



## The Effect of 1% Povidone Iodine Mouthwash on The Incidence of Oral Mucositis and Odynophagia in Patients with Head and Neck Malignancy

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### Abstract

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**Background :** Oral mucositis is an injury of normal mucosal tissue with an acute inflammation of the oral, tongue, and pharyngeal mucosa after exposure to chemoradiotherapy. Post chemoradiotherapy oral mucositis is commonly accompanied by painful swallowing or odynophagia. Povidone iodine 1% is an antiseptic mouthwash that widely used to prevent infections in the oral cavity. The aim of this study was to determine the effect of 1% povidone iodine mouthwash on the incidence of oral mucositis in patients with head and neck malignancy at Dr. Kariadi General Hospital Semarang.

**Methods :** This study was single random blinded experimental study, with total samples of 44 patients with head and neck malignancy after chemoradiotherapy. The samples divided into treatment group of 22 samples with 1% povidone iodine mouthwash and control group of 22 samples with NaCl 0.9% recruited using single random sampling at Dr. Kariadi Semarang General Central Hospital in 2022. The effect of 1% povidone iodine mouthwash on the incidence of oral mucositis and odynophagia was analyzed using the Fischer Exact and Mann Whitney test.

**Results :** In the 1% povidone iodine mouthwash group day 15<sup>th</sup>, 21 patients (95.5%) were found without mucositis and 1 patient (4.5%) with mucositis oral grade I. In the 1% povidone iodine mouthwash group, 21 people (4.5%) were found without odynophagia and 1 person (4.5%) had odynophagia. There was an association between oral mucositis and odynophagia on povidone iodine 1% group ( $p < 0.05$ ).

**Conclusion :** Povidone iodine 1% mouthwash can affect the incidence of oral mucositis in patients with head and neck carcinoma. Povidone iodine 1% mouthwash can reduce the incidence of oral mucositis and odynophagia compared to placebo in patients with head and neck carcinoma.

**Keywords :** oral mucositis, povidone iodine 1%, odynophagia, head and neck malignancy

## INTRODUCTION

Head and neck carcinoma is a malignant tumor in organs around the head and neck such as the mouth, throat, sinuses, respiratory tract and salivary glands. Treatment for head and neck carcinoma may include radiation, chemotherapy, or a combination of the two. Treatment of head and neck carcinoma often has side effects such as oral mucositis.<sup>1-3</sup>

Oral mucositis is an injury to normal mucosal tissue that occurs secondary to inflammatory and cytotoxic effects after exposure to chemoradiotherapy lasting between 7 to 98 days.<sup>4,5</sup> The incidence of oral mucositis in patients with head and neck malignancy receiving chemotherapy, radiotherapy and chemoradiotherapy respectively is 20%- 40%, 80% and 80% - 100%, respectively.<sup>4,6</sup> Oral mucositis is generally characterized by erythema, edema, mucosal ulceration and pseudomembrane formation in the oral cavity and oropharynx.<sup>5-7</sup> Severe oral mucositis causes pain, reduces oral nutrition intake, impairs quality of life, increases secondary infection due to loss of protective epithelial barrier and basal membrane, and affects medication adherence.<sup>8</sup>

Painful swallowing or odynophagia is also the most common symptom found in patients with head and neck malignancy who receive radiotherapy and/or chemotherapy. Odynophagia due to oral mucositis causes chewing, swallowing, and speaking disturbances, leading to many complications including malnutrition, dehydration, aspiration, respiratory infections, increasing the number of days of hospitalization, and even death.<sup>7</sup>

Povidone iodine mouthwash is a mouthwash with an active iodine complex that is popular, easy, inexpensive, safe, and effective in reducing inflammation and infection. Povidone iodine mouthwash is considered to have the broadest spectrum of antimicrobial action compared to other common mouthwash antiseptics such as chlorhexidine, octenidine, polyhexanide and hexetidine which show efficacy against gram-positive, gram-negative bacteria, bacterial spores, fungi, protozoa and some viruses. The antimicrobial activity of povidone iodine originates from the strong oxidizing ability of free iodine towards amino acids, nucleotides and double bonds, as well as unsaturated free fats which cause povidone iodine to damage protein and microbial DNA. The ability of povidone iodine is also found to inhibit interleukin-1 beta (IL-1 $\beta$ ) and interleukin-8 (IL-8), thus reducing inflammation.<sup>9-13</sup>

Oral mucositis requires a highlight, especially for clinicians because it is strongly associated with the quality of life of patients with head and neck malignancy after receiving chemoradiotherapy. Previous research discussing the effect of 1% povidone iodine mouthwash in patients with head and neck malignancy with

complaints of oral mucositis after administration of chemoradiotherapy in Indonesia is still very limited. This study assessed the effect of giving povidone iodine 1% mouthwash for the prevention of oral mucositis due to side effects of chemoradiation in patients with head and neck malignancy at Dr. Kariadi General Central Hospital, Semarang.

