COMPARATIVE EVALUATION OF 0.5% AZITHROMYCIN GEL AND CURCUMIN GEL AS LOCAL DRUG DELIVERY SYSTEM IN PATIENTS DIAGNOSED WITH CHRONIC PERIODONTITISAS AN ADJUNCT TO SCALING AND ROOT PLANING

Dr. Sri Sushma yarram[1], Dr. Adusumilli Srikanth[2]

[1]Consultant periodontist

[2]Professor, Department of periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of dental sciences, Chinnaoutpalli, Gannavaram mandal – 521286.

ABSTRACT:

AIM: To evaluate efficacy of 0.5% Azithromycin gel and Curcumin gel as local drug delivery system in chronic periodontitis as an adjunct to scaling and root planning (SRP).

Materials and Methods: Total of 60 patients with localised or generalised periodontitis with a pocket depth of 5-7mm were selected and they were randomized into 3 groups: Group A (SRP + 0.5% azithromycin gel), Group B (SRP + curcumin gel), and Group C (SRP only). Clinical parameters including Plaque Index (PI), Modified Sulcular Bleeding Index (mSBI), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL) have been assessed at baseline, 4 and 6 weeks.

Results: All groups showed significant clinical improvements over time. Both azithromycin and curcumin groups demonstrated greater reductions in PI, mSBI, and PPD compared to SRP alone ($p < 0.05$). Azithromycin produced superior pocket depth reduction, whereas curcumin achieved greater reduction in bleeding scores, indicating enhanced anti-inflammatory activity.

Conclusion: Both 0.5% azithromycin gel and curcumin gel are effective adjuncts to SRP. Curcumin, being natural and biocompatible, represents a promising alternative to antibiotics.

Keywords – Azithromycin, Local drug delivery, Scaling, Curcumin

INTRODUCTION:

An infectious disease that causes inflammation of tooth's supporting tissue, progressive attachment loss, and bone loss is known as chronic periodontitis.[1] The main etiologic factor for development of periodontal disease is bacterial plaque that covers teeth. Cornerstone of periodontal therapy is elimination of subgingival calculus and plaque.[2] Although the ethology of periodontitis is multifaceted, the main etiologic agents are bacterial species, and the condition is an infection. It is well known that bacteria play a significant function in etiology of periodontal pockets, [3] Therapy must therefore focus on controlling bacterial flora associated to periodontium-tooth interface. "Gold Standard" for periodontal therapy is mechanical therapy consisting of SRP. Reducing bacterial load, shrinking swollen and inflamed gingiva, and reconditioning the subgingival ecology to make it biologically compatible with optimal healing are the goals of SRP. They also allow the epithelium to reattach to the root surface.[4] Clinical response varies, although non-surgical mechanical therapy is effective for majority of patients with periodontitis. It can also caused by genetic or environmental factors, subgingival flora composition, inadequate debridement, or poor compliance to an oral hygiene regimen.[5] Systemic antibiotics, topical antiseptics, and sustained release LDD systems are

examples of anti-infective therapy, which combines mechanical therapy and chemotherapeutic agents. The side effects of systemic antimicrobials are more severe.[6]

Materials and methods:

Total of 60 subjects reported to Department of Periodontics and Implantology, Drs. Sudha and Nageswara Rao Siddhartha Institute of Dental Sciences, Chinnaoutpalli, Gannavaram mandal are included in the study.

Inclusion criteria:

- Patients aged between 25 years to 55 years.
- Patients with no history of previous periodontal surgery.
- Patients with probing pocket depth (PPD) ≥5mm, clinical attachment loss (CAL) ≥5mm
- Patients with gingival and plaque index scores ≥1.

Exclusion criteria:

- Subjects with the presence of any systemic diseases that could affect wound healing.
- Patients with history of using antibiotics and corticosteroids in past 3 months.
- Smokers
- Pregnant females and lactating mothers

Materials:

1. **.0.5% Azithromycin gel**

The recent research involved the development of an in-situ gel formulation of azithromycin, which was prepared at the Department of Pharmaceutics, JSS College of Pharmacy, Mysuru. Initially, a precise quantity of poly (D, L-lactide-co-glycolide) (PLGA; 75:25, 72 kDa) was weighed and transferred into a glass vial, to which an accurately measured volume of the biocompatible solvent N-methyl-2-pyrrolidone has been added. Resulting mixture has been subjected to continuous agitation using a magnetic stirrer while being maintained at 60 °C until complete dissolution of the polymer was obtained, yielding a clear and homogeneous solution. Subsequently, a predetermined amount of azithromycin has been incorporated into polymer solution and stirred until a uniform dispersion was achieved. The formulation was carefully adjusted to a microenvironmental pH of 7.4, facilitating physiological compatibility. This approach ensured that the preparation remained in a liquid state during manipulation and transitioned to a gel after administration, thereby enabling sustained release of azithromycin for the intended pharmaceutical application.

