Review Article

Povidone-Iodine in Dental and Oral Health: A Narrative Review

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Abstract

Aim: Proper oral care is an important contributor to overall health, and various antiseptic options are available for the prevention and treatment of oral diseases. Povidone-iodine (PVP-I) oral formulations remain popular for their broad spectrum of effect and favorable tolerability profile. Our aim was to provide a narrative review looking at the past and current studies evaluating PVP-I usage for the maintenance of oral health. **Materials and Methods:** Querying the PubMed and Web of Science databases using the terms "PVP-I," "Oral Health," and "Dental Care," we identified and systematically reviewed articles for a literature review of PVP-I applications in the area. In addition to potent antimicrobial action against common viruses, fungi, and bacteria, the absence of reported resistance to PVP-I makes it an increasingly attractive option in today's settings. **Results:** The applications for PVP-I range from routine oral care and gingivitis through to the management of oral mucositis and surgical site disinfection following dental surgeries. Evidence also suggests that PVP-I confers additional benefits that complement its antiseptic properties. These include anti-inflammatory, anti-edematous, and hemostyptic effects, which can improve clinical outcomes. **Conclusion:** The clinical benefits of PVP-I warrant its ongoing consideration as a reliable antiseptic for broad oral care needs.

Keywords: Antimicrobial Agents, Antiseptics, Dental Hygiene, PVP-Iodine

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Introduction

The oral cavity is home to a complex microbial ecosystem with a high rate of cellular turnover. Bacterial colonization of the mouth is considered normal, and several beneficial types of oral microflora help the body's immune system to fight disease-producing germs that enter the mouth. For example, some types of resident bacteria produce organic acids that kill pathogens responsible for various intestinal diseases. However, in conditions of poor oral hygiene following dental surgery, or in immunocompromised individuals, pathogenic bacteria can gain the upper hand and overwhelm the normal checks and balances, posing risks from mild local infections to life-threatening bacteremia.[1]

Various active ingredients in antiseptic mouthwashes are available, including alcohols, quaternary ammonium compounds, chlorhexidine, peroxides, permanganates, and iodine compounds, as well as fluoride-based and quinolone derivatives. The potent antiseptic properties of iodine compounds have been known for decades. Several types of elemental iodine exist in aqueous environments, with hypoiodous acid and molecular I_2 being the most potent antimicrobial forms. These iodine molecules are highly chemically reactive and attack microbes by oxidizing vital pathogen structures including nucleic acids, proteins, and membrane components.[2]

Povidone-iodine (PVP-I) refers to an iodine preparation specifically developed for widespread use in healthcare settings. The preparation is comprised of a complex of the polymer polyvinyl pyrrolidone (also known as povidone) and elemental iodine. Equilibrium is achieved when the preparation is applied as a topical antiseptic with the iodine consumed by germicidal activity being replaced by the release of more PVP-bound iodine into the solution. This equilibrium helps to maintain an extended duration of effect, while reducing the risk of irritation and cytotoxicity.

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The common formulation for oral care applications is the 1% PVP-I gargle, which contains 0.1% available iodine.[3]

The aim of this narrative review was to consolidate findings on PVP-I in oral and dental health to clarify current understanding of the area. The terms "PVP-I," "Oral Health," and "Dental Care" were queried in PubMed and Web of Science databases. Due to the relative lack of (particularly clinical) publications on the subject matter, the authors chose to include all relevant studies conducted as recently as 2020, to as far back as 1992.

