

## Magic Mouth Wash V/s Benzydamine Mouth Wash in Prophylaxis and Treatment of Radiation Induced Oral Mucositis in Patients with Head and Neck Cancers: A Prospective Study

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Received on 23.11.2017, Accepted on 05.12.2017

### Abstract

**Background:** The incidence of mucositis is increased by adding concurrent chemotherapy as well as by altered fractionation radiation. The main aim of the study is to compare the efficiency of magic mouth wash and benzydamine mouth wash in prophylaxis and treatment of radiation induced oral mucositis in patients with head and neck cancers. **Materials and Methods:** The present randomized, comparative study conducted at Department of Radiotherapy at Guru Gobind Singh Medical College and hospital a period between April 2016-June 2016. A total of 60 patients with head and neck cancer being treated with 6 or more weeks of radiotherapy to a total dose of 66Gy, 200cGy per day, 5 days a week, with shrinking field technique using 2D conventional method on cobalt teletherapy machine were randomly assigned to receive either the magic mouthwash (group A) or benzydamine (Group B) with equal number of patients i.e 30 patients in each group. All the results obtained were arranged in a tabulated form and analysed using SPSS software. **Results:** In the present study, the distribution of patients according to age was comparable in both groups. The mean age was  $57.033 \pm 12.397$  in group A and  $54.633 \pm 11.418$ . There was no development of severe mucositis (grade 3-4) until week 3<sup>rd</sup> of treatment in both the groups. 4 patients (13.3%) in group B developed grade 3-4 mucositis in 4<sup>th</sup> week. In the 5<sup>th</sup> week 1 patient (3.33%) in group A and 6 patients (20%) in group B developed grade 3-4 mucositis. In the 6<sup>th</sup> and the 7<sup>th</sup> week 3 patients (10%) in arm A and 6 patients (20%) in arm B developed severe reactions in each of these weeks respectively. **Conclusion:** From the above study,

we can conclude that mouthwashes are an effective alternative for managing cases of mucositis, with magic mouth wash giving better results but there was no significant difference between both the groups

**Keywords:** Magic Mouthwash; Benzydamine; Mucositis.

### Introduction

Mucositis is a general term referring to the inflammatory reaction and ulcerative lesions of the mouth and oropharynx that occur secondary to RT and certain chemotherapy agents [1-4]. It is a major limiting acute side effect of radiotherapy for head and neck cancer. The incidence of mucositis increases with the use of concurrent chemotherapy [5]. It has been demonstrated that patients with oral mucositis are significantly more likely to have severe pain and a weight loss of  $\geq 5\%$  [6]. Further, 11% of the patients receiving radiation therapy for head and neck cancer had unplanned breaks in radiation therapy due to severe mucositis [7]. Radiation-induced oral mucositis also has a significant economic impact due to costs associated with pain management, liquid diet supplements, gastrostomy tube placement or total parenteral nutrition, management of secondary infections and hospitalizations. In one study of patients receiving radiation therapy for head and neck cancer, oral mucositis was associated with an increase in costs ranging from \$1700-\$6000 per patient, depending on the grade of oral mucositis [6]. Viral infections such as recrudescence herpes simplex virus (HSV) and fungal infections such as candidiasis can sometimes be superimposed on oral mucositis

[8]. So keeping all the above considerations in mind, prophylaxis and treatment of mucositis has become an important area of interest. So the present study was conducted to compare the effectiveness of two mouthwashes i.e the magic mouth wash (containing a combination of antibiotic, antifungal, anti-inflammatory drugs) [9-15] and benzydamine mouth wash [16-18] (non-steroidal anti-inflammatory drug that inhibits proinflammatory cytokines including TNF-alpha) in prophylaxis and treatment of radiation induced oral mucositis.

### Materials and Methods

The present randomized, comparative study conducted at Department of Radiotherapy at Guru Gobind Singh Medical College and hospital a period between April 2016-June 2016. A total of 60 patients with head and neck cancer being treated with 6 or more weeks of radiotherapy to a total dose of 66Gy, 200cGy per day, 5 days a week, with shrinking field technique using 2D conventional method on cobalt teletherapy machine were randomly assigned to receive either the magic mouthwash (group A) or benzydamine (Group B) with equal number of patients i.e 30 patients in each group. Only subjects aged more than 18 years were included in the study. Pregnant or lactating females were excluded from the study. All the subjects were informed about the study and a written consent was obtained from them in their vernacular language. Magic mouth wash contained candid b lotion (30ml) having cotrimazole (1% w/v) and beclomethasonedipropionate (0.025% w/v); tetracycline (500 mg) and glycerine (30ml). Group B patients were given benzydaminehcl (0.15%) mouth wash.

