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Case Report

Tetracycline fiber: A drug in your pocket

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ABSTRACT

Periodontal disease is a broad phrase that refers to a variety of diseases that damage the tooth\'s supporting components. Chronic periodontitis, Aggressive periodontitis & systemic disease-associated periodontitis are all examples of periodontal disorders. The breakdown of the periodontal ligament, resorption of the alveolar bone, and migration of the junctional epithelium along the tooth surface define these diseases. It is a localized inflammatory reaction brought on by bacterial infection of a periodontal pocket, which is often accompanied by supra & sub gingival plaque.

Methodology: Different mechanisms and ways to medication release in the periodontal pocket are used in local drug delivery. Such technologies deliver the medicine directly into the periodontal pocket and provide up to 11 days of continuous release.

Conclusion: This study exhibited that albeit careful SRP is a successful therapy technique for disposal of chronic periodontal pockets, further developed outcomes can be acquired by adjunctive utilization of locally controlled antibiotic medication tetracycline fibres and others such products.

1. Introduction

Periodontal disease is a broad term that refers to a variety of diseases that damage the tooth's supporting components. Chronic periodontitis, Aggressive periodontitis & systemic disease-associated periodontitis are all examples of periodontal disorders. The breakdown of the periodontal ligament, resorption of the alveolar bone, and migration of the junctional epithelium along the tooth surface define these diseases. It is a localized inflammatory reaction brought on by bacterial infection of a periodontal pocket, which is often accompanied by supra & sub gingival plaque.[1] Bacteria create a highly organized and complicated biofilm in the periodontal pocket. As time goes on, the biofilm spreads well under the gingival margin, making it impossible for the patient to access it during dental care.[2]

Periodontal diseases are caused by gram-negative, facultative anaerobic bacteria such as B. intermedius and B. gingivalis; fusiform organisms such as Actinobacillus, A. Actinomycetemcomitans, Wolinella recta, and Eikenella species; various bacilli and cocci; spirochetes; amoebas and trichomonas.[3] The degradation of connective tissue and bone loss in periodontitis is generally known to be mediated by both bacterial infection and the host immune response. In the treatment of periodontal infection, antibacterial medicines have been used with mechanical debridement. Due to the restriction of accessibility in the periodontal pocket, the effectiveness of all techniques is not up to mark.[4] To be successful, the antibiotic must penetrate the depths of the pocket and create gingival fluid concentrations greater than the suspected bacteria minimum inhibitory concentrations (MIC).[5] Clinicians and researchers now have a multitude of diagnostic tools and techniques to help them better understand the etiopathogenesis of periodontal

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disease, which has broadened the treatment choices.[6]

Various medicines have been utilized in the treatment of periodontitis since the development of systemic antibiotics. Because of the drawbacks of systemic antibiotics, such as bacterial resistance, superimposed infections, unsure patient compliance, nausea, vomiting, and gastrointestinal problems, local drug administration was introduced as a therapy alternative.[7] Dr. Max Goodson and colleagues 1972, originally presented the notion of controlled delivery system in the treatment of periodontitis. Since then, a number of studies have been conducted with various antimicrobial drugs and in a variety of clinical settings.[8]

1.1. Local drug delivery system

Different mechanisms and ways to medication release in the periodontal pocket are used in local drug delivery. Such technologies deliver the medicine directly into the periodontal pocket and provide up to 11 days of continuous release.[9,10] There will be various benefits and limitation of local drug delivery in periodontal pocket which are as follows:[11]

1.1.1. Benefits

1. Directly reaches the target site.
2. Improvement of patient compliance.
3. Avoidance of GIT-related issues due to oral drug delivery.
4. Avoidance of first pass metabolism.
5. Enhanced therapeutic efficacy of the drug.
6. Reduced treatment cost when compared to surgical procedure.
7. Suitable for those patients where surgeries are contraindicated due to some systemic debilitating conditions.
8. Safer and convenient route of drug administration.
9. Enhanced duration of action.
10. Simple, painless and non-invasive therapy.
11. Drug concentration maintained at the target site.
12. Reduced side effects.
13. Reduction of dosing frequency.

1.1.2. Limitations

1. Dose is limited because of relatively small area.
2. Administration of peptides not feasible due to the degradation by the enzyme peptidase.
3. This route understood the needs for high potency drugs.
4. Manufacturing cost of the patches and devices is high as compared to systemic anti microbials.