Benefits of Pvp-I as an Oral Care Product

Broad spectrum

Several studies have demonstrated the efficacy of PVP-I against a broad spectrum of oral pathogens. A study involving six bacterial species (*Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, Tannerella forsythensis, Prevotella intermedia,* and *Streptococcus anginosus*) comparing PVP-I gargle and chlorhexidine mouthwash found that PVP-I reduced the viable cell count of all strains to below the limit of detection within 15 s. This was superior to the results for chlorhexidine wash and demonstrated the rapid bactericidal activity of PVP-I against strains relevant to dental disease.[4]

Activity against biofilms

Biofilms are a common feature of the oral environment and are formed by bacteria as a defensive strategy against mechanical and chemical removal. Biofilms can be notoriously difficult to penetrate, with bacteria within dental biofilms resisting the effects of antimicrobial agents. However, a combination of 10% PVP-I and 5% fluoride varnish was observed to reduce biofilm accumulation, with repeated administration suggested to augment plaque control during dental rehabilitation in children.[5]

P. gingivalis and *F. nucleatum* are two bacterial species that are known to be active in biofilm production. PVP-I has been observed to significantly reduce *P. gingivalis* and *F. nucleatum* biofilms *in vitro*. It was found that a 30-s application of 2% PVP-I was effective in suppressing both *P. gingivalis* and *F. nucleatum* in dual-species aggregates, highlighting implications for the clinical control of subgingival biofilms.[6] Meanwhile, a study of cross-kingdom oral biofilms (i.e. exopolysaccharide biofilms of both fungal and bacterial origin) determined that clinically used concentrations of PVP-I (2%) and fluconazole (0.2%, an oral antifungal agent) effectively disrupt such biofilms *in vitro*.[7] Importantly, it was shown that a combination of PVP-I and fluconazole eradicates *Candida albicans* within biofilms in a rat model of oral disease.

Lack of resistance

To date, there has been no reported resistance to iodine and this is thought to be due to the sheer number and diversity of cellular targets that are susceptible to such oxidation.[8] Antiseptics and antibiotics are both used in oral healthcare settings, but the emergence of antibiotic-resistant bacteria is placing greater emphasis on a more selective and needs-based approach to the use of antibiotics.

Hemostyptic actions

In a recent literature review focusing on the healing of oral wounds, the authors concluded that the use of PVP-I is efficacious in the local control of infection in a dose-dependent manner, eliciting a positive influence on tissue repair.[9] It concludes that PVP-I is recommended for the management of such lesions, citing its low risk of systemic toxicity and allergies, and reduced likelihood of emerging bacterial resistance.

One advantage of PVP-I in oral wound care is that it acts as a hemostyptic agent, which can be useful in preventing localized site bleeding following oral surgery.[10,11] An evaluation of the hemostyptic effect of PVP-I (2% w/v) when used as an irrigant was undertaken at low concentrations following surgical procedures.[12] Healthy patients requiring routine dental extraction were divided into treatment (n = 50) and control groups (n = 50). The patients in the treatment group had their alveolar sockets irrigated using PVP-I following routine dental extraction, while those of the control group were irrigated with normal saline (0.9%, w/v). After irrigation, the sockets were subjected to digital pressure, with the endpoint of significant hemostasis defined as the spontaneous cessation of bleeding from the socket following the procedure. The average time until bleeding cessation in the PVP-I group was 135.7 ± 11.4 s, which was superior to the saline group at 168.8± 23.7 s ($P < 0.001$).

In another clinical trial focusing on fresh bleeding after extraction socket irrigation in patients who had a tooth removed, more than three-quarters of the patients in the treatment group experienced spontaneous bleeding cessation with topical PVP-I application, compared with less than a quarter of the patients irrigated with saline. The cessation of bleeding occurred prior to dressing of the socket with gauze followed by manual compression of the sockets, with PVP-I treatment found to be statistically superior ($P < 0.01$) to saline irrigation.[10]

Anti-inflammatory and anti-edematous properties

The anti-inflammatory properties of PVP-I on host cytokine generation induced by pathogens has been observed *in vitro*, including with human neutrophils. TNF-α plays several roles as a major regulator of inflammation and has been thought to contribute to the development of several chronic diseases. Studies have shown that PVP-I suppresses human neutrophil-mediated TNF-α release following stimulation by respiratory syncytial virus and *Staphylococcus aureus* epitopes.[13] In a similar

way, the enzyme β-galactosidase is a marker of bacterial proliferation during infections, and PVP-I has been shown to reduce β-galactosidase activity in both *Escherichia coli* cultures and supernatant.[14]