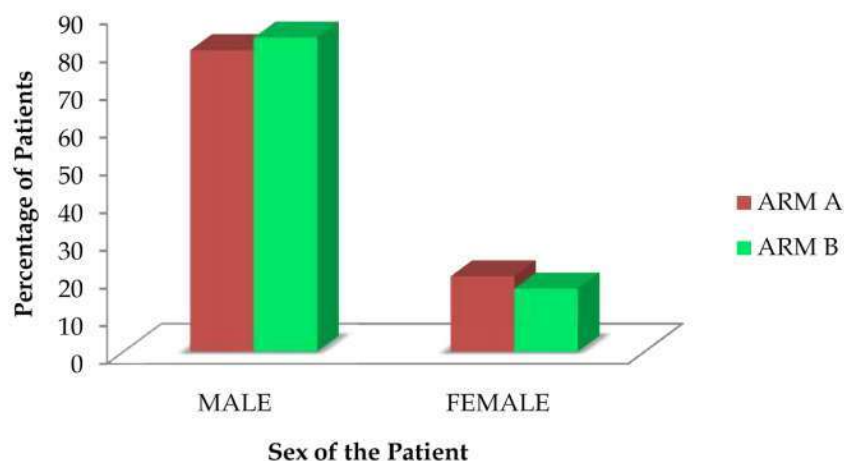
Patients were instructed to take 5ml of the magic

mouthwash solution and rinse the entire mouth for 2 minutes then spit, repeating this 4 times daily, starting on the day prior to the initiation of radiotherapy, and stopping 2 weeks after the completion of radiotherapy. Patients were asked to avoid eating or drinking for atleast 20 mins after mouth rinse so that the medication remains over the mucosa and gets time to act. Patients were also prescribed a B-complex capsule once daily and were advised to drink plenty of water (>8-12 glasses) and other liquids like fresh fruit juice, milk, buttermilk, vegetable soup etc. Also they were asked to avoid tea, coffee, spicy and oily food. Patients were evaluated every week for two weeks after completion of the radiotherapy. The oral cavity was examined thoroughly under light to look for the mucosal reactions. The final grading was done on the basis of following criteria. It ranged from 0 to 4 where 0 denoted no change and 4 denoted life threatening alteration. All the results obtained were arranged in a tabulated form and analysed using SPSS software. Chi square test was used for analysis and p value of less than 0.05 was considered significant.

### Results

In the present study, the distribution of patients according to age was comparable in both groups. The mean age was 57.033±12.397 in group A and 54.633±11.418.

Table 1, Graph 1 shows the gender distribution of the subjects. Out of sixty patients that were recruited in study were predominantly males. 24 patients (80%) in group A and 25 patients (83.3%) in group B were males, and only 6 patients (20%) and 5 patients (16.7%) were females in group a and group B respectively.



Graph 1: Gender Wise Distribution of Patients

**Table 1:** Gender Wise Distribution of Patients

Age	Group A		Group B	
	Number	Percentage	Number	Percentage
Male	24	80.0	25	83.3
Female	6	20.0	5	16.7
Total	30	100.0	30	100.0

Table 2, Graph 2 shows the distribution of subjects according to severity of mucositis. In group A, 14 patients (46.66%) had grade 2 mucositis, whereas in Arm B, 16 patients (53.33%) developed grade 2 mucositis. While looking at grade 3 toxicity, 2 patients (6.67%) in group A and 5 patients (8.33%) in group B developed it. Grade 4 toxicity that led to treatment interruptions was seen in 1 patient in group A and 4 patients in group B that came out to be statistically insignificant (p value-0.591).

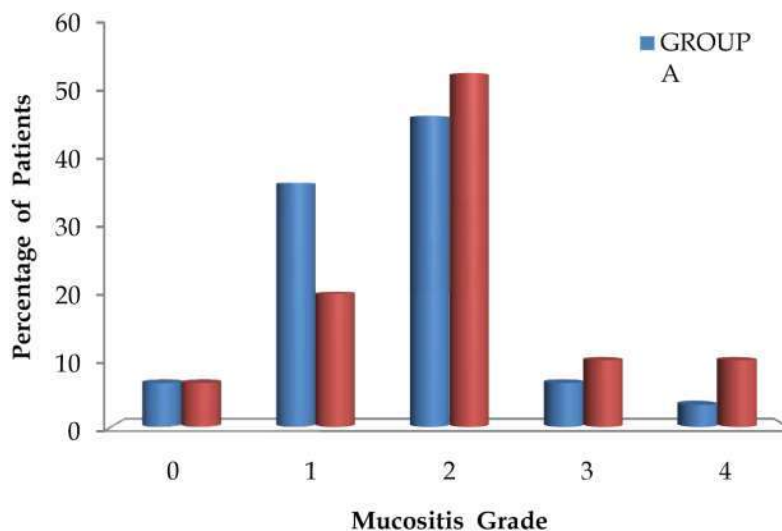
Table 3 shows the weekly results of the study. Looking at the weekly analysis of the mucositis grade, there was no development of severe mucositis (grade 3-4) until week 3<sup>rd</sup> of treatment in both the groups. 4 patients (13.3%) in group B developed grade 3-4 mucositis in 4<sup>th</sup> week. In the 5<sup>th</sup> week 1 patient

