Original Article

Role of povidone iodine in periapical surgeries: Hemostyptic and anti-inflammatory?

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ABSTRACT

Introduction: Periapical surgery needs asepsis, a bloodless field for ensuring success of the treatment. Efficacy of Povidone Iodine (PVI) in the elimination of pathogen causing periapical lesions is well established. PVI is also widely used as a disinfectant, sclerosing agent, styptic as well as an anti-odematous agent. **Materials and Methods:** This prospective pilot study done on 20 males between 20-40 years age group with periapical lesions in single rooted maxillary anterior tooth of 1-2 cm in diameter. The bleeding time, clotting time, bleeding time at the apex, drugs used and visual analogue scale of oedema on postoperative days were obtained. Descriptive statistics, paired t test and independent t-test were used. **Results and Conclusion:** Results show a statistically significant reduction in the time required to achieve a bloodless field and a marked decrease in oedema in the first and second postoperative days resulting in lesser consumption of NSAIDs. In conclusion, the effect of PVI in periapical surgery seems to reduce the bleeding time at apex, total dose of NSAIDs used, oedema on first two postoperative days with high statistical significance. Hence the routine use of saline in periapical surgeries may be effectively substituted with PVI. The finding of this pilot study has to be evaluated using wider samples for effective clinical translations.

Keywords: Apicoectomy, periapical surgery, periradicular surgery, povidone iodine

INTRODUCTION

Hemostasis and asepsis are vital in periapical surgery. Intraoperative bleeding not only masks the visual field but also hampers the setting of materials used for retrograde filling. Although local anesthetic infiltration with 1:80,000 adrenaline provides vasoconstriction, it is often not adequate for the surgical manipulation of bone in the periapical region. Many methods are routinely used to control bleeding. Thermal coagulation using cautery, cryosurgery, lasers, etc. need additional armamentarium and skill. Bone wax is known to cause foreign body granulomas.[1] Astringents and styptics such as ferric sulfate, calcium sulfate, and tannic acid can modify the local tissue environment and thereby alter healing. Although hemostasis can be achieved, they shall also act as potential irritants and increase inflammation. Usage of biologically active autogenous or allogenous materials with regenerative capacity like thrombin, gelfoam, oxycel, surgicel, fibrin glue, or platelet-rich protein may be advocated for large critical sized bone defects where spontaneous regeneration of bone is not possible. Even in those cases, hemostasis needs to be achieved to provide better visualization of the size of the defect without hampering the vascularity. However, a few of these materials are also known allergens.[2]

Periapical surgical site is an infected wound site. Because periapical surgery is often performed as an out-patient procedure under not so optimal operation theater grade aseptic environment, an additional antiseptic for the complete sterilization of the area before closure of the wound would reduce the infection and inflammation by bringing down the bacterial load. Periapical infection also signals a recalcitrant infection of bacteria that have survived rigorous debridement, sterilizing procedures, and antibiotics; to ensure the success of the treatment, meticulous disinfection of the infected site is mandatory, hence the efficacy of the safe disinfectant should be unquestionable.

Among all disinfectants, iodine and sodium hypochlorite were found to be more effective against *Prevotella intermedia, Peptostreptococcus micros, Streptococcus intermedius, Fusobacterium nucleatum*, and *Enterococcus faecalis*.[3] Sodium hypochlorite being a protein solvent can cause severe complications when used in periapical region and therefore iodine is one of the best antimicrobial agents for elimination of periapical infection.[4]

Iodine combines irreversibly with tyrosine residues of proteins of microorganisms, interferes with the formation of hydrogen bonding by some amino acids and nucleic acids, oxidizes sulfydryl groups, and reacts with sites of unsaturation in lipids and is thereby a potent disinfectant.[5] Povidone iodine (PVI), a synthetic polymer of 1-vinylpyrrollidone, is free iodine bound to polyvinyl-pyrrollidone (PVP), a solubilizing agent, which releases iodine.[6] PVI iodine is a widely used perioperative disinfectant. However, its off-label use in intraoperative procedures such as pleurodesis as sclerosing agent, checking of fallopian tube patency as irrigant, as scolicidal agent in hydatid cyst removal from peritoneal cavities, and the like are reported.[7] A meta-analysis of intraoperative PVI application to prevent surgical-site infection concludes that it significantly decreased the surgical site infection.[7] Efficacy and safety of PVI in minor oral surgical procedures have been well documented. PVI's effective use as a sclerosant in various parts of the body has also been well documented.[9-12]

The effectiveness of PVI as a hemostyptic in open extraction wounds and antiedematous agent in minor oral surgical procedure has been demonstrated. The aim of this prospective study is to analyze the hemostyptic and the antiedematous effect of PVI in close oral surgical sites of periapical surgery.