2. **Curcuma oral gel (Curenext)**

CLINICAL PARAMETERS:

- Plaque score using plaque index (silness J and Loe H1964)
- Modified sulcular bleeding index (Mombelli, Van Oosten and S. church1989)
- Probing Pocket Depth (PPD)
- Clinical attachment level (CAL)

METHODS:

A comprehensive history has been documented for all selected patients, and all clinical data have been recorded at baseline. Subsequently, SRP was conducted for each patient. Upon completion of the SRP, selected sites with probing depths ranging from 5 to 7mm have been divided at random into 3 groups, each in a different quadrant.

- Group I - Received 0.5% azithromycin gel.
- Group II - Received only curcumin gel.
- Group III- Received only scaling and root planing alone.

The study's goal and utilization were explained to 60 patients that satisfied inclusion and exclusion criteria. Patient permission was obtained in writing. Using a pre-structured proforma, a comprehensive case history was documented, including all pertinent clinical findings. Recorded were clinical measures like as plaque index, pocket depth, gingival index, and clinical attachment level. After careful SRP, 0.5% Azithromycin (AZM) gel and Curcumin gel were applied to appropriate treatment locations. Only the control group underwent SRP. Once more, clinical parameters have been evaluated at baseline, four and six weeks.

Statistical analysis:

The data was compiled with Microsoft Excel, and the statistical analysis was conducted using IBM Corp.'s Statistical Package for the Social Sciences (SPSS) version 20 (IBM Corp. Armonk, NY, USA). Descriptive statistics were utilized to generate the data. Employing one-way analysis of variance (ANOVA) alongside post hoc testing, the Azithromycin Group (Group 1), Curcumin Group (Group 2), and Control Group (Group 3) were analyzed and have been compared at baseline, four weeks, and six weeks using PI, SBI, Periodontal Pocket Depth (PD), and CAL parameters. Repeated measures ANOVA was used to compare these research parameters with the change in time within each of the three study groups. A range of line diagrams and bar charts were used to display the data. The significance criterion for each statistical test has been set at $P<0.05$.

Results:

Table 1 shows descriptive data of all study parameters (PI, SBI, PD, CAL Scores) in test and control groups at baseline, 4 and 6 weeks. The mean reduction in PI scores from baseline to 6 weeks (PI) was 1.96 + 0.45, 1.72 + 0.47 and 1.38 + 0.31 and in mSBI scores (SBI) were 1.5 + 0.42, 1.45 + 0.4 and 1.3 + 0.31 in Azithromycin Group (Group 1), Curcumin Group (Group 2) and Control Group (Group 3) respectively. No significant improvements were seen in PIScores and mSBI scores among test groups and control group. The mean Periodontal Pocket Depth (PPD) reduced significantly by 3.15 + 0.52 from baseline to 6 weeks in Azithromycin Group (Group 1), when compared to Curcumin Group (Group 2) (2.7 + 0.37) and Control Group (Group 3) (1.65 + 0.23). The CAL loss also reduced significantly from baseline to 6 weeks by 2.65 + 0.04 in Azithromycin Group (Group 1), when compared to Curcumin Group (Group 2) (2.55 + 0.2), and Control Group (Group 3) (1.35 + 0.16). Figure 1 depicts the means of all the study parameters (PI, mSBI, PPD, CAL) of the Azithromycin Group (Group 1), Curcumin Group (Group 2) and Control Group (Group 3) across various time points. i.e. baseline, 4 weeks, and 6 weeks. One way analysis of variance (ANOVA) with post hoc tests has been done to comparing test parameters between the study groups. At baseline, comparison of study parameters, revealed no statistically significant difference between Azithromycin Group (Group 1), Curcumin Group (Group 2), and Control Group (Group 3). A statistically significant difference was seen only in Periodontal Pocket Depth (PPD) (P value=0.012*) and CAL loss (P