Although the LDD seems to be cost effective as compared to surgical procedure but when compared to systemic antibiotics they are quite expensive.[12]

1.2. Classification of local drug delivery

1.2.1. Based on the application [Rams and Slots] 1996[13]

1. (a) Personally applied (in patient home self-care
   - i. Non-sustained subgingival drug delivery
     Home oral irrigation
     Home oral irrigation jet tips
     Traditional jet tips
     Oral irrigation (water pick)
     Soft cone rubber tips (pick pocket)

   (b) Sustained subgingival drug delivery
   - i. Professionally applied (in dental office
     - A. Non-sustained subgingival drug delivery
       Professional pocket irrigation.
     - B. Sustained subgingival drug delivery
       Controlled release devices.
       Hollow fibres
       Dialysis tubing
       Strips
       Films

1.2.2. Based on the duration of medicament release (Greenstein and Tonetti 2000[14]

1. (a) Sustained release devices – Designed to provide drug delivery for less than 24 hours
   (b) Controlled release devices – Designed to provide drug release that at least exceeds 1 day or for at least 3 days following application (Kornman1993)

1.2.3. Depending on degradability[6]

1. (a) Nondegradable devices (First generation)
   (b) Degradable devices (Second generation)

Fibres, films, injectable systems, gels, strips, compacts, vesicular systems, microparticles, and nanoparticles are some of the local drug delivery methods used to treat periodontitis.

Currently available locally delivered antimicrobials in periodontal therapy are: -

1.3. Minocycline

Minocycline is a broad-spectrum antibiotic that is a semi-derivative of tetracycline. It acts as an antibacterial agent by interfering with the bacterial cell's protein production.[15] Arestin is a locally administered, sustained release formulation that comprises 1mg of minocycline hydrochloride in the form of microspheres in a bioresorbable polymer (polyglycolide-co-dl-lactide) [PLG]. The antibiotic is released locally during a two-week period at a concentration of >300 microg/ml in the gingival crevicular fluid, as assessed in the gingival crevicular fluid.[16]

1.4. Metronidazole

Elyzol is a topical treatment that contains a 25% oil-based metronidazole dental gel that is administered to the pocket in a thick consistency.

1.5. Chlorhexidine

Periochip is a tiny chip made of biodegradable hydrolyzed gelatin matrix that has been cross-linked with glutaraldehyde and contains glycerine and water, as well as 2.5 mg of chlorhexidine gluconate. It is an FDA-approved little orange brown chip that measures 4.0x 0.5x 0.35mm and is encased in a biodegradable gelatin matrix.[17]

1.6. Chlo-site

Ghimas Company, Italy, manufactures Chlo-Site, a xanthan-based gel containing 1.5% chlorhexidine. Xanthan gel is a biocompatible, naturally occurring saccharide polymer with a distinct crosslinking structure that regulates drug release. The chlo-site gel gets vanished from the pocket within 10-30 days after applying and effective concentration of greater than 100 ug/mL of chlorhexidine digluconate is achieved on the first day which is then maintained for an average of 6-9 days reaching a level greater than the minimum inhibitory concentration for chlorhexidine (0.10 ug/mL). It helps in treating periodontal pockets and periimplantitis.[18]

1.7. Doxycycline

Atridox is a 10% doxycycline gel system with a syringe that has been certified by the FDA. The GCF levels hit a peak of 1,500-2,000 within about 2 hours Following treatment with Atridox these levels remained over 1000 g/mL for 182 hours, after which they began to drop.[19]

1.8. Tetracycline (TC)

Fiber containing tetracycline is the first local drug delivery system. Tetracycline, a broad-spectrum bacteriostatic drug used to treat long-term bacterial infections like acne vulgaris, and had been utilized as a periodontal disease therapy adjunct. Tetracycline fiber local drug contains monofilament ethylene/vinyl acetate copolymer fibres with diameter of 0.5 mm, containing tetracycline12.7mg per 9 inchesand tetracyclines hydrochloride get disappeared evenly, that provides continuous liberate of tetracycline for 10 days.[20]Periodontal Plus AB, a commercially available collagen film, was used to create resorbable tetracycline fibers. This product has a shelf life of 2 years and comprises 25 mg of pure fibrillar collagen with about 2 mg of uniformly impregnated tetracycline HCL, that is sterilized by gamma radiation. It releases tetracycline, which dissolves over the course of 8-12 days. And has the benefit of being biodegradable.