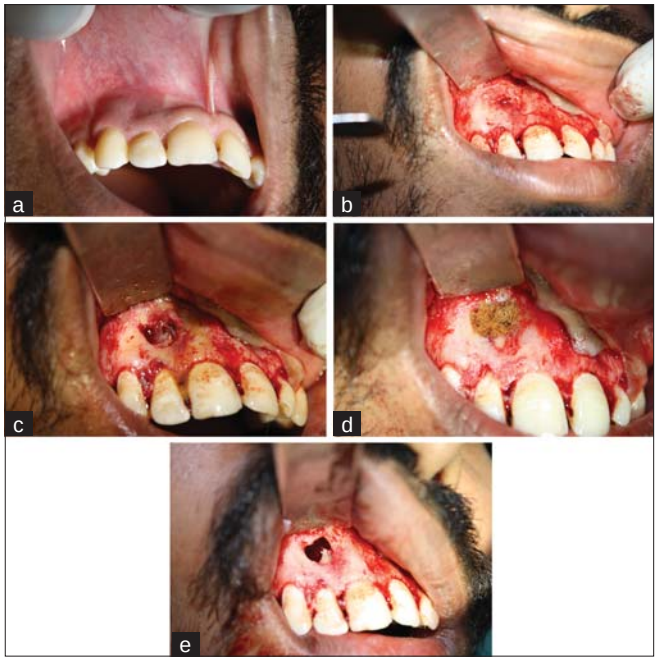

Figure 1: (a) Intraoral view of the lesion, (b) Exposure of the cystic lesion, (c) Enucleation of the lesion and curettage, (d) Betadine-soaked gauze placed in the bony crypt to sterilize the cavity and achieve hemostasis, (e) achieving of adequate hemostasis for retrograde filling

MATERIALS AND METHODS

This study was conducted in the period between June 2009 and December 2010. This pilot study included 20 males in the age group of 20–40 years with a periapical lesion of size of about 1–2 cm in diameter in a maxillary single-rooted tooth to minimize bias. Patients were screened for thyroid disorders. Informed consent was taken as a part of the procedure. As the study did not deviate from the standard care procedure of periapical surgery, it was earlier exempted from Institutional Ethical Board clearance, provided the patients were not identified through photographs and radiographs.

The routine blood examination was performed to assess the fitness of the patient and to detect abnormalities of the bleeding time (BT) and clotting time (CT). A total of 2 ml of 2% lignocaine with adrenaline (1:80,000) was given during the surgery. During surgery, randomly, in 10 cases, 0.5% diluted povidone iodine (BETADINE, G.S. Pharmabutor Pvt Ltd., Uttarakand and distributed by Win-Medicare, New Delhi, India) was used as an irrigant along with cotton, if necessary, to clear the pooled blood along with suction. After adequate periapical curettage was performed, a gauze pellet soaked in PVI was placed in the periapical cavity for a minute. The pellet was removed and wound irrigated again with saline to clear the site. The time taken for achieving optimal hemostasis to start the retrograde filling was recorded [Figures 1a to 1e].

In the rest of the cases, saline was used to irrigate the periapical surgical field along with cotton, if necessary, to remove the pooled

