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Original Article

Assessment of the Antimicrobial Effectiveness of 10% Doxycycline Gel Versus 1% Chlorhexidine Digluconate Gel on Sandblasted Acid-Etched Titanium Implant Surfaces Contaminated with Porphyromonas Gingivalis

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Abstract

The study aimed to compare the antimicrobial performance of 10% doxycycline gel and 1 percent chlorhexidine (CHX) gel in decontaminating sandblasted acid-etched titanium implant surfaces inoculated with Porphyromonas gingivalis. Titanium implants were assigned to two groups (A and B), each subdivided into 3 subgroups (A1–A3, B1–B3), and deliberately contaminated with P. gingivalis. Group A implants received 10% doxycycline gel, whereas Group B implants were treated with 1 percent CHX gel. The remaining viable bacterial load after treatment was measured using standard culture techniques. Initially, both groups showed an average bacterial load of 120,000,000 CFU. On the first day, subgroup A1 had 3291.67 CFU, while B1 showed complete eradication (0 CFU). By days three and seven, all remaining subgroups (A2, A3, B2, B3) demonstrated complete elimination of the bacteria. While repeated application of 10 percent doxycycline gel and a single application of 1 percent CHX gel both achieved complete disinfection of implant surfaces, 1% CHX gel was particularly efficient. These findings suggest that both agents could be practical and cost-effective approaches in managing peri-implant infections.

Key words: Porphyromonas gingivalis, Anti-infective Agents, Chlorhexidine, Doxycycline

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Introduction

Oral health plays a vital role in overall well-being, as proper dentition, effective chewing function, and an esthetic smile significantly influence an individual's quality of life. The introduction of dental implants has revolutionized tooth replacement therapy, offering patients a functional and appealing alternative to conventional prostheses [1]. Despite their high clinical success rates, dental implants are not devoid of complications that can compromise their longevity [2]. These complications are generally categorized as mechanical, technical, or biological in nature [3,4]. Among biological complications, peri-implantitis remains a major concern, representing an infectious inflammatory condition affecting the supporting tissues surrounding an implant.

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According to a systematic review on the microbial biofilm composition in peri-implantitis, Porphyromonas gingivalis was identified as one of the predominant red-complex bacteria frequently associated with peri-implant lesions [5]. Treatment approaches for peri-implantitis are broadly classified into nonsurgical and surgical methods. Nonsurgical strategies encompass mechanical debridement, local antimicrobial delivery, photodynamic therapy, and laser application, while surgical interventions include resective and regenerative procedures. In situations where mechanical or surgical access is limited, adjunctive antibiotic therapy can serve as an effective alternative [6].

Previous research has assessed various antimicrobial agents in conjunction with mechanical debridement—such as 0.2 percent chlorhexidine (CHX), 10 percent hydrogen peroxide, 5 percent tetracycline hydrochloride, 25% metronidazole, minocycline, citric acid, and 14 percent doxycycline—yet none have achieved complete elimination of bacterial contamination from implant surfaces [7]. Effective decontamination of implant surfaces is crucial for successful healing of peri-implant defects and prevention of early implant failure. Although peri-implantitis arises from a polymicrobial biofilm, P. gingivalis constitutes a major pathogenic species within this microbial consortium[8]. Therefore, testing antimicrobial efficacy against P. gingivalis is essential.

Chlorhexidine has been extensively investigated as an anti-infective agent in peri-implant therapy due to its high substantivity, though lower concentrations (0.05%–0.2%) in single applications have shown limited effectiveness against P. gingivalis [9,10]. Similarly, doxycycline has demonstrated short-term therapeutic benefits in peri-implantitis management [11]. However, comparative evaluation of 1% CHX gel and 10% doxycycline gel against P. gingivalis has not yet been documented. Consequently, this study aimed to assess and compare the antimicrobial efficacy of 10 percent doxycycline gel and 1% CHX gel in disinfecting sandblasted acid-etched (SAE) titanium implant surfaces contaminated with P. gingivalis.

Materials and Methods

This in vitro study received ethical approval and was conducted in the Department of Periodontics between 2018 and 2021.

A total of 72 SAE titanium implants were randomly allocated into two main groups. Group A (n = 36) was treated with 10 percent doxycycline gel, while Group B (n = 36) received 1 percent CHX gel. Each group was further subdivided into three subgroups of 12 implants each (A1, A2, A3, B1, B2, B3).

The excipients used in the formulation of the doxycycline gel—poloxamer (P407) and propylene glycol (PG)—were obtained from BASF Pharmaceuticals and Bangalore Fine Chemicals, respectively. Doxycycline hyclate was provided as a complimentary sample by Sisco Research Laboratories Pvt. Ltd.

