Case Study

PHOTODYNAMIC THERAPY - THE LIGHT WITH THERAPEUTIC POTENTIAL: A CASE SERIES

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ABSTRACT

Photodynamic therapy is a modern, rapidly evolving discipline for treating various diseases & conditions. It is a light-mediated photochemical reaction involving the activation of photosensitizing compounds leading to the generation of cytotoxic reactive oxygen species. Photodynamic therapy represents a non-invasive, non-toxic, repeatable procedure without causing any collateral damage and is used for treating periodontal and peri-implant diseases by causing light-activated microbial killing and also in the treatment of various oral potentially malignant disorders (OPMDs). Photodynamic therapy was performed using an application of photosensitizing dye (1% methylene blue) and a low-level diode laser (660nm at 50mW) for one minute. Three different modalities i.e., management of periodontitis, peri-implantitis & oral lichen planus are showcased in this case series where PDT was effective in improving the clinical parameters of periodontitis & peri-implantitis cases and overall clinical improvement of symptoms in case of oral lichen planus. Thus, proving the PDT as a promising treatment adjunctive.

Key words: Photodynamic therapy, aPDT, Oral lichen planus, Peri-implantitis, Photosensitizers, Methylene blue.

Introduction

Light as a therapy in the field of medicine and surgery can be traced from antiquity to the modern-day. Photodynamic therapy (PDT) emerged as a powerful medical tool and has now been used extensively in various fields of clinical dentistry.

It was in the year 1900 when Oscar Raab, a medical student from Munich Germany, noticed the killing of paramecium due to interaction between acridine dye and visible light in the presence of oxygen [1]. A few years later Munich dermatologists Jesionek and von Tappeiner in the year 1904, utilized the basis of this therapy to treat a case of basal cell carcinoma by using Eosin, an acidic xanthene dye as a photosensitizer, and activated that with light [2]. Nobel prize winner, Danish physician Dr. Neil Rayberg Finsen opened a new avenue in medical sciences by utilizing light sources as a therapeutic modality. In 1978 Thomas Dougherty performed successful clinical trials for the treatment of cancers and even founded the International Photodynamic Association, in 1986 [3]. Food and Drug Administration approved the usage of PDT in 1999 to treat pre-cancerous lesions.

Since then, PDT has extensively been used to treat cancers and many other diseases. Photodynamic therapy acts selectively when light with a specific wavelength causes activation of the Photosensitizer [4]. Oschner M defined Photodynamic therapy as a "Light mediated photochemical reaction involving activation of photosensitizing compound leading to generation of cytotoxic reactive oxygen species" [5]. Photosensitizer activation results in two types of reaction: Type I reaction produces highly reactive oxygen species and Type II reaction singlet oxygen ($^1O_2$) is generated which is having strong antimicrobial action and forms the basis for antibacterial photodynamic therapy. Singlet oxygen being short-lived and with a small radius of action, a localized effect of oxidative damage to microorganism cells is achieved [6].

In dentistry, Wilson *et al*. 1992 investigated the bactericidal effect of photosensitizers [7] and since then use of aPDT in dentistry started as an approach to deliver antimicrobial agents locally at diseased periodontal sites and successful results have been achieved [8]. The application of photodynamic therapy as a valuable adjunct to various mechanical procedures in treating periodontal infection has been well documented in the literature.

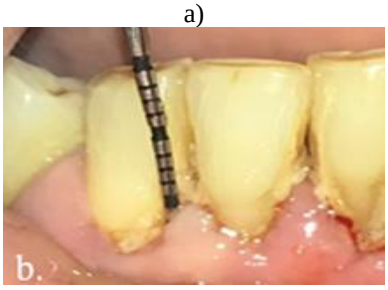
Case presentation

Photodynamic therapy has got a lot of scope as a therapeutic modality in periodontology. This clinical case presentation gives three different conditions which are successfully treated with PDT.

Case 1: PDT as an adjunct to SRP

A 49-year-old male reported to the department of periodontology with a chief complaint of bleeding gums and food lodgment in his teeth for 6 months. Clinical examination revealed positive scores of supragingival plaque, bleeding on probing, suppuration, and CAL of 6mm in upper anterior and 5mm in lower anterior teeth **(Figure 1)**, and the patient was subsequently diagnosed with Stage 2 grade B periodontitis.