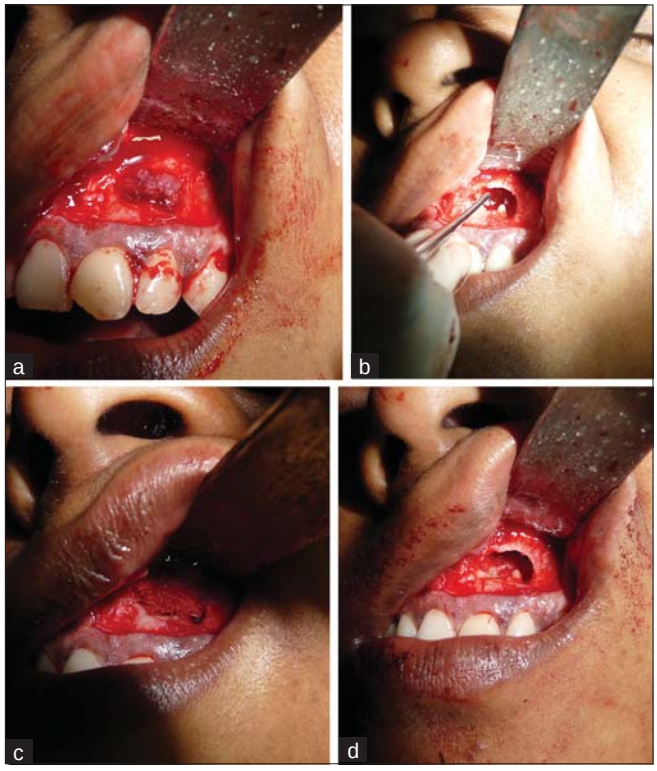

Figure 2: (a) Exposure of the cyst, (b) Enucleation and curettage, (c) Soaking of the saline pack placed in the cystic cavity within seconds, (d) Achieving optimal hemostasis for retrograde filling

blood along with suction. After adequate periapical curettage and retrograde cavity preparation, a saline-soaked pellet was placed for a minute on the bony cavity, removed, and the site irrigated well. The time taken for adequate hemostasis for placing the retrograde filling was measured [Figures 2a to 2d]. Same type suture material was used for all the cases. Same surgeon performed all the surgeries as a day care surgery in the morning between 9.00 am to 10.00 am.

The periapical bleeding time (PBT) was measured as the time that elapsed between the removal of the curette/rotary tool to the achievement of complete hemostasis (in seconds). Patient was prescribed with 500 mg of amoxycillin IP thrice daily for 3 days initially and extended as required. Similarly, ibuprofen IP 600 mg thrice daily was prescribed for 2 days and extended as required. The patient was advised to take ibuprofen as and when required only and to record the total dose taken per day. The patient was discharged on the same day by 4.00 pm after checking the surgical field. No pack (heat/cold) application was advised. Twenty-four hours after surgery, the patient's perception of edema on a visual analog scale (VAS) of 10 was asked and noted. This was repeated for all subsequent 5 days.

Statistical Package for Social Services (SPSS Version 16, IBM, IL, USA) was used to make data entry and analysis. P-P plot was initially performed to study the distribution of the data. Descriptive statistics for the outcome variable were presented. Paired *t*-test was used to find the difference between the VAS of the edema in the whole population. Independent t-test was used to find the difference between the two study groups. The mean of outcome measures and mean difference between the two study groups along with the 95% confidence interval are presented. Paired *t*-test was used to find the difference between the VAS of the edema in the whole population. *P* value of less than 0.05 was taken as significant.

Table 1: Descriptive statistics of the study population

	Minimum	Maximum	Mean	Standard deviation
BT (in minutes)	1.5	3	2.33	0.52
CT (in minutes)	4	6.5	5.60	0.82
BT at apex (PBT in seconds)	90	210	135.50	37.76
Days of ibuprofen used	2	7	4.73	1.53
Total dose of ibuprofen used (in mg)	2200	8000	5430.00	1798.57
Edema VAS on day 1	2	9	4.60	1.57
Edema VAS on day 2	2	7	5.70	2.13
Edema VAS on day 3	1	4	2.70	0.92
Edema VAS on day 4	0	2	1.15	0.49
Edema VAS on day 5	0	1	0.30	0.47

RESULTS

This pilot study had involved all males in the age group of 20–40 years with a periapical lesion of about 1 cm in diameter in a maxillary single-rooted tooth to minimize bias. The mean age in saline group was 27.8 ± 4.61, while in the PVI group it was 28.7 ± 5.5. The difference in mean age between the groups was not significant ($P = 0.696$).

The descriptive statistics of the study group are presented in Table 1. It was observed that the difference between the mean edema VAS score increased in day 2 and from third postoperative day it decreased. The difference between the days was significantly different ($P = 0.001$) [Figure 1].