value=0.005*) parameters at 4 weeks comparison between the study groups. The comparison of study parameters at 6 weeks also revealed high statistical significance in Periodontal Pocket Depth (PPD), (P value=0.001*) and CAL loss (P value=0.001*) parameters between the Azithromycin Group (Group 1), Curcumin Group (Group 2), and Control Group (Group 3). However, no statistical significance was seen in PI and mSBI parameters at both 4 and 6 weeks. Post hoc tests were done for multiple pair-wise comparisons, and a statistically significant difference was revealed for both test groups when compared with control group (Table 2). The comparison of study parameters (PI, mSBI, PPD, CAL) within each of the study groups from baseline to 6 weeks were done using Repeated Measures Analyses of Variance (ANOVA). There were statistically high significant differences in all three groups regarding all four study parameters between different time points (All P Values = 0.001*). The changes in PI, mSBI, Periodontal Pocket Depth (PPD), and CAL loss parameters in each of the three study groups with change in time are shown respectively in Figures 2, 3, 4, and 5. The comparison of these four study parameters, within each of the study groups revealed least mean scores in all the parameters with progress of time. i.e. from baseline to 6 weeks the above study findings suggest that Azithromycin (Group 1) can be a valuable adjunct to scaling and root planning in treatment of chronic periodontics than Curcumin Group (Group 2) and Control Group (Group 3).

Table 1: DESCRIPTIVE DATA OF STUDY PARAMETERS

PARAMETERS	PLAQUE INDEX			SULCUS BLEEDING INDEX		
GROUPS	AZITHROMYCIN GROUP (N=20)	CURCUMIN GROUP (N=20)	CONTROL GROUP (N=20)	AZITHROMYCIN GROUP (N=20)	CURCUMIN GROUP (N=20)	CONTROL GROUP (N=20)
BASELINE – MEAN (S.D)	2.31(0.871)	2.14(0.938)	1.67(0.694)	1.8(0.894)	1.8(0.894)	1.55(0.759)
4 WEEKS – MEAN (S.D)	1.27(0.841)	1.12(0.775)	0.89(0.645)	0.95(0.686)	0.95(0.759)	0.85(0.587)
6 WEEKS – MEAN (S.D)	0.35(0.416)	0.42(0.464)	0.29(0.379)	0.3(0.47)	0.35(0.489)	0.25(0.444)
95 % CI LOWER - UPPER	1.8152 – 2.2648	0.8948-1.2885	0.2456-0.3611	1.4982-1.9351	0.7433-1.0901	0.1806-0.4194

PARAMETERS	PROBING DEPTH			CLINICAL ATTACHMENT LEVEL		
GROUPS	AZITHROMYCIN GROUP (N=20)	CURCUMIN GROUP (N=20)	CONTROL GROUP (N=20)	AZITHROMYCIN GROUP (N=20)	CURCUMIN GROUP (N=20)	CONTROL GROUP (N=20)
BASELINE – MEAN (S.D)	6.25(0.851)	5.85(0.745)	5.95(0.887)	5.8(0.41)	5.7(0.571)	5.65(0.489)
4 WEEKS – MEAN (S.D)	4.45(0.686)	4.25(0.716)	4.9(0.641)	4.35(0.587)	4.25(0.716)	4.9(0.641)
6 WEEKS – MEAN (S.D)	3.1(0.308)	3.15(0.366)	4.3(0.657)	3.15(0.366)	3.15(0.366)	4.3(0.657)
95 % CI LOWER - UPPER	5.8014 – 6.232	4.3463-4.7204	3.3295-3.7039	5.59-5.8433	4.3189-4.6811	3.3463-3.7204

TABLE 2: COMPARISON OF STUDY PARAMETERS BETWEEN THE TEST AND CONTROL GROUP AT BASELINE, 4 WEEKS, 6 WEEKS

PARAMETER	GROUP	N	BASELINE		4 WEEKS		6 WEEKS	
			F - value	P value	F value	P value	F value	P value
PI	1	20	3.1	0.061	1.31	0.27	0.446	0.642
	2	20						
	3	20						
SBI	1	20	0.57	0.566	0.14	0.866	0.228	0.797
	2	20						
	3	20						
PD	1	20	1.25	0.292	4.76	0.012*	41.86	<\0.001*
	2	20						
	3	20						