(3.33%) in group A and 6 patients (20%) in group B developed grade 3-4 mucositis. In the 6<sup>th</sup> and the 7<sup>th</sup> week 3 patients (10%) in arm A and 6 patients (20%) in arm B developed severe reactions in each of these weeks respectively. Once the treatment was over reactions starting subsiding at the end of first week itself and only one patient in group B was left with >grade 3 mucositis. And by the end of 2<sup>nd</sup> week post treatment mucositis recovered and no patient in any group had severe mucositis.

Table 4, Graph 3 showed treatment interruptions that occurred during the study. There were 2 patients in group A and 3 patients in group B had interruption in treatment due to severe grade of mucositis. The difference was not statically significant (pvalue-0.640).

**Table 2:** Distribution of Patients According To Mucositis Severity

Grades	Group A		Group B		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
0	2	6.67	2	6.67	4	6.67
1	11	36.67	6	20.0	17	28.33
2	14	46.66	16	53.33	30	50.00
3	2	6.67	3	10.0	5	8.33
4	1	3.33	3	10.0	4	6.67
Chi square			2.804			
P value			0.591			
Significance			NS			



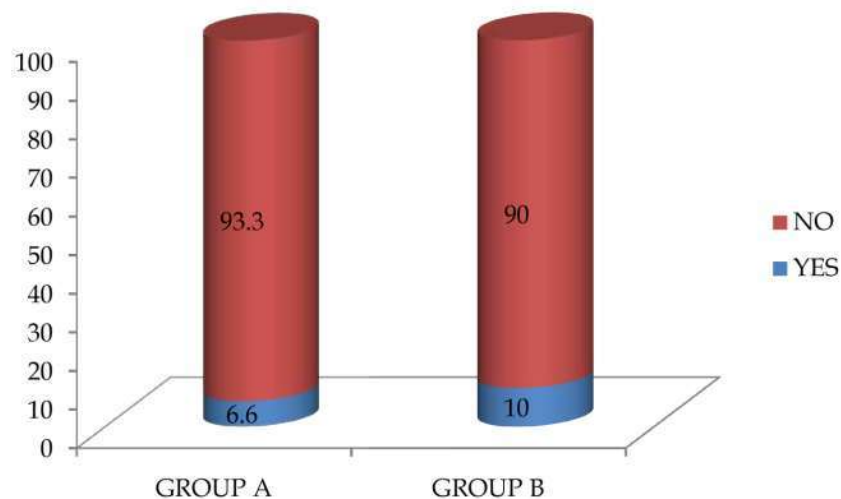
**Graph 2:** Distribution of patients according to mucositis severity

**Table 3:** Week wise analysis of mucositis (Grade 3-4)

Stage	Group A		Group B	
	Number	Percentage	Number	Percentage
Week 1	0	0.0	0	0.0
Week 2	0	0.0	0	0.0
Week 3	0	0.0	0	0.0
Week 4	0	0.0	4	13.3
Week 5	1	3.33	6	20.0
Week 6	3	10.0	6	20.0
Week 7	3	10.0	6	20.0
DAY 7 POST T/T	0	0	1	3.33
DAY 15 POST T/T	0	0	0	0

**Table 4:** Treatment Interruptions

	Group A		Group B	
	Number	Percentage	Number	Percentage
YES	2	6.6	3	10
NO	28	93.3	27	90
Chi Square			0.218	
P value			0.640	
Significance			NS	



**Graph 3:** Treatment Interruptions

## Discussion

This is a randomized, comparative study conducted at Department of Radiotherapy at Guru GobindSingh Medical College and hospital a period between April 2016-June 2016. Sixty patients with head and neck cancer being treated with 6 or more weeks of radiotherapy to a total dose of 66Gy, 200cGy per day, 5 days a week, with shrinking field technique using 2D conventional method on cobalt teletherapy machine were randomly assigned to receive either the magic mouthwash (group A) or benzydamine (Group B) with equal number of patients i.e 30 patients in each group. Development of significant

