

**Comparative evaluation of the clinical efficacy of locally delivered 1 % curcumin gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis- A Triple Blind Randomized Controlled Clinical Trial**

<sup>1</sup>Dr. Akanksha Gaud, Postgraduate Student, Department of Periodontology, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India

<sup>2</sup>Dr. Ashish Yadav, Professor, HOD, Department of Periodontology, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India

<sup>3</sup>Dr. Swati Sharma, Professor, Department of Periodontology, Mahatma Gandhi Dental College and Hospital , Jaipur-302022, India

<sup>4</sup>Dr. Meenakshi, Reader, Department of Periodontology, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India

<sup>5</sup>Dr. Gaurav Pal Singh, Professor, Department of Prosthodontics, Crown and Bridge, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India

<sup>6</sup>Dr. Saroj Nehra, Senior Lecturer, Department of Pedodontics and Preventive Dentistry, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India,

**Corresponding Author:** Dr. Akanksha Gaud, Postgraduate Student, Department of Periodontology, Mahatma Gandhi Dental College and Hospital, Jaipur-302022, India

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**Abstract**

Curcumin (diferuloylmethane), is the main yellow bioactive component of turmeric which has several biological actions including anti-inflammatory, antioxidant and antiallergic. Clinical trials indicate that human beings can tolerate a dose as high as 8 g/day with no side effects. This study aims to evaluate and compare the clinical efficacy of locally delivered 1 % curcumin gel

as an adjunct to scaling and root planing in the treatment of chronic periodontitis with the objective of evaluating and comparing the pocket depth reduction and the clinical attachment levels in the patients receiving curcumin gel as an adjunct to scaling and root planing in the management of chronic periodontitis. In total, 40 systemically healthy individuals diagnosed with chronic periodontitis were included in the study. This randomized

controlled study comprised of two groups (n=20) which were randomly allocated to test and control group. Control group (Group 1) received only scaling and root planing and test group (Group 2) received SRP with additional subgingival application of curcumin at the experimental site chosen. Parameters recorded were plaque index, gingival index and sulcus bleeding index, pocket probing depth, Clinical attachment level on day 0 (baseline), 1 month and 3 months along with proper oral hygiene instructions. Data was analyzed statistically. There was a statistically significant difference seen for the values from Baseline to 3 Months with higher values in group 2 between the groups ( $p < 0.01$ ) for Gingival Index, Plaque Index, Sulcus Bleeding Index, Probing Pocket Depth and Clinical attachment Level.

**Keywords:** Periodontitis, Scaling and Root Planing, Curcumin, Local Drug Delivery, Triple Blind, Randomized Controlled Clinical Trial.

### Introduction

Periodontitis is a chronic inflammatory disease which is seen in a state of dysbiosis in which the commensals behave as proinflammatory pathobionts; defects in the host's immune response to the bacterial insults promote dysbiosis and hence promote periodontal tissue destruction thereby generating a self-prevailing pathogenic cycle. <sup>[1]</sup>

Non-surgical periodontal therapy has always been the gold standard treatment protocol, aiming at reducing the microbial load and pocket reduction by mechanical and antimicrobial means. Phase I therapy (scaling and root planing) followed by adjunctive use of local drug delivery agents helps us to achieve this objective to an extent. <sup>[2]</sup>

Local drug delivery agents act via target specific action that helps in eliminating the periodontopathogenic bacteria with no side effects associated with its application. <sup>[3]</sup>

Curcumin is a yellow, water insoluble pigment of turmeric which has been used as a therapeutic agent in ayurvedic medicine for many years. It has various pharmacological properties such as anti-inflammatory, antioxidant, antiallergic etc which make it a potent local drug delivery agent. Clinical trials indicate that human beings can tolerate a dose as high as 8g/day with no side effects. So, the objective of this study is to evaluate the efficacy of curcumin as an adjunct to scaling and root planing (SRP) <sup>[4]</sup>

The present study was designed to evaluate the efficacy of curcumin gel as a local drug delivery agent following SRP and its effect on various clinical parameters like plaque index (PI), gingival index (GI), sulcular bleeding index (SBI), pocket probing depths (PPD), clinical attachment level (CAL).