The gel base was prepared using the cold method described by Schmolka in 1972 [12]. Measured quantities of P407 were gradually incorporated into chilled distilled water (maintained in an ice bath at 4°C) to produce a 20 percent w/v solution, which was stored overnight at 4°C for complete dissolution [13]. The resultant clear, viscous solution was allowed to reach room temperature to achieve gelation. Doxycycline hyclate was then incorporated into the P407 base to obtain a 10% gel formulation, with viscosity adjusted by adding PG **(Figure 1)**. A commercially available 1% CHX gel was used as the comparator and maintained at 4°C **(Figure 2)**.

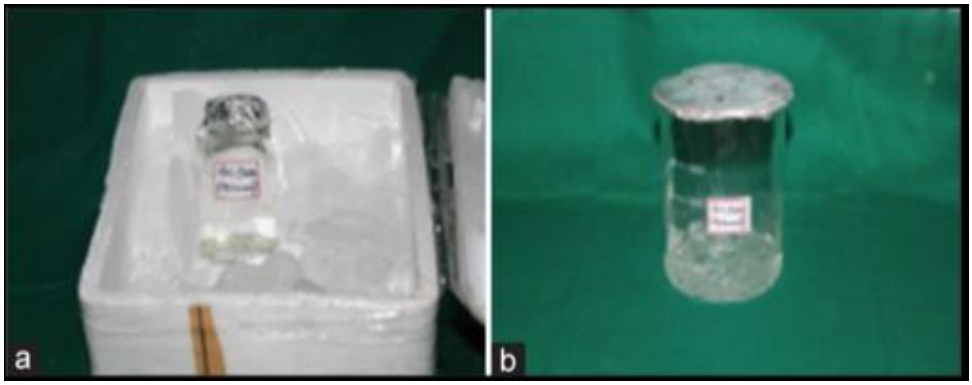


Figure 1. Preparation process of 10 percent doxycycline gel. (a) Poloxamer base maintained in an ice bath at 4°C; (b) Incorporation of doxycycline hyclate, propylene glycol, and benzalkonium chloride into the poloxamer matrix

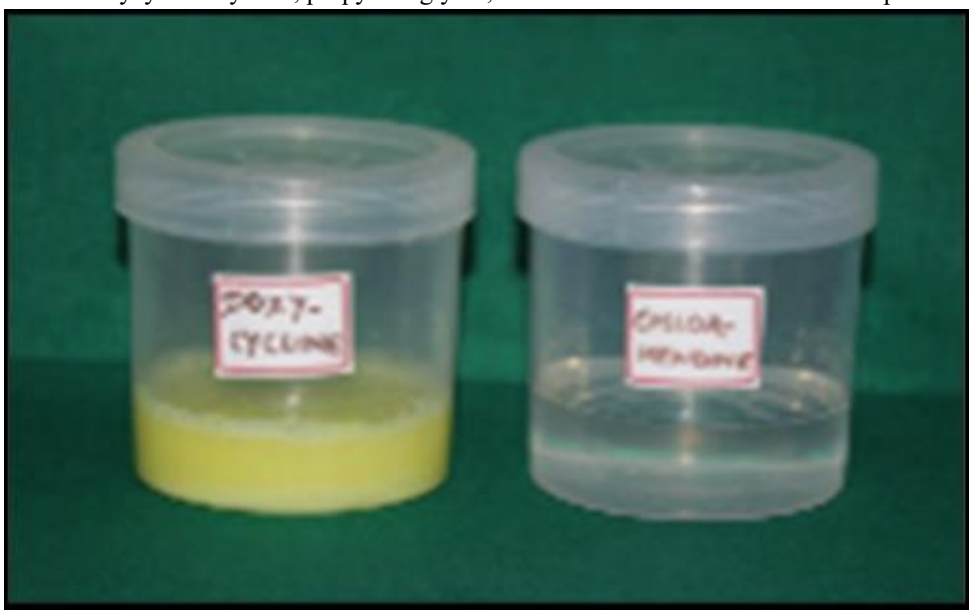


Figure 2. Antimicrobial gels applied – 10 percent doxycycline gel and 1 percent chlorhexidine gel

The Porphyromonas gingivalis ATCC 33277 strain was acquired in lyophilized form from HiMedia (KWIK-STIK™) and kept at 4°C. Each KWIK-STIK contained a dehydrated bacterial pellet, a hydrating solution, and an inoculation swab. Revival of the bacteria followed ATCC standard procedures.

Before bacterial contamination, all titanium implants were sterilized in a dry autoclave at 121°C for 15 minutes. Sterile 2 ml plastic cryovials (45 mm height × 11 mm diameter) were used to hold the implants. Thioglycolate (TG) agar at 1% concentration was prepared and sterilized under standard autoclaving conditions (120°C, 15 minutes, 1 bar).

After cooling the agar to a semi-solid state, the implants were partially embedded, leaving roughly half of each implant exposed. The exposed surfaces were then inoculated with 0.5 ml of P. gingivalis suspension containing 1.2×10^8 CFU per vial **(Figure 3)**. All vials were incubated for 48 hours at 37°C in a 5% CO_2 anaerobic chamber **(Figure 4)**.

