N | N/A | N/A | N/A | N/A | N/A |
| | 2 MO TO 3 MO | 0.12±1 | 0.16±0 | -0.0 2.4 | 0.47± 1.10 | -0.2 2.6 | 0.53 1.90 | N/A | N/A | N | N/A | N/A | N/A | N/A | N/A |
| | 2 MO TO 6 MO | 0.44±1 | 1.11±1 | 0.3 2.1 | 1.32± 1.71 | 0.3 2.1 | 1.45 1.99 | N/A | N/A | N | N/ | N/A | N/A | N/A | N/A |
| | 3 MO TO 6 MO | 0.32±1 | 0.94±1 | 0.4 2.6 | 0.85± 1.50 | 0.6 3.0 | 0.91 1.90 | N/A | N/A | N | N/A | N/A | N/A | N/A | N/A |
| RITU JAIN et al 2019 | BASE | N/A | N/A | N/A | N/A | N/A | N/A | 50.3 | 45.4 | 3 | 32. | 28.6 | 28.2 | 28.6 | 28.3 |
| | 3 MO | N/A | N/A | N/A | N/A | N/A | N/A | 14.3 | 15.1 | 2 | 20. | 12.7 | 13.4 | 14.0 | 14.0 |
| | 6 MO | N/A | N/A | N/ | N/A | N/A | N/A | 31.6 | 34.5 | 3 | 31. | 18.2 | 21.7 | 17.0 | 19.4 |
| | 9 MO | N/A | N/A | N/A | N/A | N/A | N/A | 48.9 | 55.4 | 3 | 40. | 24.8 | 19.2 | 21.6 | 25.5 |

**MICROBIAL ANALYSIS:**

In the study[2] ,the reduction in the mean red complex bacteria numbers were noted for both the groups at baseline and at 30 days. In the study[5],the mean changes in the red complex bacteria count were noted from baseline to 2months,2-3 months,2-6 months & 3-6months. In the third study[6] the mean count of the spirochetes, cocci, motile bacilli and the non-motile bacilli are noted at baseline,3,6 and 9 months. The mean changes in the microbial analysis is provided in Table 3.

**OUTCOME OF STUDIES:**

In the human studies[(1,2,3,4,5&6)].

In the study[1]showed that SRP plus the use of minocycline microspheres shows an increased efficacy in the reduction of all the clinical parameters such as PPD,CAL and BOP at the end of 9 months. In the study[2] that using minocycline HCl microspheres as an adjunct to SRP effectively reduces the PD,BOP as well as the number of red complex bacteria and their proportions to a greater extent than SRP alone. In the study[3] application of local minocycline as an adjunct to surgery in adults with moderate to severe to chronic periodontitis were associated with statistically significant reduction in probing depth than surgery alone. In the study[4] revealed that using a 2% minocycline ointment, as a adjunct to periodontal flap surgery showed a greater reduction in Gingival Bleeding Index ,PPD and gain in CAL than just open flap debridement alone. In the study[5] revealed that the local application of minocycline HCl gel (Periocline),as an adjunct to SRP, was effective for reduction in the clinical parameters as well as effective for suppressing the regrowth of periodontal pathogens. In the study[6] locally delivered 2% minocycline gel used as an adjunct to SRP, revealed that it did not show any significant advantage of using 2% minocycline gel over SRP as a effective local drug delivery system.

## 2. DISCUSSION:

All the studies were reviewed. In this study by Ray.C.Williams et al 2001,748 patients with moderate to advanced periodontitis were selected and minocycline microspheres (or) vehicle was administered to all sites with probing depth $\geq$ 5mm.The unit dose of 4mg of drug containing 1mg of minocycline & 3mg of polymer was administered for the MM+SRP group and 3mg of polymer only were administered for the vehicle group. Results revealed that MM+SRP group provided substantially more reduction in the clinical parameters, than the other treatment groups[1].