### Materials and Methods

**Experimental Design:** The experimental Study was designed as a triple-blind (participants, assessor and examiner) randomized controlled clinical trial with two parallel groups consisting of 20 participants in each group, according to the CONSORT statement <sup>[5]</sup> [CONSORT flow chart, figure 3] The study investigated two groups, group 1 (control group), group 2 (test group). Control group received only SRP and while Test received SRP with additional subgingival application of curcumin at the experimental site chosen. The experimental period was of 3 months with assessment conducted at baseline (day 0), 1 month and 3 month. The study protocol was approved by the Ethical Committee in University of Mahatma Gandhi Dental College and Hospital, Jaipur, Rajasthan. Participants were explained about the details of the study and a written informed consent was taken from them form prior to start of the study.

**Study procedure:** A total of 80 patients were assessed for eligibility, and out of those 40 participants were

included in the study and were randomized (n=20) and equally allocated into two groups .

All the participants completed the study (CONSORT flow chart, figure 3) Patients in the test group (group 2) received scaling and root planing along with 1% curcumin gel. The control group (group 1) sites received scaling and root planing only. Curcumin gel (1 mg/ml) [Curanext oral gel 10 g (ayurvedic proprietary medicine) containing C. Longa extract manufactured by Abbott Healthcare Pvt. Ltd, was taken.] For the test group patients, it was loaded and packed in a 1ml syringe and was dispensed subgingivally to base of the pocket by means of a disposable syringe in the experimental site chosen and post-operative instructions were given. Patients were re-evaluated after 7 days, 1 month and 3 month and the clinical parameters were recorded in all the 40 participants at baseline, 1 month and 3-month time period by the examiner, Akanksha Gaud (AG) who was blinded about the group allocation throughout the study period. Systemically healthy patients diagnosed with chronic periodontitis (PPD  $\geq$  5 mm, CAL  $\geq$  2 mm) and individuals who can maintain satisfactory oral hygiene after the initial treatment were included in the study. Patients who were taking medications for any systemic illness or were medically compromised were excluded from the study, pregnant and lactating females were excluded. Patients who were currently on antibiotics, steroids or hormonal therapy were not included. Patient who had undergone previous periodontal therapy in last six months were not included, also smokers and patient diagnosed with aggressive periodontitis were not included.

**Intervention:** The experimental study was performed by the examiner, Akanksha Gaud (AG). In this study there were two examiners who were blinded throughout the study period. Clinical parameter was assessed by the

blinded examiner (AG) and double blinded examiner performed conceal allocation to determine the group subject.

**Clinical parameters measured:** The following clinical measurement was assessed by a blind examiner (AG) during the experiment period:

- Plaque index (Silness and Loe, 1964)
- Gingival index (Loe and Silness, 1963)
- Sulcus Bleeding index (Mulhemann H.R. and Sons S in 1971 )
- Pocket probing depth
- Clinical attachment level

**Randomization, allocation concealment and blinding:**

A total of 80 subjects were assessed according to the inclusion criteria of the study. To allocate the subjects into the test or control group, systematic randomization was done to ensure that every 2<sup>nd</sup> individual was included in the study, such that the total sample size was of 40 participants. The allocation sequence was done by using computer generated list and was performed by the double blinded examiner. To conceal the subject allocation, it was in a sequentially numbered opaque sealed envelope which was performed by the double blinded examiner and after that, envelopes were opened to determine the group allocation and were assigned to Group 1 and Group 2. Each group consisting of 20 participants. The examiner and assessor were blind as to what group the participants were assigned as each group were coded differently and the participants were blind about whether they were assigned to the study group or control group. The code (of test or control group) was only broken after the completion of the experimental studies data analyses.

**Statistical Analysis**

The statistician was blinded as to what group the participants were allocated. Data obtained was compiled

on a MS Office Excel Sheet (v 2019, Microsoft Redmond Campus, Redmond, Washington, United States).