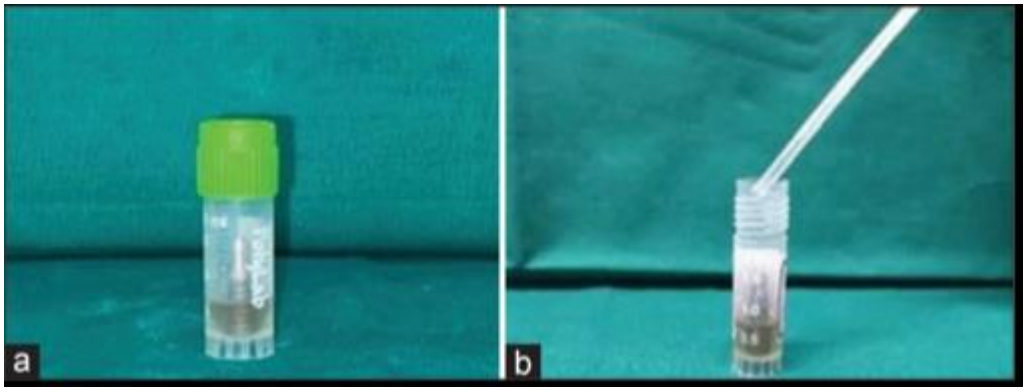


Figure 3. (a) Implant positioned within semi-solid thioglycolate agar; (b) Application of P. gingivalis suspension onto the implant surface

Figure 4. Vials containing Porphyromonas gingivalis-inoculated implants placed inside an anaerobic chamber

On day 1, implants in Group A were coated with 10% doxycycline gel using a syringe equipped with a blunt cannula and left undisturbed for roughly 3 minutes. Group B implants received 1% CHX gel, which remained on the surface for 10 minutes. After the treatment period, all implants in both groups were carefully flushed with sterile saline **(Figure 5)**.

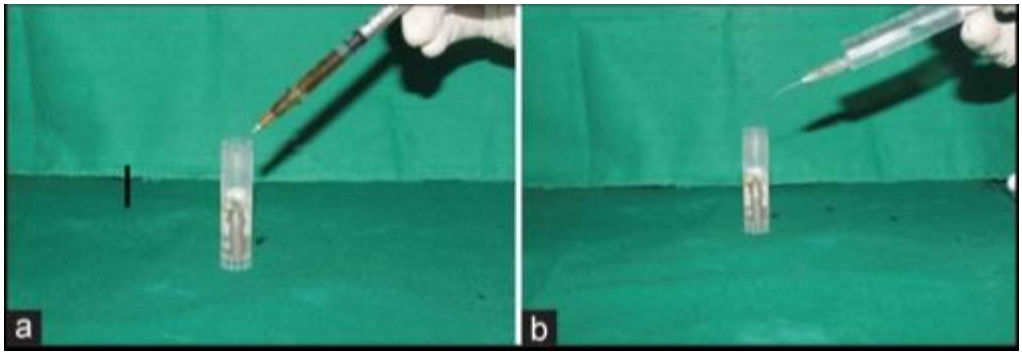


Figure 5. (a and b) Coating of implants with antimicrobial gel

For subgroups A1 and B1, each implant was placed into a sterile microtube containing ten milliliters of thioglycolate (TG) broth and agitated for 60 seconds to release adherent bacteria from the implant surface. The bacterial suspensions were then serially diluted to a 10^2 concentration **(Figure 6)** and plated onto blood agar to assess colony-forming units (CFU) **(Figure 7)**. The inoculated plates were incubated at 37°C in a 5% CO_2 environment for 48 hours. Implants belonging to subgroups A2, A3, B2, and B3 were returned to the incubator for further incubation.

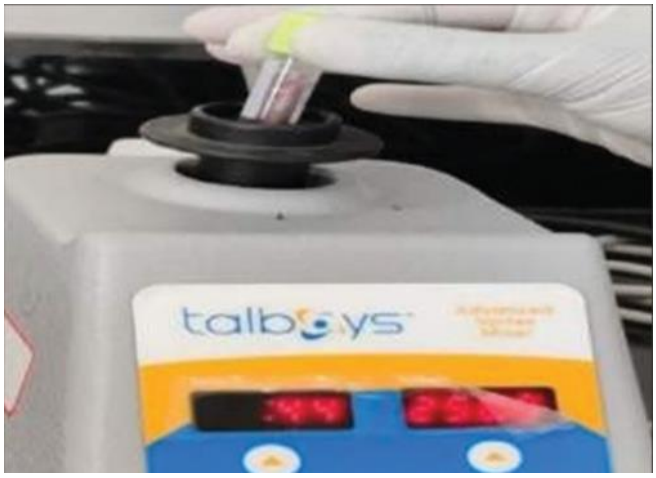


Figure 6. Agitation of disinfected implants in ten milliliters of thioglycolate broth for 60 seconds