Clinical observations have also shown that PVP-I formulations can confer anti-edematous effects. A single-blind randomized study evaluating facial swelling in postoperative patients demonstrated reduced swelling over time, leading to reduced patient discomfort.[15] The group that received 0.5% PVP-I solution (equivalent to 0.5 mg/mL) experienced significantly reduced postoperative swelling ($P < 0.01$). These anti-edematous properties of PVP-I are thought to arise from its ability to inhibit leukotriene B4 and suppress leukocyte extravasation.

PVP-I for Oral Health

Chronic periodontitis

In a long-term maintenance study of 223 patients with chronic periodontitis, treatment with 0.1% PVP-I significantly improved all clinical endpoints tested.[16] These include improved gingival conditions, reduced probing pocket depth, and an increase in probing attachment level. Importantly, these improvements were apparent at 3, 6, and 12 months after the initiation of treatment. These findings suggest that when topically applied during subgingival instrumentation, PVP-I can improve the outcome of non-surgical periodontal therapy.

Early childhood caries

Young children are particularly susceptible to the development of tooth decay, a condition referred to as early childhood caries (ECC). Less well-developed hygiene practices are common in this population and combined with a propensity for eating sweeter foods can lead to the rapid deterioration of tooth enamel. Colonization of the oral cavity by *Streptococcus mutans* can lead to tooth decay or dental caries. Antiseptic agents that act to reduce *S. mutans* numbers, therefore, help to prevent the development of caries in young children and establish a favorable oral environment to halt the progress of decay. In a study focusing on the prevention of ECC in 83 children, participants receiving 10% PVP-I exhibited a median 12-month disease-free survival rate of 95% versus the placebo group which was at 54%.[17] These findings show that topical PVP-I applied to dentition in young children increases disease-free survival. Similarly, in a clinical study evaluating the efficacy of 10% topical PVP-I against *S. mutans* counts in children with ECC, saliva samples were collected to assess postoperative baseline *S. mutans* counts. Irrigation with PVP-I caused a significant reduction in the rise of *S. mutans* levels from the baseline score following 12 months of treatment. The reduction in counts resulted in a lower incidence of caries relapse in these children compared with the deionized water-irrigated controls. Oral rehabilitation combined with regular mouth washing with 10% PVP-I is, therefore, recommended for the control of dental caries in children affected with ECC.

Use of PVP-I for Dental Procedures

The prevention and treatment of infection in the oral and maxillofacial region following oral surgery is necessary to prevent caries, periodontal disease, pulpal pathology, and trauma. Within the oral cavity and its associated structures, pathogenic bacteria including *Streptococci* and *Staphylococci* produce enzymes that breakdown fibrin and other connective tissue and sustain themselves by absorbing cellular debris.[18] Following the newly created paths through connective tissue and along fascial planes, emerging infections can spread quickly from a dental origin, causing potential serious risks to life.

Bacteremia, the presence of bacteria in the blood, is a common yet potentially serious complication that can arise after dental surgery. Application of a PVP-I solution immediately prior to dental surgery has been shown to reduce the risk of bacteremia significantly when compared with sterile water, suggesting that its efficacy is due to more than just a mechanical rinsing effect. An equivalent concentration of 0.23% PVP-I in mouthwash was shown to effectively eradicate *Klebsiella pneumoniae* and *Streptococcus pneumoniae*, as well as rapidly inactivate MERS-CoV, SARS-CoV, rotavirus, and influenza virus A (H1N1) after only 15 s exposure.[19] In another study of 120 patients, the oral cavity was disinfected with either PVP-I, chlorhexidine, or saline solution. Blood samples were drawn shortly after the dental procedure and inoculated in culture bottles. Bacteremia was identified in 28% of the PVP-I patients, 45% of the chlorhexidine patients, and 50% of the saline controls, demonstrating the advantage of using PVP-I solution immediately before a dental procedure.[20]