Data was subjected to statistical analysis using Statistical package for social sciences (SPSS v 26.0, IBM). Descriptive statistics like frequencies and percentage for categorical data, Mean & SD for numerical data has been depicted. Normality of numerical data was checked using Shapiro-Wilk test & was found that the data did not follow a normal curve; hence non-parametric tests have been used for comparisons. Inter group comparison (2 groups) was done using t test. Intra group comparison was done using repeated measures ANOVA (for >2 observations) followed by post Hoc test. For all the statistical tests,  $p < 0.05$  was considered to be statistically significant, keeping  $\alpha$  error at 5% and  $\beta$  error at 20%, thus giving a power to the study as 80%.

\* = statistically significant difference ( $p < 0.05$ )

\*\* = statistically highly significant difference ( $p < 0.01$ )

# = non-significant difference ( $p > 0.05$ )

## Results and Discussion

### Results

**Intergroup comparison:** The Plaque Index (PI) and Gingival Index (GI) values showed highly statistically significant difference ( $p < 0.01$ ) at 3-month, significant difference ( $p < 0.05$ ) at 1 month and no significant difference (day 0).

Test group developed less plaque and gingival inflammation than the control group (Table No. 1, Figure No. 3).

Sulcus Bleeding index (SBI) showed highly statistically significant difference ( $p < 0.01$ ) for the frequencies between the groups (Table No.1, Figure No. 3).

Probing pocket depth and clinical attachment levels showed no significant results ( $p > 0.05$ ) at baseline and highly significant results at 3 months ( $p < 0.01$ ) (Table No. 1, Figure No. 3)

Intergroup comparison from baseline to 3 months showed highly significant results ( $p < 0.05$ ) (Table -3, Figure 2)

**Intra group comparison:** Comparison showed a highly statistically significant difference ( $p < 0.01$ ) in both GI, PI, SBI, PPD, CAL which was observed in all the groups at various time interval with higher values at 3 months. (Table No -2)

### Discussion

Periodontal diseases occur due to colonization of subgingival biofilm by pathogenic microorganisms.<sup>[6]</sup> Scaling and root planning is one of the most commonly utilized procedures in the treatment of periodontal diseases and has been used as the “gold standard” for mechanical therapy<sup>[7]</sup>. Whenever a chemotherapeutic agent is added as an adjunct to mechanical instrumentation it provides additional properties for disease control.<sup>[8]</sup> Curcumin has been in the news since the last decade regarding its application in dentistry due to its various underlying applications which it carries, i.e., anti-inflammatory, anti-oxidant, antibacterial wound healing etc<sup>[4]</sup>. The objective of this randomized control clinical trial was to evaluate the efficacy of locally delivered curcumin gel as an adjunct to scaling and root planing over a period of 3 months.

There was a significant reduction in PI values from baseline to follow up which can be attributed to the fact that there was a reduction in supragingival plaque after SRP and oral hygiene instructions. Similarly there was a significant reduction in GI scores and SBI scores which shows that after SRP there is further elimination of the local pathological microbionts due to which there was a marked reduction in gingival inflammation and bleeding. The results of the present study were similar to the studies done by Farzana et al<sup>[9]</sup>, Davi et al<sup>[10]</sup>, Nagasri et al

<sup>[11]</sup>, Chatterji et al <sup>[12]</sup> and Parvathy Harshan et al<sup>[13]</sup> etc