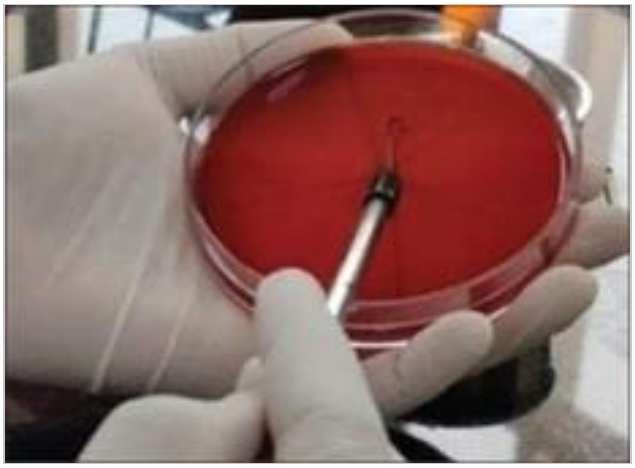


Figure 7. Blood agar culture of vortexed bacterial suspensions

On the third day, implants in subgroups A2, A3, B2, and B3 were again treated with their respective antimicrobial gels using the same protocol as on day 1. Only the implants from subgroups A2 and B2 were then transferred into sterile microtubes containing TG broth and subjected to vortexing to release adherent bacteria. The resulting suspensions were diluted, plated onto blood agar, and incubated at 37°C in a 5% CO_2 incubator for 48 hours, whereas the implants in subgroups A3 and B3 were returned to the incubator for further incubation.

On day seven, implants from subgroups A3 and B3 received the antimicrobial gels following the same procedure used on previous days. After treatment, the implants were immersed in TG broth to prepare bacterial suspensions, which were then diluted, plated onto blood agar, and incubated under the same conditions for 48 hours.

After each 48-hour incubation on days one, three, and seven, colonies of P. gingivalis were identified and counted manually using a magnifying glass **(Figure 8 and 9)**. A schematic representation of the experimental design is provided in the flowchart **(Figure 10)**.

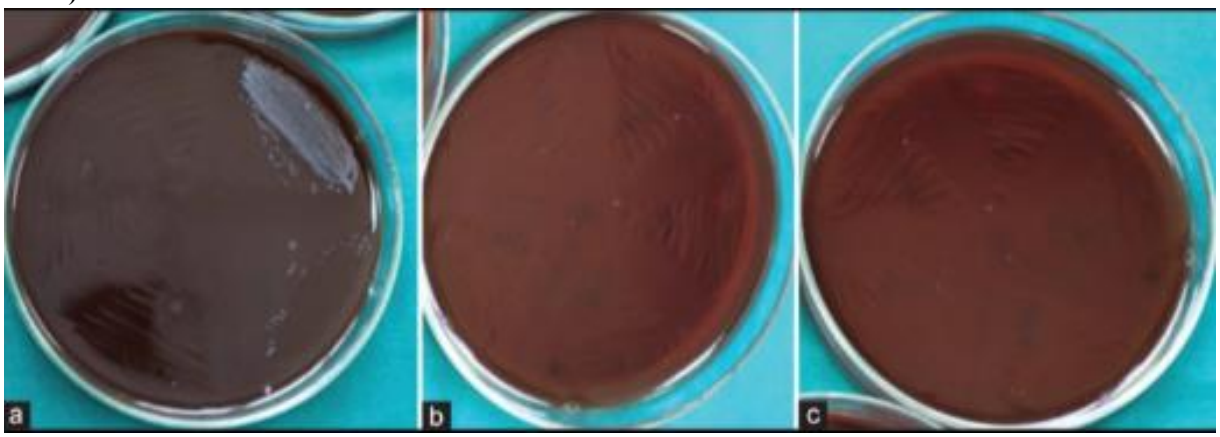


Figure 8. Blood agar growth of Porphyromonas gingivalis colonies from implants treated with 10 percent doxycycline gel in subgroups A1, A2, and A3. (a) Colony counts for subgroup A1; (b) colony counts for subgroup A2; (c) colony counts for subgroup A3