CAL	1	20	0.47	0.623	5.795	0.005*	37.78	<0.001*
	2	20						
	3	2						

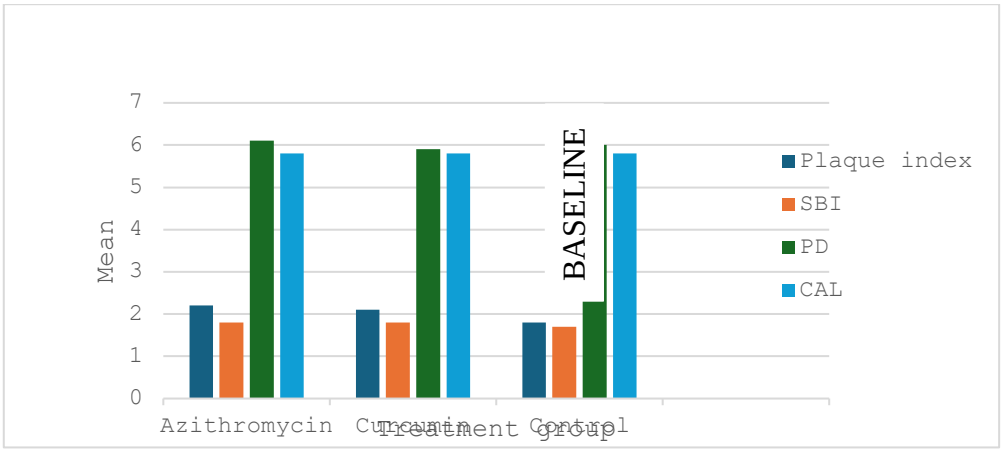
One way analysis of variance; p<0.05 considered statistically significant * denotes statistical significance with other groups in post hoc tests;

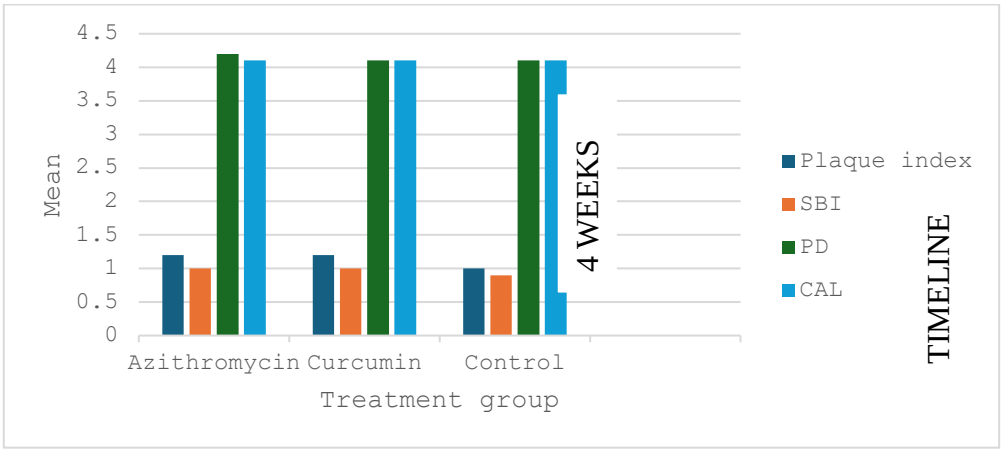
Table 3: COMPARISON OF PLAQUE INDEX, SULCULAR BLEEDING INDEX, PERIODONTAL POCKET DEPTH, AND CLINICAL ATTACHMENT LEVEL SCORES WITHIN EACH OF THW STUDY GROUPS WITH CHANGE IN TIME