<sup>[9]</sup>Farjana et al., (2014) did a pilot study to evaluate the clinical efficacy of oral curcuma gel in gingivitis management without traditional SRP employing Papillary bleeding index and GI as clinical parameters and observed significant reduction in papillary bleeding index. This finding is in accordance with the findings of studies conducted <sup>[10]</sup> Davi et al (2018) and <sup>[14]</sup> Anitha et al (2015). Madhu Bhatia et al., (2014) <sup>[4]</sup> evaluated the clinical and microbiological efficacy of locally delivered 1% curcumin gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis and found the 1% curcumin gel appeared to provide significant improvements in clinical parameters. <sup>[15]</sup> Hugar SS et al (2016) evaluate the efficacy of subgingival application of chlorhexidine gel and curcumin gel as an adjunct to SRP in the treatment of mild to moderate (4-6 mm) periodontal pockets. It concluded that both chlorhexidine gel and curcumin gel can be used as an adjunct to SRP, but the curcumin gel has shown to be more effective than the chlorhexidine gel in the treatment of mild to moderate periodontal pockets. <sup>[12]</sup> Chatterjee et al., (2017) used curcumin mouthrinse in comparison with Chlorhexidine mouthrinse and found significant reduction in plaque and GI. Similar results were obtained in the present study. <sup>[16]</sup> Ravishankar et al., (2017) evaluate the comparative effect of curcumin and ornidazole in treating chronic periodontitis. At 1-month evaluation, curcumin group showed a significant decrease in pocket PD, plaque index, and clinical attachment loss when compared to the ornidazole group. <sup>[13]</sup> Parvathy Harshan et al(2019) did a systematic review to determine the effectiveness of curcumin in the treatment of periodontitis .Nine studies were included in the systematic review of which all are clinical trials. Among which, eight studies showed that

curcumin, when used as an adjunct to scaling and root planing, had a crucial role in reducing the inflammation and improving the periodontal status. However studies done by Anuradha et al(2015)<sup>[17]</sup> and Nandini et al (2012)<sup>[18]</sup> showed contrasting results where there was no significance in both GI and PI.

In concordance with other studies, the present study could have been done with a larger sample size along with a microbial analysis , also a comparative local delivery drug could have been taken as an interventional group, getting more accurate mean values .Farzana et al <sup>[9]</sup> also evaluated the clinical efficacy of oral curcuma gel in gingivitis management without traditional SRP employing Papillary bleeding index and GI as clinical parameters and observed significant reduction in papillary bleeding index .<sup>[16]</sup> Ravishankar et al. performed local application of curcumin gel andfound reduce gingival inflammation in periodontitis patients suggesting its anti-inflammatory action on periodontium. Arunachalam et al. <sup>[19]</sup> evaluated antiplaque effects of curcumin in gingivitis by evaluating salivary reactive oxygen species and proposed that antioxidant property of curcumin can be responsible toward its anti-inflammatory action.

The difference in mean PPD reductions was significant at the test site when compared to the control site . This can be attributed to the anti- inflammatory mechanism of curcumin which modulates the inflammatory response , inhibits the production of pro-inflammatory cytokines , represses the activation of AP-1 and NF-k $\beta$ , inhibit the biosynthesis of \*inflammatory prostaglandins , enhances neutrophil functions during inflammatory response; contrasting results were shown by Anuradha et al <sup>[17]</sup>and Nandini et al<sup>[18]</sup> however the results were in accordance with <sup>[20]</sup>Colombo et al and Behal et al.<sup>[21]</sup>

Also a significant reduction was found in mean CAL levels in test than in control group . it may be due to

increased levels of transforming growth factor  $-\beta 1$  in healing tissue, earlier re-epithelization, improved neovascularization, reduced inflammatory cell infiltrate, increased collagen content and fibroblastic cell numbers, enhanced wound repair in sites treated with curcumin, contrasting results were presented by <sup>[17]</sup>Anuradha et al and <sup>[18]</sup>Nandini et al that have showed that there was an improvement in the clinical attachment level but the improvement was not statistically significant. However, the results of the present study was in accordance with Nagasri et al<sup>[11]</sup>, Behal et al<sup>[21]</sup> and Hugar et al<sup>[15]</sup>. Borgesa et al. (2020)<sup>[22]</sup> in his systemic review on preclinical studies stated that it significantly reduces alveolar bone loss in experimental models of periodontitis in rats, which further implements the importance and ongoing research on curcumin.