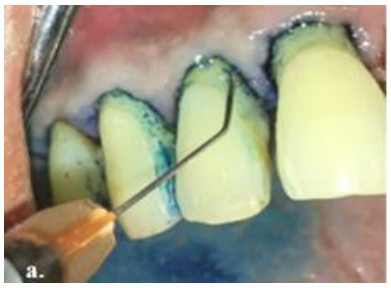
a)



b)

Figure 1. a) Pre-op Probing depth 6mm in 12, b) Pre-op Probing depth 5mm in 43

After initial mechanical debridement, PDT was utilized to bring down the infectious microbial load. Photosensitizer dye used was 1% methylene blue dye which was applied in sulcus using a blunt needle **(Figure 2a)**, keeping the dye in situ for 5 mins for uptake by diseased tissue [9]. Washing done with normal saline to remove excess dye and site is irradiated using Helbo®, a low-level diode laser of 660nm at 50mW and 100mV for 1 minute separately to all six surfaces around each tooth **(Figure 2b)**.



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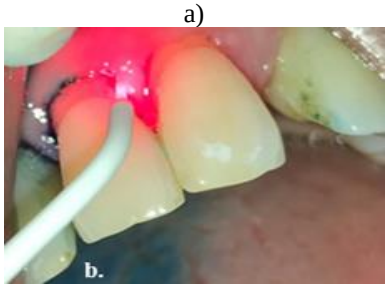

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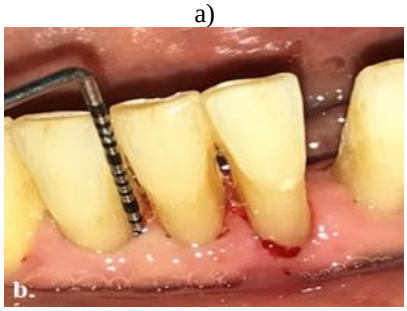
Figure 2. a) Photosensitizer dye application, b) Light Activation of Dye using diode laser

The patient was recalled fortnightly and a similar procedure with a total of 5 cycles of PDT was carried upon which has resulted in improvement of clinical parameters. Probing depth reduction from baseline 5mm to 3mm in upper anterior teeth and 6mm to 3mm in lower anterior teeth, 6month postoperatively **(Figure 3)**.

a)



b)

Figure 3. a) Post-op Pocket depth reduced to 3mm in 12, b) Post-op Pocket depth reduced to 3mm in 43

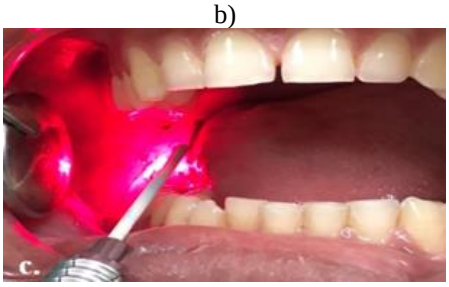
Case 2: PDT in management of oral lichen planus

A 31-year-old female reported the chief complaint of burning sensation in her mouth for the past 3 months with difficulty in having hot and spicy food. The patient did not give any relevant medical or drug history. The intraoral clinical presentation showed the presence of white lacy lines the Wickham's striae along with ulcerated lesions on her right cheek mucosa and associated slight erythema **(Figure 4a)**. Case provisionally diagnosed as a unilateral atrophic form of oral lichen planus and later confirmed histologically.

PDT was planned for the management of the lesion. 1% methylene blue applied on lesion along with 1cm of the perilesional area followed by washing which removes extra dye and selective uptake by lesion tissue was achieved **(Figure 4b)**. Diode laser activation of dye was done for 60 secs **(Figure 4c)**. The cycle repeated on the 3rd, 5th 7th, and 14th days. There was a marked reduction in patient symptoms after one month and on the 6th month follow up the significant resolution of the lesion was evident **(Figure 4d)**.

a)

b)



c)

d)

Figure 4. a) Wickham's striae with Ulcerated lesions, b) Methylene blue dye application, c) Diode laser activation of dye, d) Complete resolution of lesion 6 month Post-op

Case 3: PDT in management of peri-implantitis

A 28-year-old male reported mild pain and bleeding gums along with an unpleasant smell from the oral cavity for one month. The patient was systemically healthy and non-smoker. Clinical history revealed placement of the dental implant in the same region 7 months ago. Clinical examination showed inflammation and on palpation, suppuration was present in implant site irt 35i. Peri-implant probing showed 6mm of pocket on the distal aspect of the implant **(Figure 5a)**. The periapical radiograph showed radiolucency on both mesial and distal aspects suggestive of peri-implant bone loss which was extending till the middle 3rd of the implant **(Figure 5b)**. Based on clinical and radiological findings, a diagnosis was established as moderate periimplantitis 35i [10].

