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Clinical note on use of povidone iodine in periodontics

Dr. Vasundhara Bhaskar Rikame[*] (3rd year MDS)[1], Dr. Yogesh S. Doshi (MDS)[2], Dr. Robert A. Horowitz (DDS)[3], Dr. Mona U. Shah (MDS)[4], Dr. Cauvery N. Karbhari (MDS)[5], Dr. Talat Mohammadi (MDS)[6], Dr. Nikita Jain (2nd year MDS)[1]

[1]*Post graduate student, Department of Periodontics, Pandit, Deendayal, Upadhyay Dental College, Solapur, India.*

[2]*Professor, Department of Periodontics, Pandit Deendayal Upadhyay Dental College, Solapur, India.*

[3]*Clinical Assistant Professor, Arthur Ashman Department of Periodontology & Implant Dentistry, NYU College of Dentistry, New York, USA.*

[4]*Head of the Department, Department of Periodontics, Pandit Deendayal Upadhyay Dental College, Solapur, India.*

[5]*Reader, Department of Periodontics, Pandit Deendayal Upadhyay Dental College, Solapur, India.*

[6]*Senior lecturer, Department of Periodontics, Pandit Deendayal Upadhyay Dental College, Solapur, India.*

***Corresponding Author: Dr. Vasundhara B. Rikame.**

Email id: rikame.vasundhara@gmail.com

ABSTRACT

Povidone iodine (PVP-iodine) is one of the widely used antiseptics in the field of medicine and surgery but it has not gained significant attention in dentistry. It is one of the most potent antiseptics with a wide range of antimicrobial action and high safety profile. It is effective against periodontal pathogenic bacteria, viruses and fungi. In vitro studies have demonstrated the toxic effects of PVP-I on fibroblasts. A question exists whether to use povidone iodine as an irrigating agent in periodontal surgery. The aim of this review is to describe the potential benefits of PVP-I in periodontal infections and periimplantitis, and its possible adverse effects. This article will provide clinical notes for the use of PVP-I in dentistry, concentration to be used and precautions to be taken while using it intraorally on open wounds.

Keywords: Povidone iodine, Periodontics, Periimplantitits.

INTRODUCTION

Periodontitis is an aggressive host inflammatory response to an infectious disease of the supporting tissues of the teeth having multifactorial etiology. [1] The main etiologic agents which initiate the disease process are the microorganisms in the dental plaque. [2] Non-surgical and surgical approaches to remove dental plaque and calculus are the fundamental principles in treating the periodontitis. [3] Complete removal of these calcified deposits and plaque becomes difficult with increasing pocket depth. [4] Various

adjunctive treatment modalities such as subgingival local drug delivery, systemic antibiotics and laser therapy have been employed for additional benefits. [5, 6] Which antimicrobial should be used and in which mode of delivery is always ambiguous. Furthermore, there is fear of developing antibacterial resistance and adverse reactions. [7] Chlorhexidine digluconate is the most widely used antimicrobial agents in the periodontics. However, some of the microorganisms associated with periodontal disease are only moderately susceptible to chlorhexidine. This is a risk factor for potential development of resistance. It is cytotoxic to gingival fibroblasts even in low concentration. It reduces the production of collagen and non-collagenous proteins hampering the healing of periodontal tissues. [8-10]

Povidone iodine (PVP-iodine) is an extensively used antiseptic in medicine and surgery. To date, there is little clinical use and minimal literature documenting its use as a surgical or non-surgical adjunct in dentistry. It is possibly the most potent antiseptic with a broad range of antimicrobial action. It has deleterious actions against various periodontal pathogens even in low concentration and with little time of contact. [11] It has the ability to kill herpes virus which is resistant to chlorhexidine. [12] Cabral *et al* in 2007 conducted an *in vitro* study to compare the effect of povidone iodine and chlorhexidine on functional activity and long-term proliferation of human alveolar bone cells. The result was, chlorhexidine had higher toxicity profile than povidone iodine. [13]

METHOD OF DATA COLLECTION

An internet search was conducted using keywords povidone iodine, periodontal therapy and periimplantitis till December 2016. Collected information was thoroughly checked to analyze the efficacy of povidone iodine as an adjunct to periodontal therapy and in the treatment of periimplantitis. Appropriate conclusions were discussed in relation to the benefits and adverse reactios of povidone iodine while treating periodontitis.