## METHODS

This study was random single blinded experimental study. The total samples of this study were 44 samples distributed into two groups; 22 samples in control group using NaCl 0.9% and 22 samples in treatment group with povidone iodine 1% mouthwash given. The sample was chosen using simple random at Dr. Kariadi General Central Hospital Semarang in 2022. The inclusion criteria for this study were patients with ECOG performance status I and II, aged  $\geq$  18 years, willing to undergo the study procedure, and diagnosed with head and neck carcinoma except for oropharyngeal carcinoma (tonsil, tongue, and palate carcinoma). Exclusion criteria in this study were the patients with history of systemic diseases such as diabetes mellitus, SLE, HIV, history of taking antibiotics and immunosuppressants  $\geq$  5 days. The independent variable was 1% povidone iodine, while the dependent variable was the degree of oral mucositis and the degree of odynophagia. The degrees of oral mucositis is divided into grade 0 (no complaints), grade 1/mild (hyperemia and burning sensation in the mouth), grade 2/moderate (oral erythema, single ulceration, and still able to eat solid food), grade 3/severe (multiple ulceration and only able to eat liquid food), and degree 4/life threatening (patients can't eat and drink). The degree of odynophagia was determined based on the Visual Analog Scale (VAS) divided into no pain (VAS 0) and mild pain (VAS 1-3). The association between variables were analyzed using Fischer Exact and Mann Whitney tests. The study protocol was approved by the Health Research Ethics Commission at Dr. Kariadi General Central Hospital Semarang (1032/EC/KEPK-RSDK/2022) with research permit (DP.02.01/I.11/2170/2022).

## RESULTS

This study involved 44 head and neck carcinoma patients who previously received chemoradiation divided into control group (22 patients) using NaCl 0.9% gargle and treatment group (22 patients) with 1% povidone iodine with the characteristics of the samples shown in Table 1.

Table 1 shows that the majority of the control and treatment groups were male. The average age of the subjects in this study was 18 to 75 years with an average age of 48 years with the most common type of head and neck carcinoma was nasopharyngeal carcinoma. The

TABLE 1  
Characteristics of Samples

Demographic Characteristics	Group A (NaCl 0.9%; n=22 samples)	Group B (povidone iodine 1%; n=22 samples)	Total (Group A dan B; n=44 samples)
Sex			
Male	16 (72.7)	16 (72.7)	32 (72.7)
Female	6 (27.3)	6 (27.3)	12 (27.3)
Age (mean) (Min–Max ± SD)	53 (24–75 ± 11.51)	43 (18–63 ± 12.72)	48 (18–75 ± 12.96)
Type of Carcinoma			
Nasopharyngeal	11 (50.0)	17 (77.3)	28 (63.6)
Laryngeal	5 (22.7)	3 (13.6)	8 (18.2)
Sinonasal	5 (22.7)	2 (9.1)	7 (15.9)
CAE	1 (4.6)	0 (0.0)	1 (2.3)
Degree of Oral Mucositis			
Not found	2 (9.1)	17 (77.3)	19 (43.2)
Grade I	15 (68.2)	5 (22.7)	20 (45.4)
Grade II	5 (22.7)	0 (0.0)	5 (11.4)
Grade III	0 (0.0)	0 (0.0)	0 (0.0)
Grade IV	0 (0.0)	0 (0.0)	0 (0.0)
Microbiological Findings			
Gram-positive and -negative bacteria	4 (18.2)	0 (0.0)	4 (9.1)
Gram-positive and -negative bacteria, and fungal	1 (4.5)	0 (0.0)	1 (2.3)
Not found	17 (77.3)	22 (100)	39 (88.6)

microbiological findings in this study were a combination of gram-positive, negative, and fungal bacteria. Side effects of chemoradiation found in this study included odynophagia, tongue stiffness, and loss of taste.