Table 2 depicts the comparison of the study group and the mean values of the outcomes. It was observed that there was significant difference between the CT and BT between the study groups. However, the time taken to achieve a clear periapical field after curettage as described in Materials and Methods section was significantly lower in the PVI group ($P = 0.004$) than the saline group. Similarly, the PVI group required much lower ibuprofen

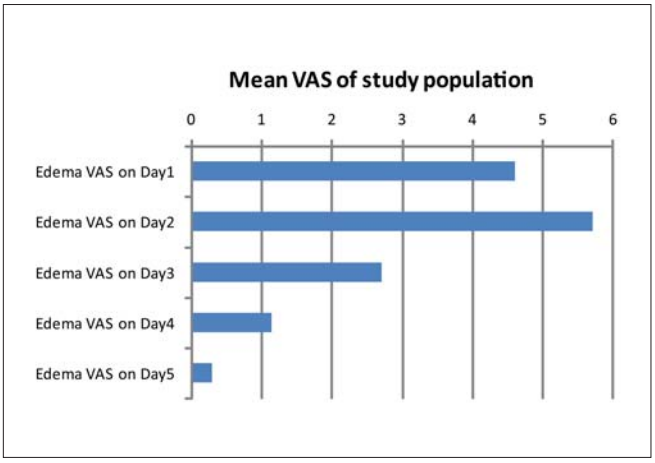

Figure 3: Comparison of edema based on Visual Analog Scale in the study population

Table 2: Difference between the type of irrigant used for the surgery and outcomes studied

	Mean		Mean difference	95% CI of difference		*P* value
	Saline	Povidone iodine		Lower	Upper	
BT (in minutes)	2.20 ± 0.59	2.45 ± 0.44	-0.25	-0.74	0.24	0.295
CT (in minutes)	5.65 ± 0.67	5.55 ± 0.98	0.10	-0.69	0.89	0.794
BT at Apex (PBT in seconds)	158.00 ± 38.02	113.00 ± 20.98	45.00	16.15	73.85	0.004$^{\$}$
Days of ibuprofen used	5.35 ± 1.33	4.10 ± 1.51	1.25	-0.09	2.59	0.065
Total dose of ibuprofen used (in mg)	6280.00 ± 1549.77	4580.00 ± 1679.81	1700.00	181.58	3218.42	0.03*
Edema VAS on day 1	5.60 ± 1.35	3.60 ± 1.07	2.00	0.85	3.15	0.002$^{\$}$
Edema VAS on day 2	6.70 ± 1.95	4.70 ± 1.89	2.00	0.20	3.80	0.032*
Edema VAS on day 3	2.80 ± 0.79	2.60 ± 1.07	0.20	-0.69	1.09	0.641
Edema VAS on day 4	1.20 ± 0.42	1.10 ± 0.57	0.10	-0.37	0.57	0.66
Edema VAS on day 5	0.40 ± 0.52	0.20 ± 0.42	0.20	-0.24	0.64	0.355

*$P \leq 0.05$, $^{\$}P \leq 0.005$

to control the postoperative pain.

There was a significant difference in perception of edema by the patient between the two study groups. The perception varied significantly on the first ($P = 0.002$) and second day ($P = 0.032$). Although on the third to fifth day the PVI group had a lower score; the difference was not statistically significant.

DISCUSSION

Wound healing is a complex biological reparative process involving a series of sequentially orchestrated physiological events. In this process, the immunological resources of the host are recruited to fight infection and debride damaged tissue.[13] In the process of healing of surgeries removing periapical lesions, like any other surgeries, blood supply is reestablished after which regeneration of bone and soft tissue occurs after replacing damaged or destroyed tissue. The area to be healed is decreased via wound contraction and bone deposition. Closure of the wound in the surface area is achieved through epithelial cell migration.[14]

The decision regarding the choice of any wound treatment involves issue of the safety and efficacy of the treatment or the material modalities. Furthermore, the effect of these on the progress of the wound through the stages of healing determines the choice of treatment. The efficacy of a wound care treatment such as PVI can be primarily judged *in vitro* by its ability to kill microorganisms. *In vivo* studies have been used to demonstrate the effectiveness in influencing the rate or severity of wound.[15]

Apicoectomy is the treatment of choice when there is a periapical infection that cannot be cleared by conventional root canal treatment and orthograde retreatment may not be possible due to obliteration of the canal, fractured instrument, or the presence of a large post and core. Success of this surgical procedure lies in the prevention of spread of bacteria from the root canal to the surrounding tissues. To achieve the same, the root-end filling should prevent microleakage and the curetted periapical region needs to be sterilized meticulously. The conventional materials used for such fillings, such as amalgam, glass ionomer cement, and the resins, are moisture sensitive and require decontamination of the resected root end from blood, moisture, and bacteria. Whatever the material of choice, success of the procedure lies in achieving a bloodless, sterile field of working.[16]

It has been reported that the Federal Drug Administration of United States has approved PVI as a nonprescription first-aid antiseptic product. It has been described as short-term treatment for about a week on superficial and acute wounds. Its efficiency in controlling infection has been already been demonstrated.[7,8] PVI is regularly available in dental clinics and much cost-effective. Use of PVI helps to maintain the asepsis of the periapical region after the surgery.