After having brief introduction of different types of local drug delivery we have used the tetracycline based local drug delivery as a case report in this article.

2. Procedure: A Case Report

A 30-year-old male patient reported to the outdoor patient department complaining of bleeding gums in upper right back tooth region since one and half month. Patient gave a history of tobacco chewing since last 6-7 years, but he quitted the habit of chewing tobacco 8months back.

Intraoral view revealed moderate stain, calculus deposits and generalized gingival inflammation. There was bleeding on probing seen in relation to teeth number 15,16,17,18,26,27,28,36,37,45,46,47. The colour of the gingiva was reddish pink, which was moderately enlarged, with blunt rolled out margin. The consistency was soft and oedematous, whereas stippling was absent and the position of gingival margin was around 2mm coronal to CEJ in posterior region of maxillary and apical to the CEJ in mandibular anterior region of jaw. There was generalised increased in probing depth and CAL ≥5mm and ≤7mm was recorded (Figure 2B). All teeth were vital.

Various investigation was advised: Radiograph (OPG) and IOPAR (Figure 5A & B)

2.1. Treatment

At first appointment, evaluation was done and supragingival ultrasonic scaling was performed. Oral hygiene instructions were given and advised for warm saline rinses for a week. Second appointment was given after a week where subgingival scaling was done. After that the area was isolated with cotton rolls. Topical LA was sprayed. Commercially available collagen fibres Periodontal Plus AB (tetracycline fibres) as a local drug was used in interdental and gingival crevice (Figure 3 A & B). Fibres were placed at the prepared site and gently pushed inside the pocket, so that the materials fill the depths and curves of the pocket. The area was sealed with coe-pack to prevent the dislodgement of fibres and the ingress of oral fluid. Patient was reinforced for the oral hygiene maintenance. Patient was recalled after 15 days for the re-evaluation.

3. Discussion

Chronic periodontitis, is one, that is widely known to be particularly difficult to cure when caused by microbial biofilms. Dental biofilms are tough to treat because they are difficult to disrupt.[21] Periodontal disease is generally caused by facultative and anaerobic bacteria, according to a growing body of research.[22] It is almost hard to completely eliminate their production in a non-sterile environment like the mouth. This objective has now been accomplished using a variety of nonsurgical and surgical treatments. Until the early 1970s, periodontal disease

Fig. 1: A: Periodontal Plus AB; **B:** content of local drug delivery tetracycline fibre; **C:** tetracycline fibre container with fibre

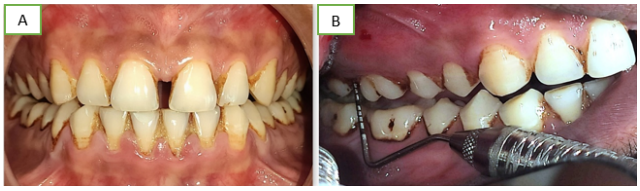

Fig. 2: A: Plaque and stain on buccal aspect of teeth; **B:** Probing pocket showing ≥6mm interdental area.

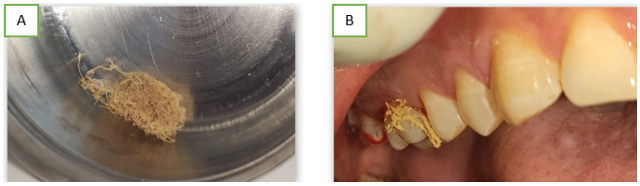

Fig. 3: A: Tetracycline fibers; **B:** Fibers are placed in interdental area and sulcus are of 15,16,17,

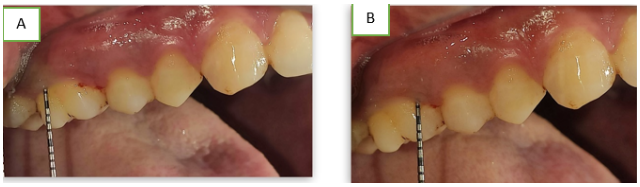

Fig. 4: A: Interdental periodontal pocket reduced to ≤ 4mm wrt to 15,16,17,; **B:** sulcus probing also reduced to ≤4mm wrt 15,16,17.

