

Effect of Povidone Iodine Versus Chlorhexidine Mouthwash on Oral Mucositis among Cancer Patients

JYOTHI¹, S LATHA², K PAVITHRA³, M NALINI⁴, SOWMYA J RAO⁵, B MAMATHA⁶



ABSTRACT

Introduction: Radiation therapy and chemotherapy are the standard treatment given for cancer, which leads to the variety of adverse effects of which Oral Mucositis (OM) is one of the common side-effects. It is responsible for patient discomfort and decreases their level of functioning. Both Chlorhexidine and Povidone Iodine have got antimicrobial and antifungal activity which decreases the severity of mucositis.

Aim: To compare the effectiveness of Povidone Iodine and Chlorhexidine mouthwash on OM among cancer patients undergoing radiation therapy or chemotherapy.

Materials and Methods: A prospective observational study was conducted in the tertiary care hospital of Mangaluru, Karnataka, India for the duration of one year and three months from December 2015-March 2017. Fifty cancer subjects aged between 25 to 65 years and who developed OM after radiation therapy or chemotherapy were selected by purposive sampling technique. Data were collected using the demographic profile, clinical proforma and World Health Organisation (WHO) OM grading scale (2004) from 19.09.2016 to 17.12.2016. Experimental group I received 10 mL of diluted Povidone Iodine mouthwash and group II

received 10 mL of diluted chlorhexidine mouthwash. Level of OM in the group I and group II were assessed on the 1st, 3rd, 5th and 7th day using WHO OM grading scale (2004). The data were analysed by descriptive and inferential statistics (Wilcoxon signed-rank test, Mann-Whitney U test, Repeated measures ANOVA) using SPSS version 16.0.

Results: Among the 50 cancer subjects, majority 30 (60%) were in the age group between 55-64 years and majority 35 (70%) were receiving radiation therapy. On day seven, in the group I (Povidone Iodine) majority 14 (56%) subjects had mild level of mucositis whereas in the group II (Chlorhexidine) majority 14 (56%) subjects had moderate mucositis. Comparison of the effect of Povidone Iodine and Chlorhexidine mouthwash using Friedman's ANOVA showed that there was a difference in the level of mucositis ($p < 0.05$) at 5% level of significance among two groups. The study findings also revealed a difference in the level of mucositis between day 1 to day 3, 5 and 7 (Mann-Whitney U test) ($p < 0.05$) in both the groups.

Conclusion: Povidone Iodine mouth wash was more effective than Chlorhexidine mouthwashes in reducing OM, and the patients were more comfortable after the use of the mouthwash.

Keywords: Anti-infective agents, Head and neck cancer, Neoplasms, Prospective studies, Radiochemotherapy, Stomatitis

INTRODUCTION

Cancer is a significant public health problem worldwide and is the second leading cause of death. Approximately, 1,806,590 cancer cases are diagnosed in a year which is equivalent to 4950 new cases each day [1]. Non surgical treatment modality for cancer are chemotherapy and radiotherapy that are widely used methods which prolong life and are commonly used in India. However, radiochemotherapy causes various side-effects among which OM is a common one. The clinical evidence of radiation-induced OM is 80-91% [2].

A descriptive study on the incidence and risk factors for the development of OM in the outpatients undergoing cancer chemotherapy highlighted that 51.7% of the outpatient cancer patients had OM [3]. Oral mucositis is one of the most severe non haematological complications of cancer therapy, affecting more than 40% of patients undergoing chemotherapy and radiation therapy, specifically in all head and neck cancers [4].

Oral mucositis is characterised as an inflammatory process that disrupts the mucous lining of the oral cavity and parts of the pharynx. Symptoms include oedema, ulceration and bleeding, with patients often having difficulty swallowing or talking. The associated ulcers and oral lesions that develop can cause significant pain, to the extent where patients may be unable to eat solid food or even ingest liquids at severe stages of OM. Therefore, good oral hygiene practices are emphasised to prevent lesions from becoming infected with pathogenic microbial flora [4].

The researcher during the clinical posting, observed that there were patients undergoing chemotherapy, radiation therapy or both as a

treatment regimen. The researcher observed symptoms like pain, difficulty in swallowing, oral ulcers etc., among those patients on chemotherapy, radiation therapy or both.

The use of an antimicrobial mouth rinse by the patients receiving radiochemotherapy is based on the similar principle of reducing the severity of mucositis and reducing the number of microorganisms in the mouth [5]. The objectives of the study were to assess the degree of OM and to compare the effectiveness of Povidone Iodine and Chlorhexidine mouthwash on OM among the cancer subjects undergoing radiation therapy or chemotherapy.