### Conclusion

The results of this study shows that the inhibitory effects of curcumin is helpful in restoring the gingival health and can be used as an adjunct to mechanical therapy to prevent early recolonization of pathogens. To further elucidate the use of this local drug delivery system, a longitudinal study with large sample of subjects should be carried out.

### References

1. George Hajishengallis - Immunomicrobial pathogenesis of periodontitis: keystones, pathobionts, and host response - Trends in Immunology-2014;35(1):3-11
2. Rajeshwari H.R, Dinesh Dhamecha, Satveer Jagwani, Meghana Rao, Kiran Jadhav, Shabana Shaikh, Lakshmi Puzhankara, Sunil Jalalpure- Local drug delivery systems in the management of periodontitis: A scientific review-Journal of Controlled Release 307,2019, 393–409
3. P.L. Ravishankar et al - Effect of local application of curcumin and ornidazole gel in chronic periodontitis patients-Int J Pharm Investig. 2017; 7(4): 188-192
4. Madhu Bhatia et al -Novel Therapeutic Approach for the Treatment of Periodontitis by Curcumin- journal of clinical and diagnostic research-2014;8(12): ZC65-ZC69
5. P.I. Di'az, P.E. Kolenbrander, Subgingival biofilm communities in health and disease, Rev. Clin. Periodon. Implantol. Rehabil. Oral,2009, 2 (3) 187–192.
6. Nagasri M, Madhulatha M, Musalaiah SV, et al. Efficacy of curcumin as an adjunct to scaling and root planning in chronic periodontitis patients: A clinical and microbiological study. Journal of Pharmacy & Bioallied Sciences. 2015;7(Suppl 2): S554-8.
7. Tan OL, Safii SH, Razali M. Commercial local pharmacotherapeutics and adjunctive agents for nonsurgical treatment of periodontitis: A contemporary review of clinical efficacies and challenges. Antibiotics 2019.
8. Farjana NH, Chandrasekaran SC, Gita B. Effects of oral curcumin gel in gingivitis management – A pilot study. J Clin and Diagn Res. 2014;8: ZC08–10.
9. Davi DH, Patel P, Shah M, Dadawala SM, Saraiya K, Sant AV. Comparative evaluation of efficacy of oral curcumin gel as an adjunct to scaling and root planning in the treatment of chronic periodontitis. Adv Hum Biol. 2018; 8:78–92
10. Nagasri M, Madhulatha M, Musalaiah SV, Aravind Kumar P, Murali Krishna CH, Mohan Kumar P. Efficacy of curcumin as an adjunct to scaling and root planing in chronic periodontitis patients: A clinical and microbiological study. J Pharm Bioallied Sci. 2015;7(Suppl 2): S554–8

11. Chatterjee A, Debnath K, Rao KN. A comparative evaluation of the efficacy of curcumin and chlorhexidine mouthwash on clinical inflammatory parameters of gingivitis. A double blind randomized controlled trial. *J Indian Soc Periodontol.* 2017; 21:132–7.
12. Parvathy Harshan et al -*J. Pharm. Sci. & Res.* Vol. 11(9), 2019, 3174-3180
13. Anitha V, Rajesh P, Shanmugam M, Priya BM, Prabhu S, Shivakumar V. Comparative evaluation of natural curcumin and synthetic chlorhexidine in the management of chronic periodontitis as a local drug delivery: A clinical and microbiological study. *Indian J Dent Res.* 2015; 26:53–6
14. Hugar SS, Patil S, Metgud R, Nanjwade B, Hugar SM. Influence of application of chlorhexidine gel and curcumin gel as an adjunct to scaling and root planing: A interventional study. *Journal of natural science, biology, and medicine.* 2016 Jul;7(2):149.
15. Ravishankar PL, Kumar YP, Anila EN, Chakraborty P, Malakar M, Mahalakshmi R. Effect of local application of curcumin and ornidazole gel in chronic periodontitis patients. *Int J Pharm Investig.* 2017;7:188–92.
16. Anuradha BR, Bai YD, et al. Evaluation of anti-inflammatory effects of curcumin gel as an adjunct to scaling and root planing: a clinical study. *J Int Oral Health* 2015;7(7):90–93.
17. Nayyar N, Vidya D, et al. Comparative evaluation of 1% curcumin solution and 0.2% chlorhexidine irrigation as an adjunct to scaling and root planing in management of chronic periodontitis: a clinico-microbiological study. *J Pharm Biomed Sci* 2012;14(03) :1–7.
18. Arunachalam LT, Sudhakar V, Vasanth J, Khumukchum S, Selvam VV. Comparison of antiplaque and antigingivitis effects of curcumin and chlorhexidine mouthwash in the treatment of gingivitis, A clinical and biochemical study. *J Indian Soc Periodontol.* 2017;21:478–83.
19. Colombo AP, Teles RP, et al. Effects of non surgical mechanical therapy on the subgingival microbiota of Brazilians with untreated chronic periodontitis: 9-month results. *J Periodontol* 2005;76:778–784.
20. Behal R, Mali AM, et al. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: a clinical and microbiological study. *J Indian Soc Periodontol* 2011;15(1):35–38.
21. Borgesa SJ, Paranhos RL, de Souza LG, Matosa FD, Bernardinoc MI, Moura GC, et al. Does systemic oral administration of curcumin effectively reduce alveolar bone loss associated with periodontal disease? A systematic review and meta-analysis of preclinical in vivo studies. *J Funct Foods.* 2020;75:1–1.