The gingival sulcus refers to the natural space found between the tooth and the gum tissue that surrounds the tooth and is considered to be a major site from which bacteremia can spread following dental procedures. In one investigation, the effect of local irrigation of the gingival sulcus was compared using three different antiseptic solutions including hydrogen peroxide, chlorhexidine, and PVP-I. The frequency of bacteremia after tooth extraction was determined with all of the solutions tested found to reduce bacteremia to various degrees. PVP-I was the most effective with the frequency in the PVP-I group at 35% compared with the control group at 70%.[21] In contrast, chlorhexidine reduced the frequency to 40% and hydrogen peroxide to 50%, and these differences were not statistically significant from the control group.

In a randomized clinical trial involving 30 patients requiring mandibular third molar removal, trismus (maximum interincisal opening), swelling (orotragus and mentotragus distances), and pain (visual analogue scale)

were assessed at 2 and 7 days postoperation using a split-mouth design.[22] A PVP-I solution at a concentration of 0.5 mg/mL was used as the irrigant solution and was compared with saline in the control group. There was a significant reduction in swelling and trismus observed at both postoperative visits compared with the control group. Although the sensation of pain in the study group was not statistically reduced at either of the visits, more patients (63%) in the PVP-I group reported subjective satisfaction with their treatment. In a similar study focusing on postsurgical bacteremia during mandibular third-molar surgery, although both PVP-I (5%) and chlorhexidine (2%) solutions reduced bacteremia in patients compared with sterile water, PVP-I had a statistically significant superiority over chlorhexidine in terms of the number of surviving organisms detected in the blood.[23]

Another study sought to identify microorganisms appearing in the bloodstream following oral surgery and the effect of a preoperative dose of antibiotics in the presence or absence of a postoperative antiseptic.[24] The prevalence of bacteremia was assessed pre- and postoperatively in three different groups with blood samples drawn for microbiological analysis. Healthy subjects serving as the control group were compared with maxillofacial trauma patients, where a breach of oral mucosal integrity was not surgically planned. The presence of bacteremia was highest in the group that did not receive prophylaxis, while the most effective treatment outcomes were observed in the group receiving the preoperative antibiotic together with 1% PVP-I rinse. These results serve to highlight the importance of combination approaches when dealing with pathogenic bacteria in the oral cavity. It should be noted that although indispensable for their broad-spectrum antimicrobial effects, antiseptics like PVP-I cannot completely eliminate bacteria in the oral cavity during surgical procedures when used alone. It is, therefore, recommended that patients in the high-risk groups undergoing dental procedures be treated with PVP-I as an adjuvant to systemic prophylaxis.

PVP-I for the Management of Oral Mucositis

Oral mucositis is a painful inflammatory condition that is characterized by ulceration of the mucous membranes lining the mouth and digestive tract, often following damage to soft tissue as a side effect of chemotherapy and radiotherapy treatment for cancer. This arises because the normal process of rapid cellular turnover in the oral mucosa is susceptible to the anti-proliferative effects of cancer therapies.[25] The condition is known to develop in >40% of patients receiving certain forms of chemotherapy and virtually all head and neck cancer patients who receive radiotherapy.[26,27] The diverse ecosystem of microflora in the mouth can lead to further complications in immunosuppressed individuals, and wholesome approaches to patient care in OM requires consideration of the microbial aspects.[28] Careful attention to oral care is recommended to prevent pathogenic organisms infecting emerging lesions.[29] As mentioned earlier, PVP-I has potent antiseptic, anti-inflammatory, anti-edematous, and hemostyptic effects which can benefit patients suffering from OM. Multiple clinical lines of evidence support the usage of PVP-I in treating its symptoms, with studies demonstrating reduced incidence, severity, time to onset, and duration of OM.[30] These clinical benefits contribute to improved quality of life for cancer patients undergoing chemo-radiotherapy.