MATERIALS AND METHODS

A prospective observational study was conducted among cancer subjects who underwent radiation or chemotherapy in a tertiary care hospital, Mangaluru, Karnataka, India. The Institutional Ethics Committee approval was obtained (NUINS/CON/NU/IEC/2015-16 dated 16/01/2016 to 31/03/2017). The study extended for a duration of one year and three months from December 2015- March 2017 and the data collection period was three months from September 2016-December 2016.

Inclusion criteria: Cancer subjects aged between 25 to 65 years, all types of cancer and who developed OM after radiation therapy or chemotherapy were included in the study.

Exclusion criteria: The therapy was continued in both groups during the study period. However, patients who underwent oral surgery and with rinsing difficulty were excluded.

Informed consent was obtained from the respondents after proper explanation about the purpose, the usefulness of the study and assurance was given about the confidentiality of their responses.

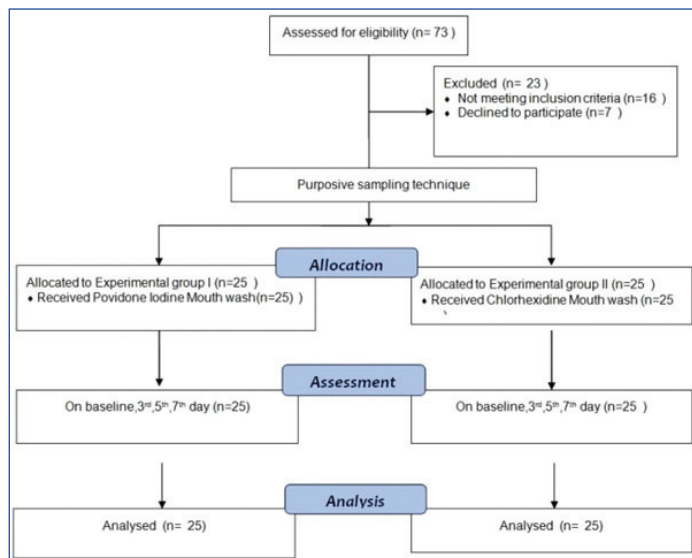
The period of data collection extended from 19.09.2016 to 17.12.2016. During the intervention, the researcher assessed the level of OM in the group I and group II on the baseline (first day) and repeated on 3rd, 5th and 7th day using WHO OM grading scale (2004) [Table/Fig-1] [6].

Grade	Description
0 (none)	None
I (mild)	Oral soreness, erythema
II (moderate)	Oral erythema, ulcers, solid diet tolerated
III (severe)	Oral ulcers, liquid diet only
IV (life-threatening)	Oral alimentation impossible

[Table/Fig-1]: WHO grading of oral mucositis.

The level of mucositis ranges from 0-4, where 0 is none and four denotes life threatening OM.

Fifty subjects with OM were selected using purposive sampling technique. Out of 50 subjects, 25 were assigned to group I (Povidone Iodine) and 25 were assigned to group II (Chlorhexidine). Socio-demographic and clinical characteristics of the subjects were assessed using the socio-demographic profile and clinical proforma developed by the researcher. Group I received 10 mL of Povidone Iodine mouthwash and group II received 10 mL of Chlorhexidine mouthwash. Both the mouthwashes were diluted with 10 mL of water, and the oral cavity was gargled with the solution for one minute thrice a day for three days [Table/Fig-2].



[Table/Fig-2]: Flow chart of research methodology (n=50).

STATISTICAL ANALYSIS

The data were analysed by descriptive and inferential statistics using SPSS version 16.0. Wilcoxon signed-rank test was used to find the effectiveness of Povidone Iodine and Chlorhexidine mouthwash on OM. Comparison of the effectiveness of Povidone Iodine and Chlorhexidine mouthwash on OM were analysed by using Mann-Whitney U test and Friedman ANOVA.