Historical perspective

Iodine in its elemental form was first discovered by Dijon chemist Bernard Courtis in 1811. [14] The name iodine was derived from the Greek word *ioeides* which mean violet colored, because of its deeply violet colored vapors. Its bactericidal action was first described by Davaine in 1880. [14] Earlier it was used as a remedy for the injured soldier as extracts from seaweed, which was rich in iodine. But the active ingredient was not known. The elemental iodine was highly unstable and had aggressive action on skin and mucosa. Detoxification of iodine was carried out by H. A. Shelanski and M. V. Shelanski in Philadelphia, at the Industrial Toxicology Laboratories in 1955 leading to the formulation of povidone iodine. [15]

Povidone iodine

Povidone iodine or iodopovidone is a chemical complex compound of povidone i.e. polyvinylpyrrolidone (PVP), hydrogen iodide and elemental iodine. It is an idophor which is bound to a stabilizing macro-molecule, hydrophilic polymer polyvinylpyrrolidone (PVP). It is obtained by heating iodine with polyvinylpyrrolidone in the presence of water at 60^{o} for 24 hours so that the hydrogen bonds are formed. [16] The 10% PVP-iodine which is formed by this reaction contains 90% water, 8.3-8.5% polyvinylpyrrolidone, 1% elemental iodine and iodide.[16,18] It is highly soluble in water ethyl alcohol, isopropyl alcohol, polyethylene glycol, and glycerol. Combining iodine with povidone increases its stability, water solubility, maintains equilibrium and decreases tissue irritability. [17]

Mechanism of action of pvp-iodine

Povidone iodine is a potent bactericidal agent having a broad spectrum of action. It's antimicrobial actions are seen against gram-positive and gram-negative organisms, including anaerobic and sporulated organisms, fungi, protozoa, and viruses. [18, 19] Polyvinylpyrrolidone does not have antibacterial activity per se, but it has the affinity for the bacterial cell membrane. PVP acts as a carrier for iodine and delivers it inside the bacteria through pores. When the iodine comes in contact with the bacterial cell wall and various cell organelles, it causes oxidation of amino acids and nucleotides. This results in the denaturation of proteins and inactivation of substances that are essential of biologic activity of the bacterial cell. [18]

Potential benefits of povidone iodine in gingival and periodontal infections

As periodontitis is a multifactorial disease it needs to be treated with multifaceted approaches. It should include proper surgical as well as non-surgical therapy and appropriate antimicrobial coverage. [20] Maruniak *et al* demonstrated the use of various antimicrobial agents in decreasing bacterial plaque and their effectiveness in treating gingivitis. It was observed that povidone iodine was more effective against bacteria than thymol, chlorhexidine and hydrogen peroxide because lower concentrations of povidone iodine killed bacteria within 5 minutes of contact in vitro. Synergistic results were obtained when povidone iodine was combined with hydrogen peroxide for the management of gingivitis in study patients. [21] Caufield and coworkers checked the susceptibility of anaerobic periodontopathic bacteria *in vitro* using membrane transfer assay. They reported lower minimum bactericidal concentration (MBC) for iodine than sodium fluoride, stannous fluoride and chlorhexidine. [22]