Tolerability and Precautions

Staining

Studies conducted with PVP-I gargle and mouthwash have not shown any staining effect on tooth enamel, unlike chlorhexidine,[31] with short-term use causing no discoloration of the teeth or tongue. In some cases, where staining occurs with PVP-I products, the discoloration effect has been reported to be transient and can be washed out.[8]

Taste alteration

Short-term use of PVP-I gargle has not been associated with alterations in taste.[8] In one publication which included a survey of 33 respondents who used PVP-I gargle and two other commercially available gargles, many of the respondents preferred the PVP-I gargle over the other two gargles due to taste and odor.[32]

Safe for use in children

Gargling is a commonly practiced protective hygiene measure in Japan to aid in the management of upper respiratory tract infections such as influenza. Studies have been conducted on the use of gargling with PVP-I to determine its utility on the management of upper respiratory tract infections in Japanese middle school children.[32,33] In both studies, children were required to gargle with PVP-I for 4–5 times daily within a period of 2–3 months. No adverse events in the children were identified in both studies.

Iodine levels and thyroid function

Studies have been conducted to monitor thyroid function in patients using PVP-I gargle. Two authors have published data showing that among patients using PVP-I gargle for oral mucositis prophylaxis, no pathologic rise in thyroid hormone levels was observed despite gargling for 9 weeks.[34,35] Resorption of iodine by the oral mucosa did not lead to any disturbances in thyroid function in patients without pre-existing thyroid gland diseases. Although PVP-I mouthwash and gargle is indicated for short-term use, caution must be exercised for patients with thyroid disorders.[36]

PVP-I gargle and mouthwash generally contain 1% w/v or 1.0 mg/mL PVP-I. Since only 10% of the PVP-I is 0.1 mg iodine or 100 mcg of iodine, it is available in solution form. If the gargle is expelled rather than swallowed and not used for longer than 14 days, it is unlikely that a significant amount of iodine will be absorbed by the user.[36]

Applications in the management of COVID-19 patients

With the COVID-19 pandemic currently causing significant disruptions to healthcare systems worldwide, ventilators are required to keep patients in critical condition breathing.[37] The use of such medical devices, particularly where a shortage necessitates the sharing of equipment between patients, represents a potential source of infection. A recent randomized Phase 2 study conducted in 2020 has shown that topical application of PVP-I in clinical settings after cleaning and irrigation of the oral cavity inhibits bacterial growth in the oropharyngeal fluid of patients on mechanical ventilation while not disrupting the balance of the oral microbiota.[38] Another recent study showed that PVP-I gargle and mouthwash (1% w/v) was effective in vitro against SARS-CoV-2, the virus causing COVID-19.[39] The product achieved >5 log10 reduction in the virus titres in just 15 seconds, demonstrating strong and rapid in vitro virucidal activity. We concur with the study authors that PVP-I oral products may help reduce the risk of COVID-19 transmission in healthcare settings, such as in dental practice.

Conclusion

PVP-I is widely recognized as a broad-spectrum antiseptic that has potent effects against a wide range of organisms that cause oral diseases. Topical antiseptics are required for the routine use in surgical dentistry, particularly in patients at high risk of bacteremia. The use of a PVP-I antiseptic together with a systemic antibiotic is complementary, because many oral antibiotics have a limited spectrum of activity and may not always reach the infection site at sufficient concentrations. PVP-I irrigation is an inexpensive, effective, and well-tolerated approach that can be used to reduce the postoperative sequelae of routine dental procedures like third-molar surgery. Further studies are needed to focus on identifying the specific conditions and therapeutic combinations in which PVP-I oral solutions are most effective.

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Authors contributions

Both authors have equally contributed and given final approval for publication.

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Data can be available on valid request on contacting to corresponding author mail.

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