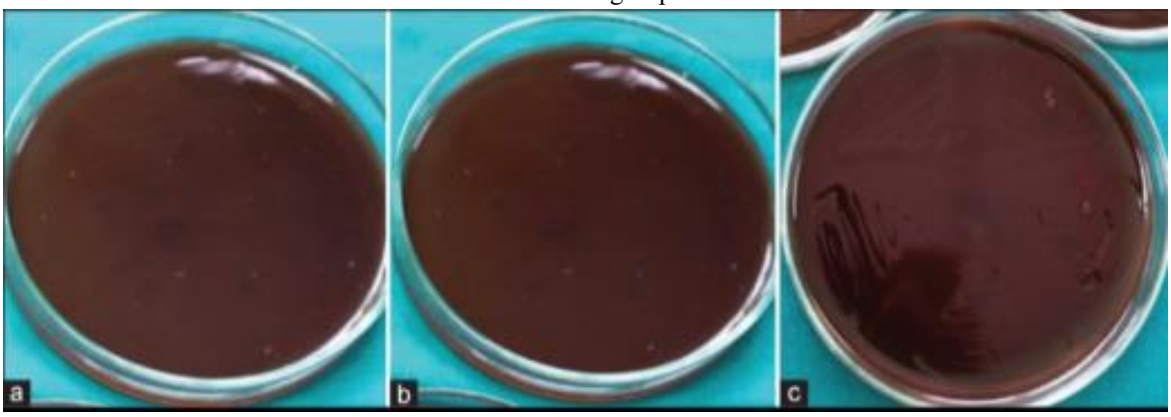


Figure 9. Blood agar growth of Porphyromonas gingivalis colonies from implants treated with 1 percent chlorhexidine gel in subgroups B1, B2, and B3. (a) Colony counts for implants in subgroup B1; (b) colony counts for subgroup B2; (c) colony counts for subgroup B3

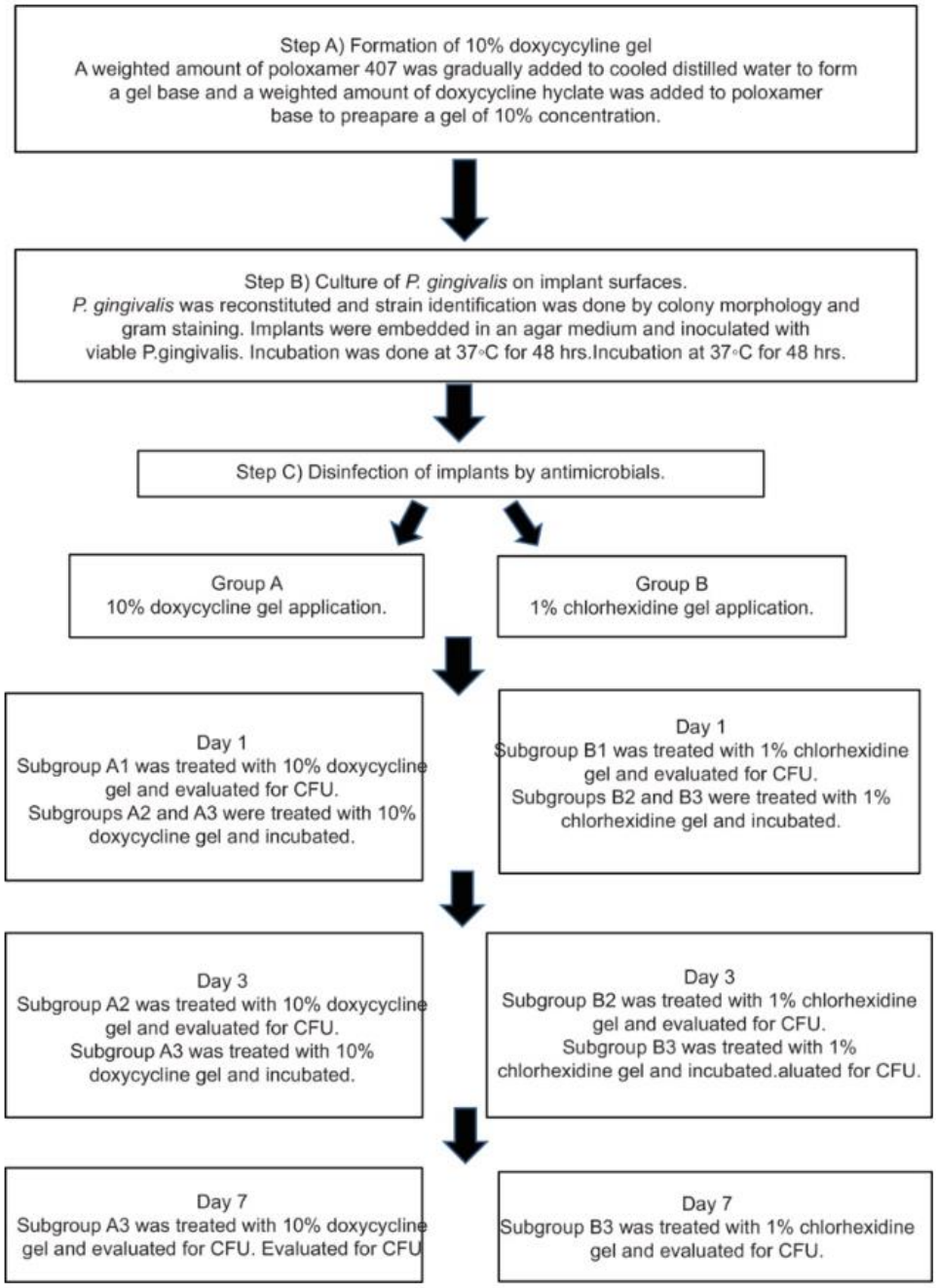
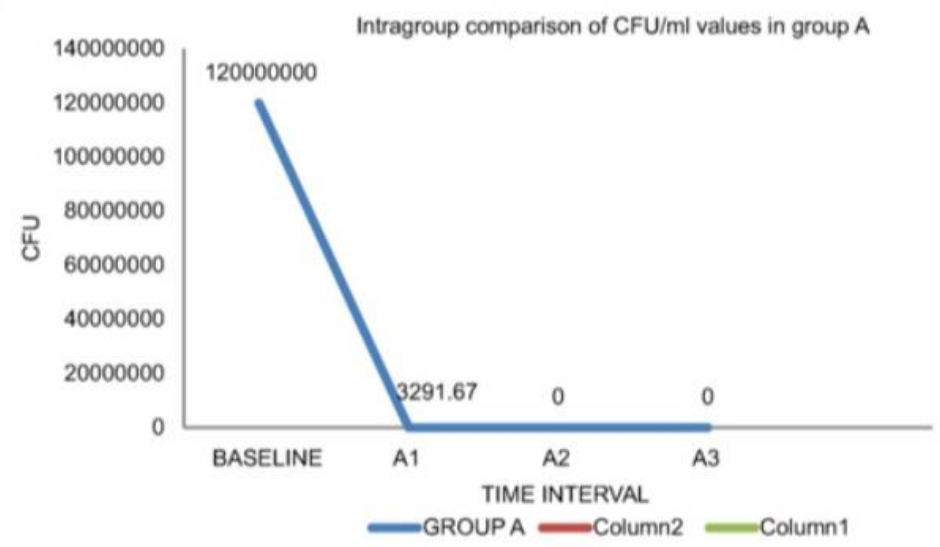