RESULTS

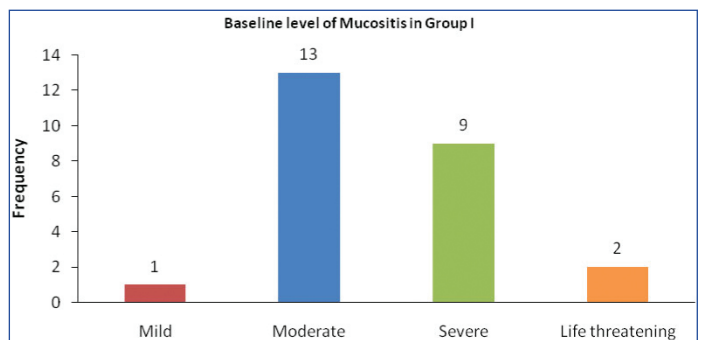
Majority 30 (60%) of the subjects were in the age group of 55-64 years, and 37 (74%) of the subjects were males. Majority 29 (58%) of the subjects had completed primary education. Based on personal habits, 22 (44%) subjects were smokers and 44 (88%) subjects were consuming semisolid diet.

Section I: Level of Mucositis among group I and group II at baseline

Level of mucositis in group I, at baseline 13 subjects had a moderate level of mucositis [Table/Fig-3]. Nine subjects had severe mucositis and two had life-threatening level of mucositis. There was one case with a mild level of mucositis [Table/Fig-4].



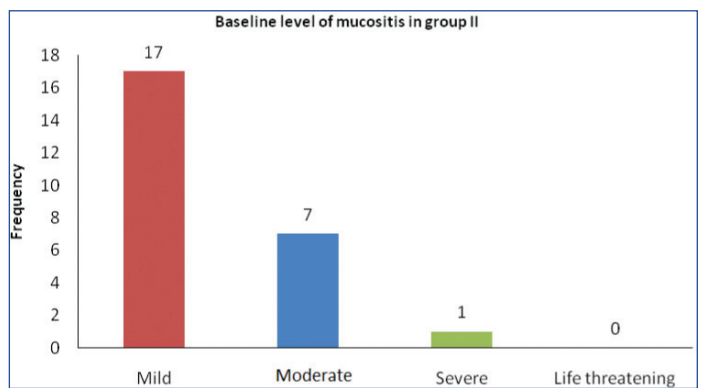
[Table/Fig-3]: Photograph of baseline Oral Mucositis (OM) before the intervention.



[Table/Fig-4]: Bar diagram depicting the baseline level of mucositis in group I (n=25).

Baseline Level of Mucositis in Group II

At baseline 17 subjects had mild level of mucositis. Followed by seven subjects of moderate level of mucositis, and there was one case with a severe level of mucositis [Table/Fig-5].

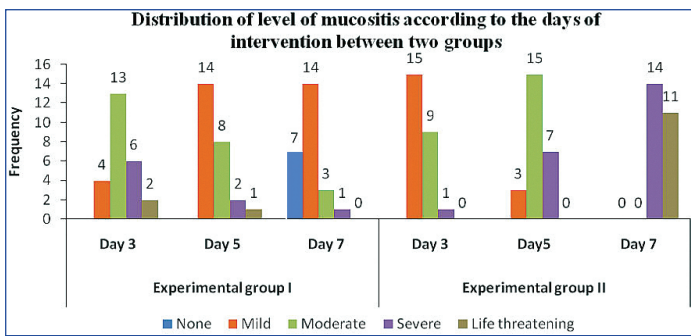


[Table/Fig-5]: Bar diagram depicting the baseline level of mucositis in group II (n=25).

Level of mucositis according to the days of intervention between two groups

[Table/Fig-6] represents frequency and percentage distribution of level of mucositis between two groups. On day three, among the group I, majority 13 (52%) of the subjects had a moderate level of mucositis. But in group II majority, 15 (60%) had mild mucositis. On day five among the group I, majority 14 (56%) of the subjects had mild level of mucositis. But in group II majority, 15 (60%) subjects had moderate mucositis. On Day seven among the group I, majority 14 (56%) of the subjects had mild level of mucositis. But in group II majority, 14 (56%) subjects had moderate mucositis.

The mean, standard deviation and median of the group I and group II on the baseline, day three, day five and day seven is depicted in the [Table/Fig-7].



[Table/Fig-6]: Bar diagram depicting the level of mucositis according to the days of intervention.

Mucositis	Experimental group I (Povidone)		Experimental group II (Chlorhexidine)	
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)
Baseline	2.48±0.71	2 (2.0-3.0)	1.36±0.56	1 (1.0-2.0)
Day 3	2.24±0.83	2 (2.0-3.0)	1.44±0.58	1 (1.0-2.0)
Day 5	1.60±0.81	1 (1.0-2.0)	2.16±0.62	2 (2.0-3.0)
Day 7	0.92±0.75	1 (0.0-1.0)	2.44±0.50	2 (2.0-3.0)

[Table/Fig-7]: Mean, standard deviation and median of the experimental group I and II (n=50).