**Legend Tables**

Table 1: Intergroup comparison of outcome variables

\* = statistically significant difference (p<0.05), \*\* = statistically highly significant difference (p<0.01), # = non-significant difference (p>0.05)

	G1		G2		G1		G2		G1		G2	
Clinical Parameters	Baseline				1 Month				3 Month			
	Mean	S.D	Mean	S.D.	Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
GI	2.32	.225	2.25	.296	1.92	.246	1.72	.300	1.48	.280	1.16	.332
p value	.440#				.027*				.002**			
PI	2.36	.179	2.34	.157	1.97	.195	1.84	.176	1.46	.330	1.18	.207
p value	.780#				.033*				.002**			
SBI	2.46	.256	2.46	.345	2.04	.244	1.93	.279	1.53	.270	1.33	.184
p value	.918#				.173#				.009**			
PPD	6.48	.938	6.47	.822	6.04	.700	5.54	.570	5.58	.753	4.43	.552
p value	.986#				.018*				.000**			
CAL	6.30	.865	6.20	.894	4.80	.768	4.60	.754	3.80	.768	2.55	.686
p value	.721#				.411#				.000**			

Table 2: Intragroup comparison of outcome variables

	Group 1					Group 2				
	GI	PI	SBI	PPD	CAL	GI	PI	SBI	PPD	CAL
Total Mean	1.90	1.93	2.01	6.03	4.97	1.71	1.79	1.91	5.48	4.45
Total S.D	.424	.441	.457	.873	1.301	.544	.515	.541	1.064	1.692
F value	55.105	67.604	65.091	6.266	49.317	62.476	209.370	83.793	48.096	109.189
p value	.000**	.000**	.000**	.003**	.000**	.000**	.000**	.000**	.000**	.000**

Table 3: Intergroup comparison of differences from Baseline to 3 Months

Group	Mean	Std. Deviation	Std. Error Mean	T value	P value of t test	
GI B to 3M	1	.84	.181	.041	-4.800	.000**
	2	1.10	.161	.036		
PI B to 3M	1	.90	.295	.066	-3.743	.001**
	2	1.17	.145	.033		
SBI B to 3M	1	.92	.186	.042	-3.362	.002**
	2	1.14	.208	.047		
CAL B to 3M	1	2.50	.607	.136	-6.090	.000**
	2	3.65	.587	.131		