Figure 10. Study design flowchart

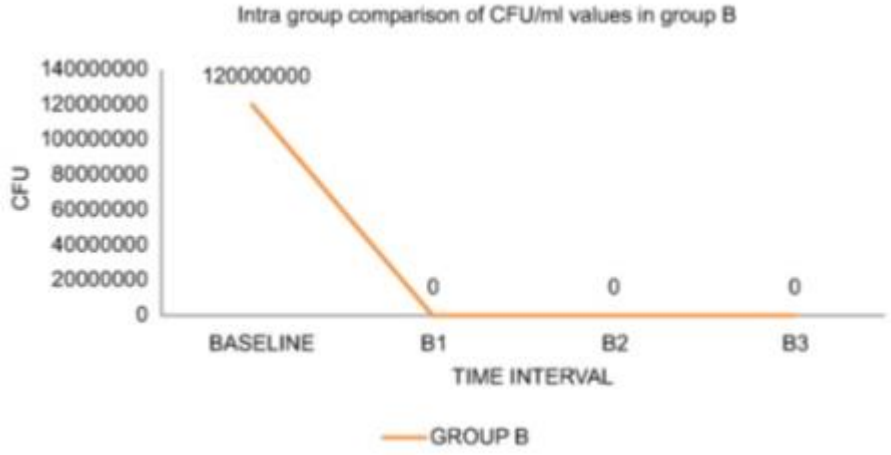
Results

The initial bacterial load for both Groups A and B was 1.2×10^8 CFU. On the first day, implants in subgroup A1 showed a mean CFU of 3291.67, while no bacterial colonies were detected for subgroup B1. By the third and seventh days, all other subgroups (A2, A3, B2, and B3) exhibited complete absence of bacterial growth.

Intragroup analysis using Friedman's test revealed highly significant reductions in CFU values from baseline across subgroups A1, A2, and A3 ($P < 0.01$), as illustrated in **Table 1** and **Graph 1**. Within Group A, CFU counts were greatest in A1 compared to A2 and A3, with these differences being statistically highly significant ($P < 0.01$). For Group B, **Table 2** and **Graph 2** demonstrated a significant drop in CFU values from baseline across subgroups B1, B2, and B3 ($P < 0.01$), although differences among these subgroups themselves were not statistically meaningful ($P > 0.05$).