Table 2 shows the degree of oral mucositis in the control group and the 1% povidone iodine mouthwash treatment group at 0<sup>th</sup>, 5<sup>th</sup>, 10<sup>th</sup>, and 15<sup>th</sup> chemoradiations. These findings were significantly different between the degrees of oral mucositis in head and neck carcinoma patients who received 1% povidone iodine mouthwash at the 15<sup>th</sup> chemoradiation (p = 0.019).

Table 3 shows odynophagia in the control group and 1% povidone iodine mouthwash treatment group. The result of this study showed no significant difference in swallowing pain between patients with head and neck carcinoma who received 1% povidone iodine mouthwash at the 5<sup>th</sup>, 10<sup>th</sup>, and 15<sup>th</sup> chemoradiation.

Table 4 shows the association between the degree

of oral mucositis and the degree of odynophagia. A significant association was found between the degree of oral mucositis and the degree of odynophagia (p < 0.05) in patients with head and neck carcinoma receiving 1% povidone iodine mouthwash at the 10<sup>th</sup> and 15<sup>th</sup> chemoradiation.

## DISCUSSION

Povidone iodine 1% mouthwash is a mouthwash that is currently widely used to prevent oral infections due to its antiseptic effect.<sup>10-12</sup> In this study, the control group using NaCl 0.9% and treatment group with 1% povidone iodine mouthwash samples were dominated by male, which was in accordance with previous studies which showed that there were generally more patients with head and neck carcinoma in males.<sup>13,14</sup> Nasopharyngeal carcinoma is one of the most common types of head and neck

**TABLE 2**  
**The degree of oral mucositis in control group and 1% povidone iodine mouthwash treatment group at 0<sup>th</sup>, 5<sup>th</sup>, 10<sup>th</sup>, and 15<sup>th</sup> chemoradiation**

Degree of Mucositis	Day of Chemoradiation							
	0 <sup>th</sup>		5 <sup>th</sup>		10 <sup>th</sup>		15 <sup>th</sup>	
	A (%)	B (%)	A (%)	B (%)	A (%)	B (%)	A (%)	B (%)
(-)	20 (90.9)	22 (100)	18 (81.8)	20 (90.8)	16 (72.7)	20 (90.9)	15 (68.2)	21 (95.5)
I	2 (9.1)	0 (0)	3 (13.6)	2 (9.1)	4 (18.2)	2 (9.1)	5 (22.7)	1 (4.5)
II	0 (0)	0 (0)	1 (4.5)	0 (0)	2 (9.1)	0 (0)	2 (9.1)	0 (0)
III	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
IV	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
p value	0.244 <sup>£</sup>		0.365 <sup>‡</sup>		0.107 <sup>‡</sup>		0.019 <sup>‡</sup>	

Fisher exact test (£); Mann Whitney (‡), \*Significant (p < 0.05);

**TABLE 3**  
**The degree of odynophagia in control group and 1% povidone iodine mouthwash treatment group at 0<sup>th</sup>, 5<sup>th</sup>, 10<sup>th</sup>, and 15<sup>th</sup> chemoradiation**

Odynophagia (VAS)	Day of Chemoradiation					
	5 <sup>th</sup>		10 <sup>th</sup>		15 <sup>th</sup>	
	A (%)	B (%)	A (%)	B (%)	A (%)	B (%)
Painless (VAS 0)	19 (86.4)	21 (95.5)	17 (77.3)	19 (86.4)	18 (81.8)	21 (95.5)
Mild pain (VAS 1–3)	3 (13.6)	1 (4.5)	5 (22.7)	3 (13.6)	4 (18.2)	1 (4.5)
p	0.303		0.349		0.172	

Analyzed using Fisher exact test; \* Significant (p < 0.05); A: control group, B: povidone iodine 1% mouthwash treatment group

carcinoma and is endemic in Southeast Asia. According to the International Agency for Research on Cancer, there were 129,079 new cases of nasopharyngeal carcinoma in 2018, more than 70% of new cases of nasopharyngeal carcinoma were reported in East and Southeast Asia.<sup>15-17</sup>

Mucositis oral occurring throughout radiation therapy is due to multifactor etiologies.<sup>12</sup> Infection plays a significant role in the pathophysiology of oral mucositis. Oral microorganisms can cause infections of the oral mucosa and antiseptic agents can reduce the incidence and severity of these infections by reducing the number of these microorganisms.<sup>11,12</sup>