In this study by J.Max.Goodson et al 2007,130 patients were categorised into 2 groups, where the test group was treated with MM+SRP where a single dose of minocycline microspheres containing 1mg minocycline & 3mg polyglycolic acid in a microsphere formulation was administered to all periodontal pockets $\geq$5mm. Results suggested that the locally delivered MM enhances clinical and microbiological outcomes. T.f, T.d and P.g showed significant reduction in the time periods compared to baseline. Also greater reduction in PD,BOP and gain in CAL were noticed[2].

In this study by Hellstrom.M.K et al 2008,60 patients were categorised into two treatment groups and were treated with modified widmann flap(MWF+MM) surgery along with minocycline HCl microspheres and modified widmann flap(MWF) surgery group only. Results suggested that a statistically significant reduction in PPD was observed in modified widmann flap(MWF)+locally administered minocycline microspheres(MM),to modified widmann flap surgery(MWF) surgical therapy alone[3].

In this study by Sara Abbas et al 2016,60 patients were recruited into two treatment groups. Group-A were treated with periodontal flap surgery followed by the application of 2% minocycline HCl ointment. Group -B, were treated with periodontal flap surgery alone. Results indicated that there was a significant mean reduction in the PPD,PI,GI and a significant gain in CAL ,reveals that the application of minocycline ointment, as an adjunct to open flap debridement in generalized chronic periodontitis provides better results[4].
In this study by Y.Soeroso et al 2018,81 subjects with moderate to severe periodontitis, were assigned to SRP alone group and SRP followed by four times of local application of minocycline HCl gel group. The results showed that local application of minocycline, as an adjunct to SRP, was effective for the significant reduction in the clinical parameters such as PD,BOP and a significant gain in CAL[5].
In this study by Ritu Jain et al 2019,patients with moderate to severe chronic periodontitis with a defined attachment loss of 4mm-5mm was chosen and assigned to 2 groups, as SRP alone group and SRP+2% minocycline gel(locally delivered) as an adjunct group. Results revealed an overall improvement in all parameters at various time intervals in both the groups. A significant reduction were also noted in the number of spirochetes, cocci, motile and non-motile bacilli in both the groups. Between the treatment groups, no significant differenced were observed ,leading to uncertain results on the efficacy and the efficiency of 2% minocycline containing gel as an effective local drug delivery system[6].
In other studies which were discussed,study[7] results indicated differences between treatment and SRP-only groups in the baseline-to-follow-up period typically favoured treatment groups even when the differences were statistically significant. Effects for CAL gains were smaller and statistical significance was less common.

In the study[8] the results concluded that treatment with Minocycline microspheres
and Metronidazole gel improved PPD and CAL in patients with periodontitis compared to SRP alone.

In the study[9] the reduction in clinical probing depth, on usage of subgingival minocycline as an adjunct to SRP may produce significant clinical benefits over SRP alone in patients with adult Periodontitis.

This study[10] could not show any significant difference in the levels
of bacterial species or groups at any time point between the two antimicrobial agents
tested. The use of a local antibiotic as an adjunct to mechanical treatment demonstrated improvements in probing depths that was sustained over 12 months.

The study[12]demonstrates that local subgingival delivery of 10% minocycline-loaded microcapsules as an adjunct to scaling results in reduction in the percent sites bleeding on probing greater than scaling and root planing alone and induces a microbial response more favourable health than scaling and root planing.

## 3. CONCLUSION:

The conclusion derived from this review is that scaling and root planning plus minocycline microspheres as a local adjunct provided a significant effect in the reduction of the clinical parameters as well as the microbiological parameters suggesting that the therapeutic effect of minocycline microspheres were more pronounced in patients with compromising conditions at local levels. The use of locally delivered antimicrobial agents should be incorporated as part of an optimal non-surgical therapeutic regimen. Further studies is needed with larger

samples, different criteria and in systemically compromised patients, so that the efficacy of minocycline microspheres as an antimicrobial can be proven in a wide array of phenomenon.

## CONFLICT OF INTEREST:

The authors report no conflicts of interest related to this study.

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