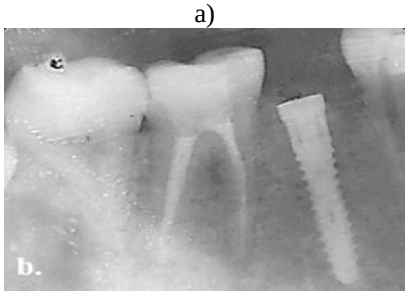
a)

b)

Figure 5. a) Peri-implant probing showing 6mm of pocket, b) Peri-implant radiolucency in IOPA

Surgical exploration of the defect was done by raising the full-thickness flap, the surgical site was debrided using titanium curettes. Post debridement and before graft placement, the peri-implant area was treated with aPDT **(Figure 6a)** using methylene blue dye providing anti-infective therapy and implant surface decontamination. This was followed by regenerative therapy with particulate xenograft and resorbable membrane and the flap was reapproximated using 5-0 polypropylene sutures. The patient was advised with analgesics and antibiotics recalled after 10 days for suture removal. A further recall was done 6 months postoperatively and an intraoral radiograph revealed peri-implant bone fill which was suggestive of the success of photodynamic antimicrobial therapy **(Figure 6b)**. A temporary crown was placed and kept under occlusion and after 6 months Implant was restored with a cement-retained PFM crown.

a)



b)

Figure 6. a) PDT on peri-implant surgical site, b) 6-month Post-op IOPA

Results and Discussion

Photodynamic therapy evolved as a revolutionary treatment modality and found its place in a variety of fields of medicine

as well as in dentistry where it is presently utilized in premalignant conditions like oral submucous fibrosis, periodontal diseases, endodontic lesions, and peri-implantitis.

The present case series showcases the therapeutic utility of photodynamic therapy in three different cases. The use of PDT as an adjunctive procedure in the management of periodontitis is based on the PACT i.e. photodynamic antimicrobial chemotherapy. Periodontal disease is caused by dental plaque biofilms, removal of which is the mainstay in its treatment. Periodontopathic bacteria are susceptible to photosensitizer activated low-level laser wherein singlet oxygen causes the antibacterial action. PDT provides an added advantage of prevention of the development of antimicrobial resistance and enhanced local efficacy. Multiple systematic reviews conclude that utilization of aPDT as an adjunct to nonsurgical periodontal treatment provides therapeutic benefits [11]. However, the use of PDT as a mainstay in the clinical management of periodontitis is not recommended and cannot substitute SRP but to be used as adjunctive therapy is well supported in the literature [12].

PDT has proven its therapeutic effectivity in oral potentially malignant disorders like oral lichen planus [13]. In recent times multiple studies were done on exploring the healing effect of PDT in oral lichen planus. Aghahosseini *et al*. in 2006 put forward PDT as an alternative treatment modality in 13 patients and observed resolution of lesions [14]. It has been seen that PDT offered better results in alleviating the clinical symptoms of burning sensation and even pain in some atrophic forms of oral lichen planus. Efficacy of PDT was found as effective as topical corticosteroids which are considered the gold standard in treating the painful lesions of OLP with the additional benefit of prevention of side effects of long-term use of steroids [15]. In terms of VAS, again the use of the diode laser performed better clinical response in the treatment of OLP. A systematic review and meta-analysis by Jajarm *et al*. in the year 2015 concluded Low-level laser therapy is a reliable alternative to corticosteroids.

Periimplantitis is also a clinical challenge to manage due to its complication associated with the chance of dental implant failures. The prime etiological factor in peri-implantitis is the accumulation of biofilm around the mucosal margins of implants. Due to the presence of gram-negative anaerobic bacteria in and around the implant in periimplantitis, the condition becomes even more challenging. However multiple clinical studies were done for the efficacy of antimicrobial photodynamic therapy (aPDT) in decreasing the bioburden and thus achieving effective implant surface decontamination [16]. The photosensitizer such as methylene blue is capable of binding to the targeted cells and upon activation, it reacts with the substrate, which produces highly reactive singlet oxygen which is toxic for the microorganisms. With the use of PDT, it's quite unlikely to development of any kind of bacterial resistance which makes it a suitable alternative to antibiotics in the treatment of peri-implantitis and periodontitis [17].

Conclusion

This case series has showcased multiple therapeutic uses of photodynamic therapy. As an independent treatment modality, PDT was effective in the management of oral lichen planus, and in cases of periodontitis, aPDT can be utilized as an adjunctive modality to scaling and root planing. PDT is a noninvasive, selective treatment modality that provides desired treatment results without causing any adverse reactions. The selective uptake of photosensitizer and localization of drug prevents systemic toxicity and more importantly prevention of development of antibiotics resistance. This makes PDT the future of periodontal therapy. However, limitation in terms of cost & issues of photosensitivity still limits its use and warrants large-term clinical trials to establish PDT as a mainstay in the treatment of periodontal diseases.

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Conflict of interest: None

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Ethics statement: All the treatment performed was in accordance with the principles embodied in the Declaration of Helsinki and in accordance with local statutory requirements as per department protocol and written consent was obtained from each patient.

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