Graph 1. Bar chart illustrating the changes in Porphyromonas gingivalis colony-forming units (CFU) on implants of subgroups A1, A2, and A3 before and after treatment with 10 percent doxycycline gel. CFU – Colony-forming unit



Graph 2. Bar chart depicting changes in Porphyromonas gingivalis colony-forming units (CFU) on implants from subgroups B1, B2, and B3 before and after application of 1% chlorhexidine gel. CFU – Colony-forming unit

Table 1. Colony-forming unit count of *Porphyromonas gingivalis* for Group A implants before and after treatment with 10% doxycycline gel

	n	**Mean**	**SD**	**Minimum**	**Maximum**	**Median**	**Mean rank**	χ^2	***P* value of Friedman test**
Baseline	36	120,000,000	0.000	120,000,000	120,000,000	120,000,000	4.00	33.545	0.000**
A1 (day 1)	12	3291.67	5451.34	0	20,000	2300.00	2.75		
A2 (day 3)	12	0.00	0.000	0	0	0.00	1.63		

A3 (day 7)	12	0.00	0.000	0	0	0.00	1.63

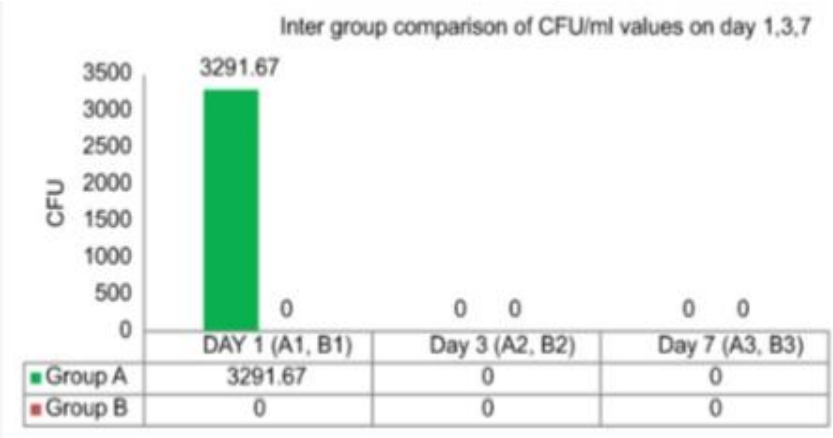
SD – Standard deviation; *P* - Probability value, *n* - Sample size, **$P < 0.01$ - Highly significant

Table 2. Colony-forming unit count of *Porphyromonas gingivalis* for Group B implants before and after treatment with 1% chlorhexidine gel

	n	**Mean**	**SD**	**Minimum**	**Maximum**	**Median**	**Mean rank**	χ^2	***P* value of Friedman test**
Baseline	36	120,000,000	0.000	120,000,000	120,000,000	120,000,000	4.00	36.000	0.000**
B1 (day 1)	12	0.00	0.000	0	0	0.00	2.00		
B2 (day 3)	12	0.00	0.000	0	0	0.00	2.00		
B3 (day 7)	12	0.00	0.000	0	0	0.00	2.00		

SD – Standard deviation; *P* - Probability value, *n* - Sample size, **$P < 0.01$- Highly significant

Comparisons between Groups A and B were conducted using the Mann–Whitney U test. **Table 3** shows that CFU counts for subgroups A1 and B1 differed highly significantly ($P < 0.01$) [Graph 3]. However, as presented in **Table 4** and **Table 5**, no significant differences were observed in CFU values between subgroups A2 and B2 or between A3 and B3 ($P > 0.05$) **(Graph 3)**.



Graph 3. Bar chart comparing Porphyromonas gingivalis colony-forming units (CFU) between implants treated with 10% doxycycline (subgroups A1, A2, A3) and those treated with 1% chlorhexidine (subgroups B1, B2, B3). CFU – Colony-forming unit

Table 3. Colony-forming unit count of *Porphyromonas gingivalis* for implants in subgroups A1 and B1 treated with 10% doxycycline gel and 1% chlorhexidine gel, respectively

Groups	***n***	**Mean**	**SD**	**Median**	**Mann-Whitney *U* value**	***Z***	***P* value of Mann–Whitney *U*-test**
A1 (day 1)	12	3291.67	5451.348	0	18.000	−3.585	0.000**
B1 (day 1)	12	0.00	0.000	0			

SD – Standard deviation; *P* - Probability value, *n* - Sample size, *Z* - Standard score, **$P < 0.01$- Highly significant

Table 4. Colony-forming unit count of *Porphyromonas gingivalis* for implants in subgroups A2 and B2 treated with 10% doxycycline gel and 1% chlorhexidine gel, respectively

Groups	***n***	**Mean**	**SD**	**Median**	**Mann–Whitney *U* value**	***Z***	***P* value of Mann–Whitney *U*-test**
A2 (day 3)	12	0.00	0.000	0	72.000	−0.448	1.000#
B2 (day 3)	12	0.00	0.000	0			

SD – Standard deviation; *P* - Probability value, *n* - Sample size, *Z* - Standard score, #*P* > 0.05 - Nonsignificant

Table 5. Colony-forming unit count of *Porphyromonas gingivalis* for implants in subgroups A3 and B3 treated with 10% doxycycline gel and 1% chlorhexidine gel, respectively

Groups	*n*	Mean	SD	Median	Mann–Whitney *U* value	*Z*	*P* value of Mann–Whitney *U*-test
A3 (day 3)	12	0.00	0.000	0	72.000	0.000	1.000#
B3 (day 3)	12	0.00	0.000	0			

SD – Standard deviation; *P* - Probability value, *n* - Sample size, *Z* - Standard score, #*P* > 0.05 - Nonsignificant

Discussion

Successful management of peri-implant diseases requires thorough decontamination of implant surfaces to eliminate bacterial colonization. Although mechanical and chemical methods are often combined to achieve this, many in vivo studies have reported inconsistent or suboptimal results [14]. This in vitro investigation focused on evaluating the disinfectant efficacy of doxycycline and chlorhexidine (CHX) gels, applied either once or multiple times, against Porphyromonas gingivalis on contaminated implant surfaces.