PPD B to 3M	1	.90	.645	.144	-4.826	.000**
	2	2.05	.843	.188		

Figure 1: Intra group comparison of mean values

Intragroup comparison of mean values

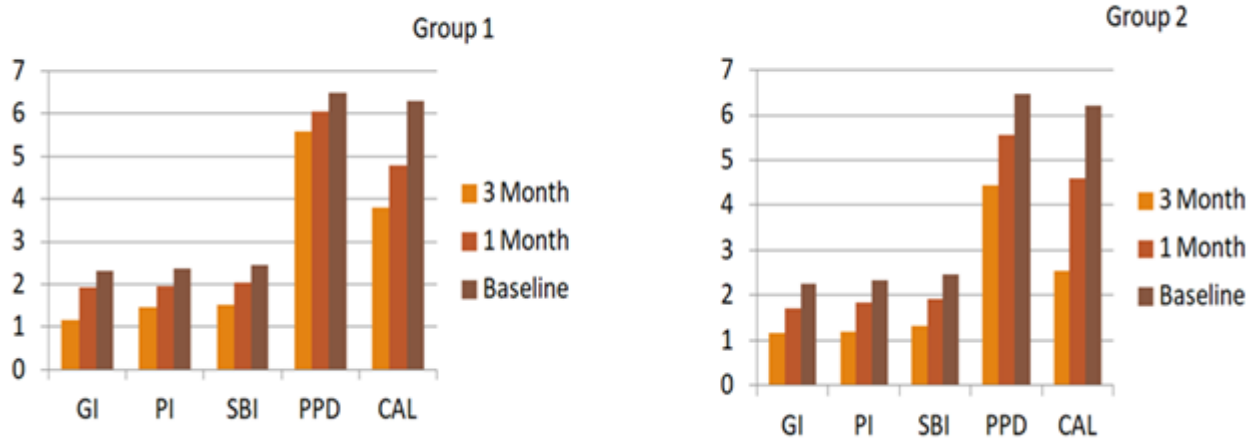


Figure 2: Intergroup comparison of differences from baseline to 3months

Intergroup comparison of mean values

**Intergroup comparison of differences from Baseline to 3M**

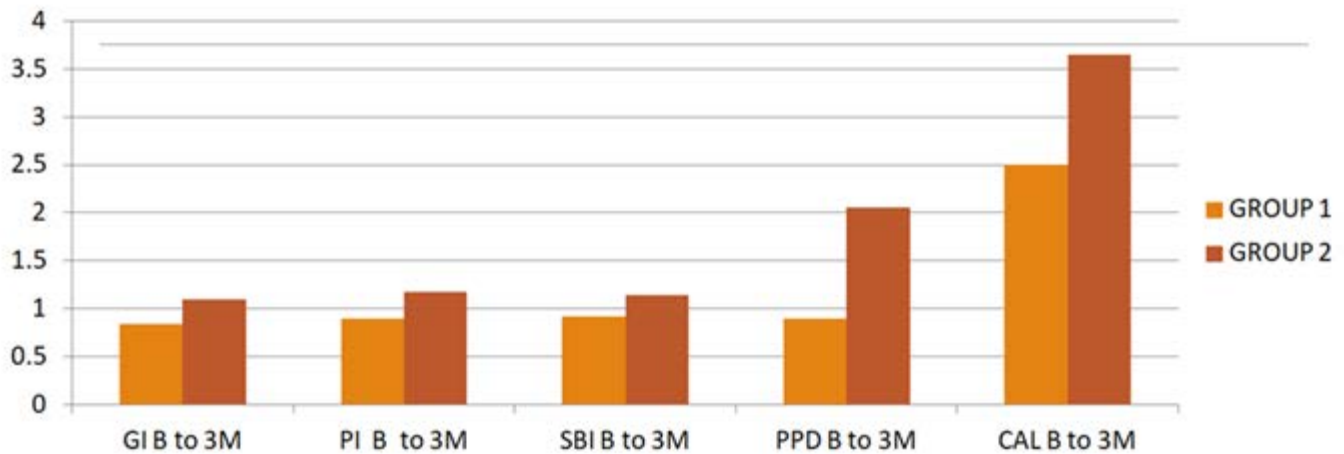


Figure 3: Consort Flow Chart