Literature is full of contradiction on the safe limits of the PVI concentration to be used in surgeries. It has been found that PVI at concentrations greater than 0.05% can be toxic to granulocytes[17] while at concentration greater than 0.004% to be entirely toxic to keratinocytes.[18] Several studies have identified PVI of concentration 0.05% to be safe for fibroblasts.[18] Lineaweaver and associates found PVI to be an effective bactericidal agent at a concentration of 0.001%.[19] Findings, based on qualitative evaluation using vital micrography, electron micrography, and vital angiography, showed "a very slight reaction" in wound microcirculation when exposed to a 1% solution of PVI.[20]

Similarly, the optimal method of application of PVI has not been clearly established. It has been reported that the brief contact such as wound irrigation, especially if followed by a saline rinse, or use of extremely diluted solution might minimize the risk of cytotoxicity.[21] On the contrary, prolonged contact such as packing the wound with gauze saturated with PVI, however, might enhance the bactericidal effects. No toxicity has been reported clinically with PVI used as a brief rinse or soak.[22]

The effect of spraying of dry powder PVI into intra-abdominal surgical wounds on wound healing was assessed experimentally (in Wistar rats) and clinically. It was inferred from this study that PVI did not interfere with wound healing macroscopically, histologically, or mechanically in Wistar rats and that it did not affect wound healing in any way.[23]

Study on the short- and long-term effects of PVI on osteoblast number, viability, and function after short exposure to PVI with and without additional bone-morphogenetic protein-2 (BMP-2) concludes that short-time application of PVI in concentrations of 1:10 and higher lead to decreased viability and impaired differentiation. However, surviving cells showed good recovery and mineralization potential.[24]

In this study, the study group did not demonstrate significant difference between BT and CT. However, the PBT varied significantly among the study group. This indicates the efficacy of the PVI as a hemostyptic that has been demonstrated earlier in exodontia cases. In this study, we had significant reduction in BT in the PVI group resulting in a faster procedure, better setting, and cleaner field of working. It concurs with earlier finding of PVI when used for irrigation of extraction sockets reduced postextraction bleeding significantly.[25] The explanation provided was that iodine, being corrosive (owing to its oxidizing potential) and povidone, is a thickening and granulating agent. Combined they produced a chemocauterizing effect that could be the reason for the cessation of bleeding.[25]

PVI, reported as an antiedematous agent earlier,[26,27] in this study have been proved once again. As demonstrated in Figure 3, there was a significant difference between each postoperative day with high statistical significance. However, the difference between the two study groups varied significantly only on the first and second postoperative day. The difference in the perception of edema varied significantly between the PVI group and the saline group. There had been a less amount of swelling perceived by the PVI group than the saline. Similar observation is seen in the literature.[26,27] This effect of PVI was suspected due to its inhibitory effect on leukotriene B4 and leukocyte extravasation (chemotaxis).[27] It could have also reduced inflammation by eliminating the pathogen from the infected area, thereby halting the disease process. *In vitro* and *in vivo* studies have shown that PVI also decreases leucocyte chemotaxis and its extravasation,

thereby bringing down edema.[28] PVI also could possibly cause a denudation of mesothelial cells and resulting in a complex sequence of events leading to an acute inflammatory response to the local injury, followed by the regeneration of the damaged cells, and the wound strength established by the migration of connective tissue cells, the synthesis of extracellular matrix proteins, and finally collagenization.[26] Moreover, PVI also decreases the availability of cytochrome oxidase thereby altering the prostaglandin synthesis, thereby influencing initial phases of healing, as observed in this study.[29,30] From these studies and our results, it could be safely concluded that PVI produces lesser edema during the initial phases of healing. This would effectively translate as a significantly reduced morbidity to the patient when used in clinical situation.

CONCLUSION

This study establishes the efficacy of PVI as an effective hemostyptic and antiedematous agent in periapical surgery when compared with saline. Further clinical trials could establish the usage of PVI as an ideal hemostypic antiseptic for periapical surgery and a 1-minute saturation of the periapical cavity with the solution may be incorporated in the regular procedure for the treatment. The difference in the effect of various stages of the sequale of periapical diseases needed to be studied in depth. Future direction in this regard would warrant large-scale studies.

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