Even though in vivo biofilms are composed of diverse microbial communities, red-complex bacteria have consistently been associated with peri-implantitis [5]. Ghensi *et al.* [15] identified P. gingivalis as the most frequently detected pathogen at peri-implantitis sites compared to healthy controls. This bacterium plays a critical role in biofilm development and architecture, as its Arg- and Lys-gingipains facilitate colonization by other pathogens such as Treponema denticola and Tannerella forsythia.[8] Furthermore, commonly used implant surfaces like sandblasted acid-etched (SAE) implants favor adhesion of P. gingivalis more than other microbial species [16]. These observations underscore the importance of developing antimicrobial agents specifically targeting P. gingivalis, a keystone pathogen in peri-implantitis.

The current study used 10% doxycycline, a bacteriostatic antibiotic, and 1% CHX, which exhibits bactericidal activity at this concentration [17]. The 10% doxycycline formulation was chosen based on previous studies demonstrating its reliable efficacy in implant decontamination [18, 19]. Patianna *et al.* [20] reported successful bacterial reduction with a 3-minute doxycycline gel application, which informed the exposure duration used in this study. Likewise, 1% CHX gel, supported by studies from Renvert *et al.* [21] and Paolantonio *et al.* [22] was applied for 10 minutes, as recommended by Sbricoli *et al.* [23] for achieving complete implant surface decontamination.

Compared to solution-based antimicrobials, gels provide prolonged contact with the target surface, enhancing their effectiveness, since solutions are rapidly cleared from gingival crevicular fluid and often require higher concentrations or repeated applications to maintain antimicrobial activity [24]. Lollobrigida *et al.* [25] demonstrated that gel-based formulations outperform liquid counterparts in reducing microbial load, justifying the choice of gel formulations in the present study.

The results showed a significant reduction in P. gingivalis CFU counts from baseline following doxycycline treatment, consistent with previous findings using 14% doxycycline gels [20]. Notably, bacterial reduction improved on day 3 compared to day 1, supporting the benefit of repeated applications, as also observed in clinical studies by Trajano *et al.* [26] with improvements over sequential treatment intervals. Similarly, CHX-treated implants showed a marked decrease in CFU counts at all assessed time points (days 1, 3, and 7), corroborating the findings of Paolantonio *et al.* [22], who reported effective bacterial suppression with 1% CHX.

Regarding implant surface integrity, Wheelis *et al.* [27] reported that 1% CHX caused only surface discoloration without corrosion, while higher doxycycline concentrations (50%) led to pitting, discoloration, and loss of oxide layer. Energy-dispersive spectroscopy indicated titanium content of 0.06%–0.85% in swab samples, and most agents increased surface roughness. While these findings highlight potential surface alterations from chemical treatment, they were beyond the scope of the current study and warrant further investigation.

Since no single decontamination approach has consistently achieved complete bacterial removal in peri-implantitis, this study aimed to determine the effectiveness of locally applied antimicrobials against P. gingivalis and to explore strategies for

optimal disinfection. The results emphasize that application frequency significantly impacts antimicrobial efficacy. For example, a single application of 1% CHX effectively decontaminates implant surfaces, making it suitable for surgical interventions, whereas 10% doxycycline gel may require multiple applications for similar outcomes. Furthermore, local delivery of antimicrobial gels reduces systemic side effects and enhances patient compliance, offering a practical alternative to systemic antibiotic therapy. If validated in vivo, these findings could inform standardized protocols for chemical decontamination of implants, supporting clinicians in the effective management of peri-implantitis.

Conclusion

The antimicrobial agents tested in this study were effective in fully decontaminating implant surfaces contaminated with P. gingivalis, although the number of applications needed differed according to the agent used. A single application of 1% CHX gel immediately eliminated viable bacterial colonies and prevented regrowth with subsequent applications. In contrast, 10 percent doxycycline gel substantially reduced CFU counts after the first application, with complete bacterial eradication achieved only after repeated applications. Since this investigation was conducted in vitro, further in vivo studies are required to confirm these results in clinical practice. Additionally, evaluating the effects of these antimicrobials on various implant surface types is essential for establishing a standardized protocol for implant decontamination.

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Conflict of interest: None

Financial support: None

Ethics statement: None

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