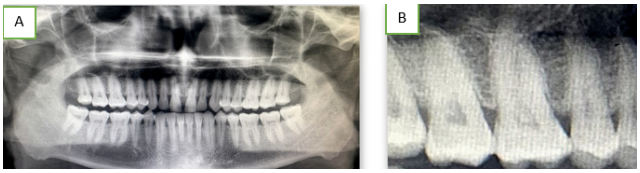

Fig. 5: A: Orthopantomagraph (OPG); **B:** IOPAR wrt 15,16,17

was treated with mechanical debridement with or without surgical interventions to disturb the subgingival flora and create clean, smooth, and biologically compatible root surfaces. However, due to the pathogenic bacteria's position within gingival tissues or in other regions inaccessible to periodontal instruments, so mechanical treatment may fail to remove them.[8] Tetracycline, as reported by Goodson,[23] Metronidazole and Chlorhexidine by Addy et al.[24] and Ofloxacin by Hoffler et al.,[25] are the most often utilised local drug delivery system reports in periodontal literature. Collagen-impregnated tetracycline fibres were utilised in this study, and they were proven to be more effective than other medicines.

Tetracyclines are preferable to other antibiotics because they are the only antibiotics that can adhere to the tooth cementum and soft tissues. The 4-membered tetracycline ring is the foundation of this category of antibiotics' chemical structure, which influences their physicochemical qualities, such as alkaline nature, poor water solubility, and durability. The action of tetracyclines work by interfering with protein production and phosphorylation in bacterial cells. Tetracycline resistance may be classified into two types: nonspecific and specific.[26,27] The former is a type of low resistance that occurs when tetracycline transport through purine channels in the outer membrane to the interior of the cell is reduced. Specific resistance can be linked to one of three mechanisms: enzymatic inactivation of drug molecules, active pump removal of tetracyclines from inside bacterial cells, or ribosome protection against tetracyclines.

Golub et al.[28] found that tetracycline inhibited collagenase activity, collagen breakdown, and bone resorption. Maiden et al.[29] reported that during vitro testing has proven probable periodontal pathogens which includes P. gingivalis, Fusobacterium nucleatum, P. intermedia, Eikenella corrodens, Wolinella recta, and A. actinomycetemcomitans are prone to neighbourhood Tetracycline concentrations finished in periodontal pocket with a managed launch device. Therefore, tetracycline is appropriate to neighbourhood transport and as adjuncts to mechanical remedy in control of periodontal disease. Betty N.A. Vandekerckhove,[30] reported that treatment with tetracycline-impregnated fibres converted refractory sites to stable areas. The efficacy of locally delivered tetracycline to prevent recurrent disease could also be related not only to its antibacterial effect,[31] but also to its secondary effects on the

collagen breakdown. It also enhances Fibroblast attachment to root structure. Additionally, there's a substantivity of tetracycline through its binding to dentin, as proven in vitro and in vivo.

3.1. Tetracycline fibres

Periodontal Plus AB (Advanced Biotech Products (P) Ltd., (Figure 1 A, B & C) Chennai, India) is a biodegradable collagen fibre soaked with 8% tetracycline, that releases drug in periodontal pocket within 10-14 days. About 1.7 mg of tetracycline hydrochloride is carried by a collagen to comprising 25 mg of pure filamentous type I collagen. Because this collagen strand is not transversely cross-linked, the drug is released in a systematic manner depending on how the collagen fibres are destroyed [34].

The present case demonstrates the successful periodontal pocket treatment was achieved by tetracycline fibre in reducing probing pocket depth ≥ 5mm to ≤7mm to 4mm (Figure 4 A & B).

4. Conclusion

According to the existing data, local drug administration into the periodontal pocket can enhance periodontal health while ensuring patient compliance. Local drug delivery, as opposed to systemic antimicrobials, would minimise the development of drug-resistant bacterial strains, which is now a global problem. This study exhibited that albeit careful SRP is a successful therapy technique for disposal of chronic periodontal pockets, further developed outcomes can be acquired by adjunctive utilization of locally controlled antibiotic medication tetracycline fibres and others. Although it is still debatable whether LDD agents are cost effective in composition to systemic antimicrobial but surely it is cost effective when compared to surgical and other regeneration procedures.

5. Conflict of Interest

The authors declare that there is no conflict of interest.

6. Source of Funding

None.

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