Microbiological findings in this study included gram-positive bacteria, *Streptococcus viridans* and *Staphylococcus aureus*. Findings of the fungal component include the finding of pseudohyphae (a sausage-like appearance) and yeast which known as pathognomonic signs in commensal *Candida albicans* infections which are usually found in the oral mucosa and in the lumen of the digestive tract which are responsible

for more than 80% of head and neck infections that more commonly found in control group compared to 1% povidone iodine group.<sup>12,18</sup>

Chemotherapy or radiotherapy procedure, especially when combined, can increase the incidence of acute side effects, such as oral mucositis, followed by odynophagia, loss of taste, tongue stiffness, xerostomia, nausea, vomiting and fatigue. All of these can lead to significant dehydration and weight loss.<sup>15,19,20</sup>

In this study, the incidence of oral mucositis was mostly found in the first to second weeks of chemoradiotherapy with predominance of grade I-II. These findings are in accordance with previous studies which showed that most patients with head and neck malignancy who received chemoradiotherapy had grade I-II oral mucositis. Grade III and IV mucositis were frequently observed in the fourth and sixth (last week) weeks, which can lead to discontinuation of treatment or even hospitalization.<sup>16,17</sup> Some literature had observed a significant reduction in the incidence, severity, and

TABLE 4

**Correlation between the degree of oral mucositis and the degree of odinofagia in the control group and povidone iodine 1% mouthwash treatment group at the 5<sup>th</sup>, 10<sup>th</sup> and 15<sup>th</sup> chemoradiation**

Degree of Mucositis	Odynophagia Degree at the Day of Chemoradiation					
	5 <sup>th</sup>		10 <sup>th</sup>		15 <sup>th</sup>	
	Painless	Mild Pain	Painless	Mild Pain	Painless	Mild Pain
(-)	35 (92.1)	5 (83.3)	35 (97.2)	1 (12.5)	36 (100)	3 (37.5)
I	3 (7.9)	1 (16.7)	1 (2.8)	7 (87.5)	0 (0)	5 (62.5)
P	0.456		<0.001*		<0.001*	

Analyzed using Fisher exact test; \* Significant (p < 0.05)

duration of oral mucositis during chemoradiation in a group of patients using the common mouthwash of povidone iodine solution.<sup>11,12</sup> The results of this study showed a decrease in the degree of oral mucositis in the 1% povidone iodine mouthwash treatment group compared to the control group at the 15<sup>th</sup> chemoradiation (p = 0.019). The results of this study are in accordance with previous studies which showed that among 76 samples, patients in the povidone iodine group had significantly lower mucositis scores when compared to the control group from the first week, saline/soda solution, and chlorhexidine from the fourth and fifth weeks after radiotherapy, respectively.<sup>11</sup>

In this study, there was no significant association between the use of mouthwash and odynophagia. These results are in line with previous studies which showed that mouthwash tolerability (assessed at VAS 1-5) was significantly better in the normal saline group than in the povidone iodine group.<sup>11,15</sup>

This study showed a correlation between the degree of oral mucositis and the degree of swallowing pain in both the control group and the 1% povidone iodine mouthwash treatment group (p < 0.05). The severity of oral mucositis including odynophagia/dysphagia can be reduced by oral hygiene care (to reduce oral infections with opportunistic pathogens that can exacerbate mucositis) through gargling activities with antiseptic solutions, one of which is povidone iodine.<sup>10-12</sup> Previous research showed that 50% of patients reported dysphagia/odynophagia in the first week after cancer therapy (25% with VAS 1 odynophagia and 25% with VAS 3 odynophagia) with 30% of these patients experiencing grade I and II oral mucositis in the same week. The study also showed that there was a transition in the severity of oral mucositis and odynophagia/dysphagia at 2-3 weeks in patients who did not perform oral hygiene care with mouthwash so understanding the natural course of acute oral complications is important by informing patients about the importance of maintaining adequate oral hygiene to help minimize symptoms of

acute oral complications.<sup>16</sup>

The limitation of this study was the short evaluation time. The research findings required to be thoroughly interpreted to reduce research bias.

**CONCLUSIONS**

Povidone iodine 1% mouthwash can affect the incidence of oral mucositis in patients with head and neck carcinoma. Povidone iodine 1% mouthwash can reduce the incidence of oral mucositis and odynophagia compared to placebo in patients with head and neck carcinoma.

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