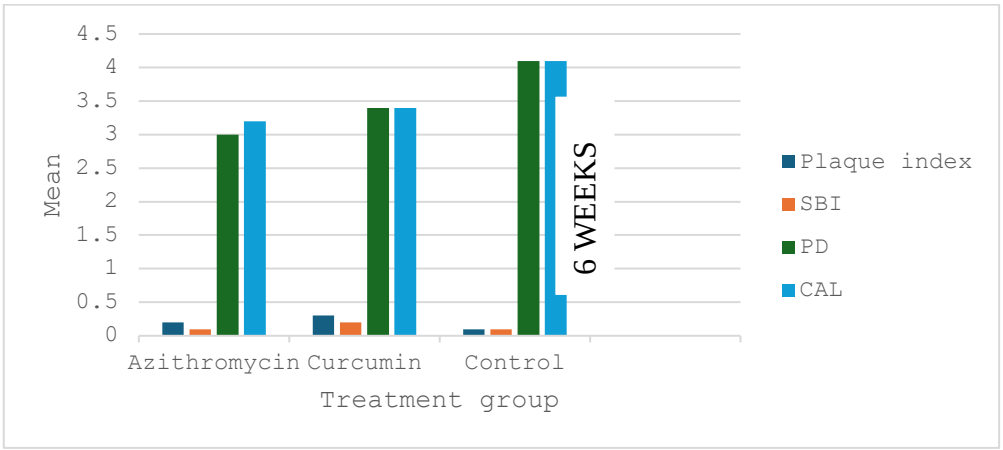
Repeated measures analysis of variance: p<0.05 considered statistically significant* denotes statistical significance

		PLAQUE INDEX		**SULCULAR BLEEDING INDEX**		**PERIODONTAL POCKET DEPTH**		**CLINICAL ATTACHMENT LEVEL**	
Group	**Time**	**F value**	**P value**	**F value**	**P value**	**F value**	**P value**	**F value**	**P value**
1	BASELINE	153.11	<0.001*	64.18	<0.001*	201.21	<0.001*	273.1	<0.001*
	4 WEEKS								
	6 WEEKS								
2	BASELINE	77.449	<0.001*	66.13	<0.001*	223.55	<0.001*	237.56	<0.001*
	4 WEEKS								
	6 WEEKS								
3	BASELINE	155.85	<0.001*	63.5	<0.001*	78.34	<0.001*	69.07	<0.001*
	4 WEEKS								
	6WEEKS								

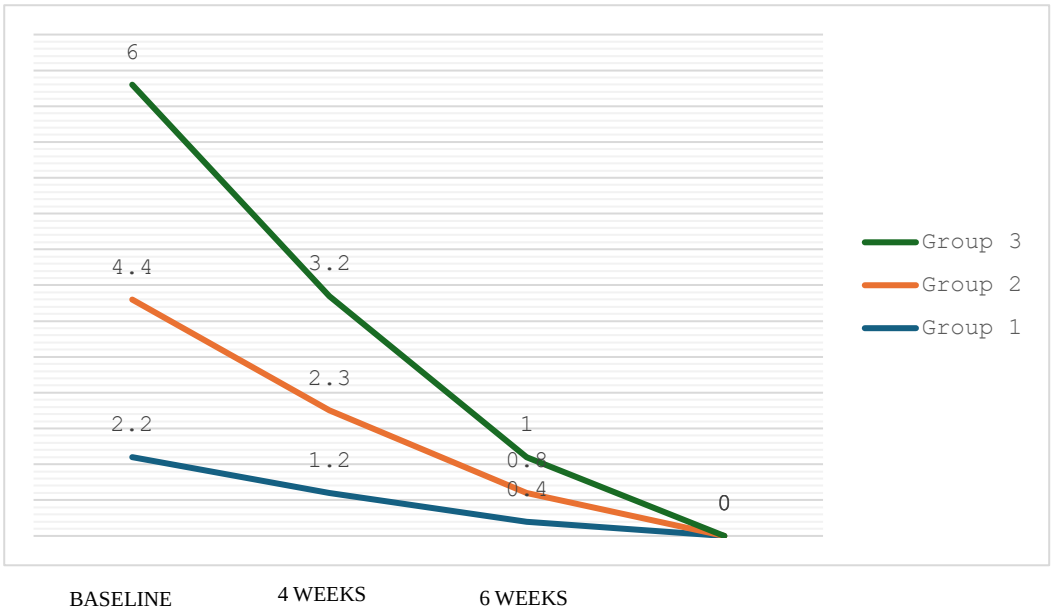
Comparison of study parameters between the test and control groups at baseline, 4 weeks and 6 weeks