Section II: Comparison of pre-test and post-test level of mucositis in group I and group II

[Table/Fig-8] depicts that Wilcoxon signed-rank test p-values are <0.05 for both the groups, which indicates that there was a difference in the level of mucositis in group I (Povidone) at 5% level of significance and group II (chlorhexidine) except in baseline and Day 3 (p-value=0.15) at 5% level of significance.

Days		Experimental group I (Povidone)		Experimental group II (Chlorhexidine)	
		Z (Wilcoxon signed rank)	p-value	Z (Wilcoxon signed rank)	p-value
Baseline	Day 3	-2.44	0.01*	-1.41	0.15
	Day 5	-4.49	<0.001*	-4.26	<0.001*
	Day 7	-4.51	<0.001*	-4.66	<0.001*
Day 3	Day 5	-4.00	<0.001*	-4.24	<0.001*
	Day 7	-4.56	<0.001*	-4.63	<0.001*
Day 7	Day 5	-4.12	<0.001*	-2.64	<0.001*

[Table/Fig-8]: Pre test and post test level of mucositis among Experimental group I and II (n=50).

*Indicates significant (p<0.05) (Wilcoxon signed rank test)

Section III: Comparison of the effectiveness of mouthwashes among group I and group II

[Table/Fig-9] shows the Friedman’s ANOVA test values on comparison of the effect of group I versus group II (64.20, p<0.001) versus group II (60.34, p<0.001). There was a difference in the level of mucositis at the 5% level of significance.

	Friedman’s ANOVA	p-value
Povidone (n=25)	64.20	<0.001*
Chlorhexidine (n=25)	60.34	

[Table/Fig-9]: Comparison of the effectiveness of mouthwashes among group I and II.

Section IV: Comparison of the level of mucositis between the group I and I group II

[Table/Fig-10] depicts that Mann-Whitney U test p-values for both the groups are <0.05, which indicates that there was a difference in the level of mucositis between the groups. Based on the median values [Table/Fig-7], it is revealed that in group I, the level of mucositis at baseline was 2.48±0.71 with median score 2 and on day seven it was declined to 0.92±0.75 with median score 1. In group II, the level of mucositis at baseline was 1.36±0.56 with median score 1,

and on day seven, it was increased to 2.44±0.50 with median score 2. Hence, it was concluded that Povidone iodine was more effective than Chlorhexidine mouthwash in reducing OM.

Days	Z (Mann-Whitney U)	p-value
Baseline	-4.81	<0.001*
Day 3	-3.52	<0.001*
Day 5	-2.92	0.003*
Day 7	-5.49	<0.001*

[Table/Fig-10]: Comparison of level of mucositis between the group I and II. n=25 in each group.

DISCUSSION

Povidone Iodine is a broad spectrum antimicrobial having its affinity against bacteria, virus, fungi and protozoa. It is an iodophor in which iodine is loosely bound to povidone thereby, delivering free iodine to the bacterial cell membrane. It reduces plaque formation and decreases the severity of gingivitis, is a broad spectrum antimicrobial agent used in the clinical setting in various forms. It is one of the commonest agent with good tolerability. The lack of unpleasant effects after its use has resulted in frequent use as a preventive and therapeutic drug in radiotherapy and chemotherapy-induced mucositis [7].

The present study was conducted to evaluate the effect of Povidone Iodine mouth wash on oral mucositis, and results indicated that Povidone Iodine mouth wash had a positive effect in reducing OM. The findings are in concordance with the study on the efficacy of Povidone Iodine mouthwash in the prophylaxis of mucositis on radio and chemotherapy treatment in head and neck cancer patients which revealed that the duration of healing of OM was 2.75 weeks in the experimental group and 9.25 weeks in the control group [8].

Hence, the study findings proved that Povidone Iodine mouthwash was effective in reducing the incidence, severity and duration of radiotherapy and chemotherapy-induced OM. Chlorhexidine mouthwash had a positive effect in reducing OM. A study conducted by Prathiba PM and Nagarathnam (2015) on the efficacy of normal saline versus chlorhexidine mouthwash in the prevention of OM in Tirupathi also proved that the administration of chlorhexidine mouthwashes significantly prevented the occurrence of OM when compared with normal saline mouthwash [9].