Collins *et al* used combination therapy to treat refractory periodontitis in which they delivered povidone iodine intrasulcularly. Substantial reduction in the level of *Porphyromonas gingivalis* was reported in culture positive patients. [23] Von Ohle *et al* compared the efficacy of one single pocket irrigation by using povidone iodine and chlorhexidine without any subgingival instrumentation. Microbial vitality was reduced to 35-80% of initial levels at 7 days and remained persistent for 31 days after only irrigation using povidone iodine. [24] Rahn *et al* tried to prevent the occurrence of bacteremia following dental procedures by irrigating the gingival sulcus using 10% povidone iodine and 0.2% chlorhexidine. The authors reported decreased levels of bacteremia in povidone iodine group. [25] Povidone iodine can be used as an effective subgingival pocket irrigant because it can lower the occurrence of bacteremia by 30%-50%. [26] Peciuliene *et al* used iodine potassium iodide as root canal irrigating solution in the cases of chronic apical periodontitis. They reported marked suppression of *Enterococcus faecalis*, Enteric rods (*Escherichia coli, Klebsiella pneumonia* and *Proteus mirabilis)* and yeasts. [27]

Rosling *et al* performed a study to check the efficacy of povidone iodine, additional to non-surgical therapy in 223 patients with chronic periodontitis. They observed improved gingival conditions, reduced probing depths and improvement in clinical attachment level. [28] Christersson *et al* demonstrated 2 mm or more increase in clinical attachment level in 80% of the deep pockets by using povidone iodine topically adjunct to non-surgical therapy. [29]

Hoang *et al* conducted a split-mouth study investigate the role of PVP-I as a periodontal pocket disinfectant. It was observed that 95% or greater decrease is attained in total bacterial count in 44% pockets having ≥6 mm pocket depth as compared to 6-13% sites in the water irrigation group. They advocated using povidone iodine after thorough scaling and rooting planing so as to achieve penetration in biofilm and break the shielding effect of calculus for pathogens. [30]

It has been reported that the use of povidone iodine as an irrigant in the treatment of generalized aggressive periodontitis reduced the bacterial count of *Aggregatibacter actinomycetemcomitans* but no improvements were noted in clinical and immunological findings. [31] Reilly *et al* conducted a study in pediatric patients to check the short term effects of combined application of 10% povidone iodine and 5% sodium fluoride varnish. They reported decreased accumulation of dental plaque biofilm. [32]

Erica Del Peloso Ribeiro *et al* reported no additional benefits with an adjunctive use of povidone iodine in the non-surgical treatment of class II furcation involvement. [33] Pereyil *et al* conducted clinical-microbial study to compare the efficacy of 2% povidone iodine and tetracycline hydrochloride as a subgingival irrigating solution in moderate periodontitis patients. Both the agents showed nearly comparable effects with tetracycline hydrochloride being slightly superior. [34]

The definitive goal of periodontal therapy is regeneration of lost tissue including alveolar bone. Cristina Trigo Cabral *et al* performed an in vitro study to check the effect of povidone iodine and chlorhexidine on the functional activity and long term proliferation of human alveolar bone cells. The behavior of these was altered by both the agents in concentration dependent manner. Chlorhexidine was more cytotoxic than povidone iodine and caused immediate cell death at 1.2-2 mg/ml concentration. [13]

Povidone iodine and implants

Due to the broad spectrum of antimicrobial activity and good safety profile povidone iodine have been suggested in the treatment of peri-implantitis. [35] Interestingly, iodine coated titanium implants were used successfully in the treatment and prevention of implant failures after orthopedic surgeries. [36] Cytotoxicity, adverse effects, thyroid gland dysfunction and infection were not reported. Excellent bone fill was obtained inside and around all hip and tumor prosthesis. Behneke *et al* effectively treated peri-implantitis around maxillary and mandibular dental implants and achieved bone fill and reduction in probing depth and bleeding on probing. [37]