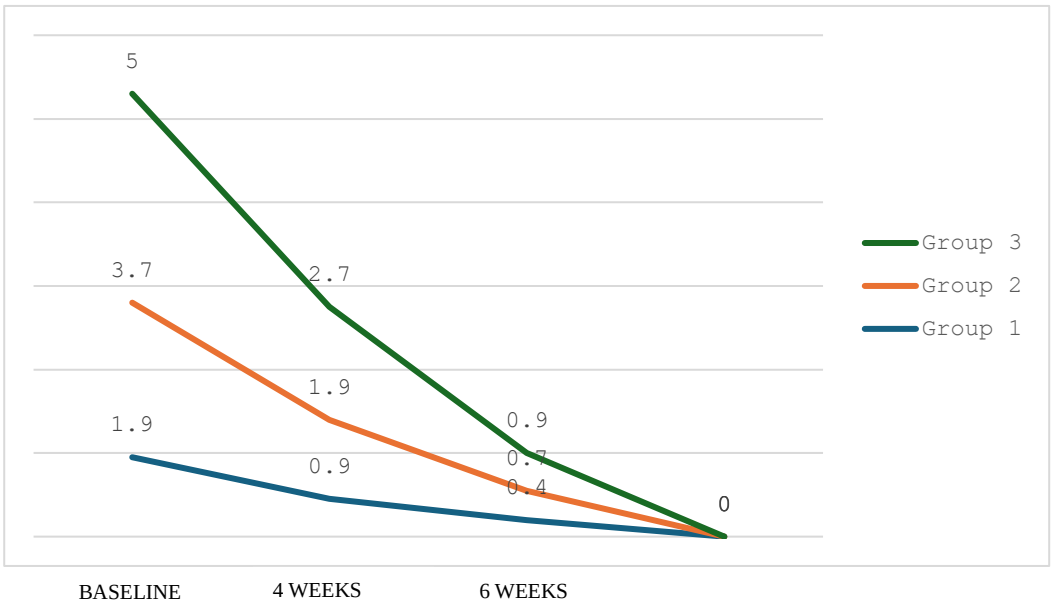




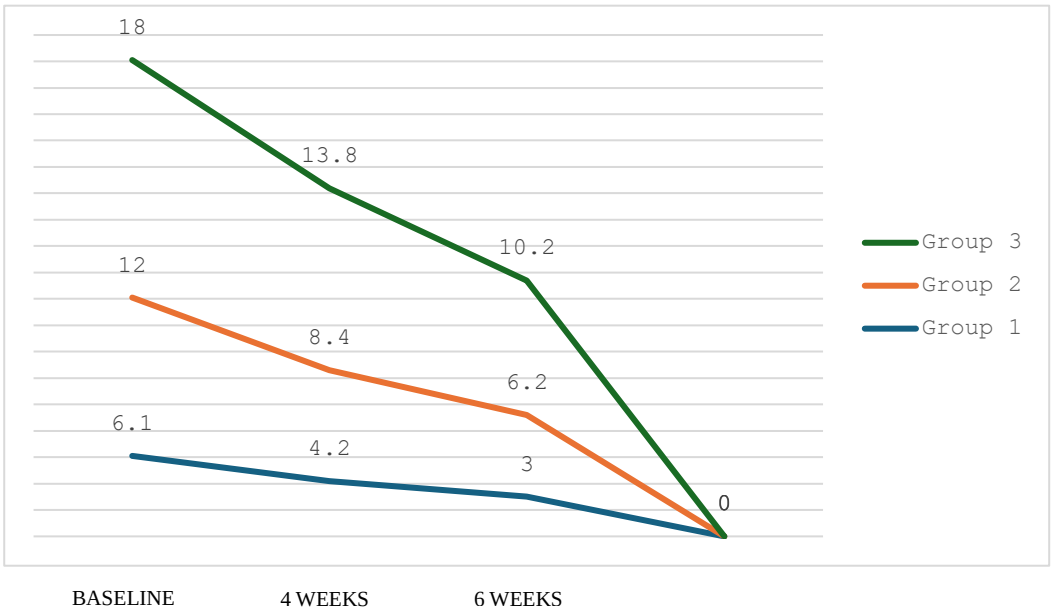
Graph 2: Comparison of plaque index scores within each of the study groups with change in time