Comparison of Povidone iodine and chlorhexidine mouthwash on OM revealed that there was a difference in the level of mucositis between the two groups. Similar findings were reported in a randomised controlled trial study on the effects of Povidone Iodine and chlorhexidine mouthwash on radiation-induced OM patients with head and neck cancer in a tertiary cancer hospital, Belagavi which also showed that there is a significant difference in the radiation therapy-induced mucositis in both the groups and it revealed that both types of mouthwash were effective in controlling radiation-induced OM [10]. Mouthwashes can be used for preventive and therapeutic purposes in order to treat oral infections as well as to reduce inflammation. Chlorhexidine has broad-spectrum antimicrobial property. It is effective against both gram-positive and gram-negative bacteria including aerobes and anaerobes, yeasts, fungi and lipid enveloped viruses. It increases the permeability of the cell membrane, followed by coagulation of cellular macromolecules [7]. In the present study, it was observed that both the mouthwashes were individually effective on OM, but on the comparison, it revealed that Povidone Iodine mouth wash was more effective than Chlorhexidine mouthwash on reducing OM. Similar findings were reported by a randomised controlled trial on the effect of three types of mouthwash that included Povidone Iodine, Chlorhexidine and salt/sodium bicarbonate on radiation-induced OM. Povidone Iodine significantly reduced mucositis scores from the first week of radiotherapy compared with the control group. By weeks four and five mucositis scores in patients treated with Povidone Iodine were significantly lower

than the salt/sodium bicarbonate group and the chlorhexidine group, respectively [11]. These findings are further supported by a systematic review assessing the effectiveness of commonly used mouthwashes in the prevention and treatment of chemotherapy-induced OM. No beneficial effects of Chlorhexidine were noted, while Povidone Iodine (PVP-I) was found to reduce the severity of OM by as much as 30% compared with sterile water [12]. Another study conducted by Shin RA and Nam SH on the effects of various mouthwashes on oral environment change for oral healthcare in Korea which revealed that Povidone Iodine was the most effective mouthwash in improving the oral environment by reducing the oral bacteria count [13].

A systematic review on the efficacy of chlorhexidine on OM in cancer patients revealed that chlorhexidine is not significantly effective in reducing the severity of mucositis nor significantly effective in preventing OM. It is also observed that teeth, tongue staining, and alteration in taste perception were the commonest reversible side-effects of Chlorhexidine [14]. In the oncology setting, patients with laryngeal cancer undergoing radiation therapy are treated with Povidone Iodine mouthwash for six weeks and nasopharyngeal cancer for eight weeks. Povidone Iodine mediates localised effects and sparing or preventing the use of antibiotics. They provide a viable option in the treatment of oropharyngeal infections [15].

Limitation(s)

The limitation of the present study is that effectiveness of the interventions were assessed for a shorter duration (one week), the study is confined only to a specific geographical area, and the sample size was minimal (50) which imposes limits to larger generalisation.

CONCLUSION(S)

Oral mucositis is a common side-effect of cancer therapy. Therefore, it is essential that the Oncology nurses should have the knowledge of prevention of OM. Based on the results of the study, it can be concluded that Povidone Iodine Mouth wash appears to be beneficial for the treatment of OM over Chlorhexidine mouthwash. Povidone Iodine mouth wash helps not just only in delaying the progression of mucositis but also reduces the intensity of pain. Hence, it is recommended that routine use of Povidone Iodine mouth wash can be a regular practice in oncology ward when caring for patients with head and neck cancer. The study further recommends conducting a study on a larger population and for specific types of cancer.

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PARTICULARS OF CONTRIBUTORS:

- Lecturer, Department of Medical Surgical Nursing, Yenepoya Nursing College, Mangaluru, Karnataka, India.
- Associate Professor and Head, Department of Medical Surgical Nursing, Nitte (Deemed to be University), Nitte Usha Institute of Nursing Sciences (NUINS), Mangaluru, India.
- Lecturer, Department of Medical Surgical Nursing, Yenepoya Nursing College, Mangaluru, Karnataka, India.
- Associate Professor and Head, Department of Mental Health Nursing, Nitte (Deemed to be University), Nitte Usha Institute of Nursing Sciences (NUINS), Mangaluru, India.
- Reader, Department of Oral Pathology, Sharavathi Institute of Dental Sciences, Shimogga, Mangaluru, Karnataka, India.
- Lecturer, Department of Medical Surgical Nursing, Dr. M.V. Shetty College of Nursing, Mangaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

S Latha,
Nitte Usha Institute of Nursing Sciences, Kotekar Beeri Road, Deralakatte,
Mangalore, Karnataka, India.
E-mail: latha@nitte.edu.in

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