Clinical note for use of povidone iodine

Use of povidone iodine during the periodontal surgical procedure has become controversial because of its deleterious effects on wound healing and growth of fibroblasts. Most of the studies have reported delayed healing and cytotoxic effects of PVP-I are directly proportional to the concentration of iodine present in the irrigating solution. However, various studies recommend that 1% solution of povidone iodine is the most beneficial concentration and have desired properties as an irrigating agent. [18] It was found that concentration of 250-500 µg/ml of povidone iodine was cytotoxic to in vitro cultured keratinocytes and fibroblasts. But the data acquired from *in vitro* experiments cannot be directly applied for in vivo use. The in vitro cultured cells are monolayered and devoid of any blood supply which makes them vulnerable to cytotoxic impacts. On the other hand, *in vivo* cells are multilayered and vascularized. Hence they have the ability to overcome the noxious changes. [38] It should be taken into account that, whenever used as an adjunct to non-surgical periodontal therapy, gingival crevicular fluid will dilute the povidone iodine making it safer for periodontal tissues. [39] Still it is not recommended to use it on open wounds where regeneration is desired. [40] No adverse effects were reported on epitheliazation of partial thickness sites[41]. Povidone iodine (10%) must be diluted by three parts of water and one part povidone iodine for use in oral cavity. This will give the concentration of 2.5% povidone iodine solution that will contain 0.25% of elemental iodine. [42]

Adverse effects of povidone iodine

Well-known side effect of iodine is staining of tissues and linen. It causes transient discoloration of teeth and oral mucosa which disappears after discontinuing the use. [43] It is contraindicated in patients having thyroid gland dysfunction. [44] No serious complications have been reported after using in the oral cavity. Still, it is indicated to monitor the patient when used for a prolonged duration on non-intact wounds. When used intraorally it is beneficial to use high-speed suction to avoid ingestion of this antiseptic. [43]

In *in vitro* studies it has demonstrated that PVP-I causes inhibition of chemotaxis of polymorphonuclear neutrophils and toxic effects on fibroblasts lymphocyte, monocyte and granulocyte culture. [18] *In vitro* observations cannot be applied straight to *in vivo* results as it is, because of lack of inherent protective mechanisms in cultured cells. Intra oral findings will be influenced by salivary flow, protein degradation and protective inflammatory response in living tissues. [43]

Povidone iodine is highly biocompatible and sensitivity to PVP-I is very rare. Only 0.73% of 600 individuals reported epicutaneous sensitization to iodine. [43]

Development of resistance to povidone iodine

It is highly unlikely to develop resistance to povidone iodine. This is mainly because its rapid action on the cell wall of the bacteria causes cell death. Bacteria would have to develop alterations in cell wall proteins so as to generate resistance to povidone iodine. [45] On the other hand, antibiotics interfere with the biochemical pathway of the bacteria and alteration in these pathways is commonly reported. [19] Numerous studies have revealed that short or long-term exposure to povidone iodine has not developed bacterial resistance. Moreover, bacterial resistance to antibiotics did not affect their sensitivity to povidone iodine. [43]

CONCLUSION

Considering the broad spectrum of antimicrobial activity, high safety profile, low cost and availability povidone iodine may be used as a

potential irrigating solution in treating the periodontal disease. Although, *in vitro* studies have documented the toxic effects of povidone iodine; human studies have demonstrated significantly positive results in various aspects. However, it is recommended to avoid prolonged contact with living, uncontaminated tissues. No histological studies have been reported to check the efficacy of povidone iodine on oral wound healing. Further clinical trials using various concentrations of povidone iodine are needed to provide predictable results.

Key messages

1. Povidone iodine is effective against various periodontal pathogens even in low concentration and with little time of contact. It has the ability to kill herpes virus which is resistant to chlorhexidine.
2. Due to the broad spectrum of antimicrobial activity and good safety profile povidone iodine have been suggested in the treatment of peri-implantitis.
3. Povidone iodine (10%) must be diluted by three parts of water and one part povidone iodine for use in oral cavity.
4. Considering the broad spectrum of antimicrobial activity, high safety profile, low cost and availability povidone iodine may be used as a potential irrigating solution in the treatment of periodontal disease.

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