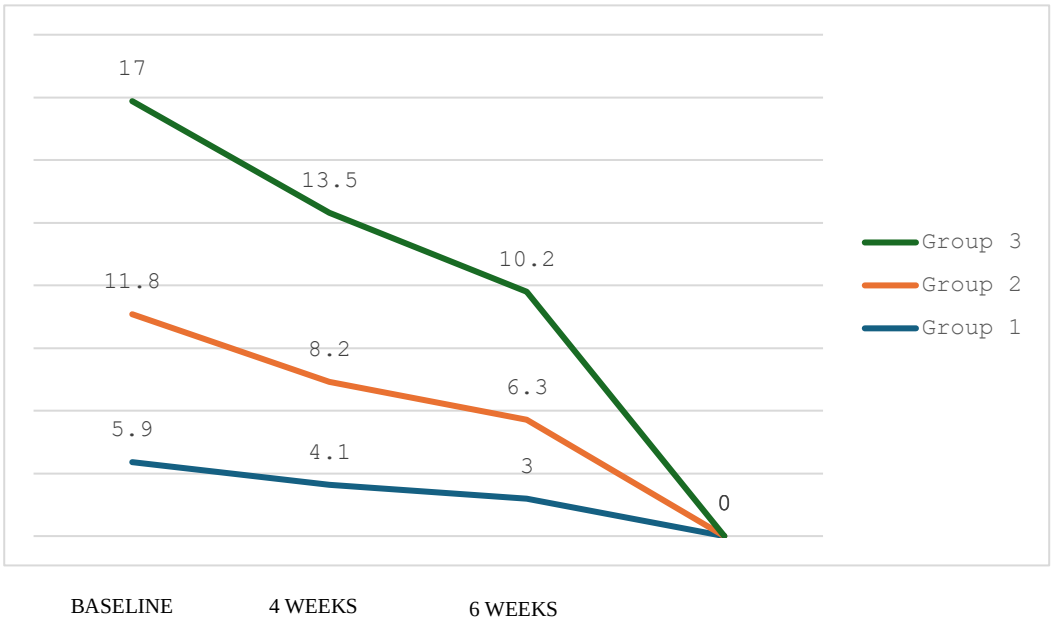
Graph 3: Comparison of modified sulcular bleeding index scores within each of the Study groups with change in time



Graph 4: Comparison of Periodontal Pocket Depth scores within each of the Study groups with change in time



Graph 5: Comparison of Clinical Attachment Level scores within each of the Study groups with change in time



DISCUSSION

Main reason of chronic inflammatory periodontal disease is microbial plaque. Most of time, SRP reduce the microorganism load, but they are unable for removing tissue-invasive pathogens. Adjunctive chemotherapy agents, which have been utilized to deliver mechanical debridement a further boost by systemic antibiotics, significantly improve clinical outcomes, despite the fact that they have inherent adverse effects. To get over these restrictions, LDD techniques have been created. In this context, it has become increasingly common to utilize antimicrobial drugs in different forms to inhibit these microorganisms. Long-term systemic treatment with antibiotics carries a number of concerns, including difficulties with compliance and resistant strains and superimposed infections. Locally administered antibiotics could be a helpful treatment for these problems. Compared to systemic therapy, LDD gives 100 times higher therapeutic doses of agent in subgingival regions.[3]

The semisynthetic, acid-stable antibiotic azithromycin (AZM) is a prototype of a new class of macrolides known as azalides. It penetrates tissues well and has a prolonged half-life.[7] AZM displays a varied antibacterial range of activity against Gram-negative and anaerobic microorganisms.[8] It has antibacterial effectiveness against periodontal infections such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans. [9,10] suggesting that it could be used to treat periodontal infections. In comparison to other commonly prescribed antibiotics, AZM exhibits reduced bacterial resistance to subgingival microflora associated with chronic periodontitis.[11] GCF concentration produced by the locally administered AZM gel has been 2041g/ml, which persisted at the location for 28 days and was detectable on day 28.[12] AZM gets concentrated in fibroblasts and phagocytes.

Novel adjunctive therapies, such as systemic host modulatory approaches and adjunctive local and systemic antimicrobial agents, may be beneficial when used in combination for the long-term clinical care of periodontitis, to improve the efficiency of existing mechanical procedures. [13,14] There is still a need to find chemotherapeutic agents that can be used with maximum effectiveness, safety, and fewer adverse effects, even though a few have been suggested.[15,16] Ancient medicines and herbal remedies are becoming more popular. A number of factors, including as affordability, availability, proximity, family influence, community opinion, and cultural familiarity, highlight usage of herbs as alternative medicine. Advances in alternative medicine have encouraged the use of a variety of natural and herbal items, such as turmeric, propolis, neem, and aloe vera, for 62 different medical purposes.[17,18] Turmeric is dried rhizome of perennial herb Curcuma longa.

Anti-inflammatory, antioxidant, anti-carcinogenic, antibacterial, antifungal, anti-protozoal, as well as antiviral properties are all exhibited by turmeric.[19,20] Curcumin, the most active component found in turmeric, was first chemically characterized in 1910 and also accelerates wound healing.[21] It is an unsaturated β-diketone that is bis α-β. Curcumin alters inflammatory response by inhibiting synthesis of inflammatory cytokines, including migration inhibitory protein, IL (interleukin)-1, -2, -6, -8, and -12, MCP (monocyte chemoattractant protein), TNF-α (tumour necrosis factor-alpha). Additionally, it alters the function of transcription factors and signaling pathways, specifically mitogen-activated protein kinases (MAPKS), activating protein 1, and nuclear factor kB (NF-kB) [22]. A highly pleiotropic compound, curcumin can interact with a diverse range of inflammatory molecular targets. It was proposed because of its anti-inflammatory properties. Singh et al., 1998 [23] found that curcumin reduces vascular engorgement of connective tissue, shrinking of inflammatory edema, and a reduction in inflammatory mediators. It encourages fibroblast migration into the wound bed, which lowers vascularization and results in connective tissue fibrosis. Curcumin enhances wound healing through transforming growth factor β and raising fibronectin. These advantageous properties of curcumin suggest that it may be used to treat periodontal diseases. Numerous mediators of tissue destruction and chronic inflammation, including enzymes, ions, hormones, proteins, and cytokines, including IL-1α, were discovered in whole saliva from patients with periodontitis. Pro-inflammatory cytokine IL-1β has been proposed in the pathogenesis of periodontitis. The compounds that are active in turmeric include volatile oils (turmerone, zingiberone, as well as atlantone), proteins,

carbohydrates, resins, and 3 curcuminoids: demethoxycurcumin, bisdemethoxycurcumin and curcumin (diferuloylmethane). Curcumin regulates the inflammatory response by suppressing the production of inflammatory cytokines and reducing the activity of the enzymes lipoxygenase, cyclooxygenase-2, and inducible nitric oxide synthase.[24]

Numerous clinical trials have demonstrated that azithromycin, a novel macrolide antibiotic, can be used as an adjunct to treat periodontal infections. It has also shown promise in treating aggressive and chronic periodontitis. According to the review of the literature, azithromycin is safe drug with a low incidence of side effects when compared to other antibiotics. It also has an appropriate antimicrobial spectrum and pharmacologic properties for treating periodontal infections. Further research is beginning to suggest that macrolide antibiotics are more than mere antimicrobials that help in the elimination of the microorganisms that cause chronic inflammation. Azithromycin provides a broad range of anti-inflammatory and immunomodulatory properties, along with cell modulatory effects that alter the activity of neutrophils, macrophages, and fibroblasts, as demonstrated by clinical trial. For these valid reasons, the current study was carried out, and the clinical trial demonstrated that local delivery of 0.5% Azithromycin in situ gel in the treatment of chronic periodontitis has significantly increased pocket depth reduction and CAL gain at 6 weeks, even in the presence of systemic disease. Curcumin is a naturally occurring agent with strong antibacterial as well as anti-inflammatory properties. Application of curcumin gel as a LDD system in adjunct with SRP was elucidated by this study. By enhancing clinical metrics such as CAL and PPD, it demonstrated noticeable improvement in restoring gingival health. When utilized for LDD, its properties were shown to be just as effective as those of numerous commercially available agents. However, as curcumin is a natural substance, there aren't many adverse effects. It is an superior adjunct to root planning and scaling.

CONCLUSION

Current research proved that 0.5% AZM and curcumin gel are equally effective as adjuncts to SRP in chronic periodontitis treatment.

Declarations

Funding: self-funded

Ethics approval: Ethical approval was obtained from Institutional Ethics Committee (IEC/DRS.S&NRSIDS/2025/PG/017/2019)

Consent for publication: consent for publication was obtained from all study participants.

Financial relationship with a commercial interest: None

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Date availability: The da ta supporting this study are available from the corresponding author upon reasonable request.

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