mucositis leads to unwanted interruptions in radiotherapy especially after the 5th week of initiation leading to accelerated repopulation of resistant clones and compromised disease control [7]. Various international groups including Radiation Therapy Oncology Group (RTOG) and World Health Organization (WHO) have graded the severity of oral mucositis. The most widely used is the RTOG grading. The degree and extent of oral mucositis that develops in any particular patient and site appears to depend on factors such as age, gender, underlying systemic disease and race as well as tissue specific factors (e.g. epithelial types, local microbial environment and function) [19,20,21]. In radiation-induced oral mucositis, lesions are limited to the

tissues in the field of radiation, with non-keratinized tissues affected more often [22]. The clinical severity is directly proportional to the dose of radiation administered. Most patients who have received more than 5000 cGy to the oral mucosa will develop severe ulcerative oral mucositis [22]. The clinical course of oral mucositis may sometimes be complicated by local infection, particularly in immunosuppressed patients. In the present study, in group A, 14 patients (46.66%) had grade 2 mucositis, whereas in Arm B, 16 patients (53.33%) developed grade 2 mucositis. While looking at grade 3 toxicity, 2 patients (6.67%) in group A and 5 patients (8.33%) in group B developed it. Grade 4 toxicity that led to treatment interruptions was seen in 1 patient in group A and 4 patients in group B that came out to be statistically insignificant ( $p$  value=0.591). In a study conducted by Renata Lazari Sandoval et al. [23], there were 3 patients (16.6%) with grade II mucositis, 7 patients with grade III (38.8%), and 8 patients with grade IV (44.4%) mucositis. In their study low energy laser was used for managing cases of mucositis and there was immediate pain relief in 66.6% subjects. In a study conducted by Bensadoun et al. [24] in 1999, comparing the use of prophylactic laser therapy amongst subjects of head and neck cancer, they found that there were 7.6% subjects in laser group who developed Grade 3 mucositis compared to 35.2% subjects in non laser group. In the present study we used mouthwash for managing cases of mucositis. In this study, only one patient in group B was left with >grade 3 mucositis and by the end of 2<sup>nd</sup> week post treatment mucositis recovered and no patient in any group had severe mucositis.

## Conclusion

From the above study, we can conclude that mouthwashes are an effective alternative for managing cases of mucositis, with magic mouth wash giving better results but there was no significant difference between both the groups. Since mucositis after radiotherapy cannot be prevented but efficient measures if taken at an appropriate time can help manage it better and thus reducing the suffering of the patients.

## References

1. Beck SL. Mucositis. In: Yarbro CH, Frogge MH, Goodman M, eds. *Cancer Symptom Management*. 2nd ed. Sudbury, Mass: Jones and Bartlett; 1999. pp.328-43.

2. Dudjak LA. Mouth care for mucositis due to radiation therapy. *Cancer Nurs*. 1987;10(3):131-40.
3. Sonis ST. Oral complications of cancer therapy. In: DeVita JVT, Hellman A, Rosenberg SA, eds. *Cancer Principles and Practice in Oncology*. Philadelphia, Pa: JB Lippincott; 1993:2385-94.
4. Carl W. Oral complications in cancer patients. *Am Fam Physician*. 1983;27(2):161-70.
5. Bossi P, Numico G, De Santis V, RuoRedda MG, Reali A, Belgioia L, CossuRocca M, Orlandi E, Airolidi M, Bacigalupo A, Mazzer M, Saibene G, Russi E. Prevention and treatment of oral mucositis in patients with head and neck cancer treated with (chemo) radiation: report of an Italian survey. *Support Care Cancer* 2014;22(7):1889-96.
6. Elting LS, Cooksley CD, Chambers MS, Garden AS. Risk, outcomes, and costs of radiation-induced oral mucositis among patients with head-and-neck malignancies. *Int J Radiat Oncol Biol Phys*. 2007 Jul 15;68(4):1110-20.
7. Trotti A, Bellm LA, Epstein JB, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. *Radiother Oncol* 2003 Mar;66(3):253-62.
8. Roche LK, Loprinzi CL, Lee JK, et al. A randomized clinical trial of two different durations of oral cryotherapy for prevention of 5-fluorouracil-related stomatitis. *Cancer* 1993 Oct 1;72(7):2234-38.
9. Woo SB, Sonis ST, Sonis AL. The role of herpes simplex virus in the development of oral mucositis in bone marrow transplant recipients. *Cancer* 1990 Dec 1;66(11):2375-2379.
10. Lapeyre M, Charra-Brunaud C, Kaminsky MC, Geoffrois L, Dolivet G, Toussaint B, Maire F, Poured N, Simon M, Marchal C, Bey P. Management of mucositis following radiotherapy for head and neck cancers. *Cancer Radiother*. 2001 Nov;5 Suppl 1:121s-130s.
11. The Erie St. Clair Palliative Care Management Tool. January 2007. [http://ccacont.ca/Upload/esc/General/Palliative\\_\\_Care\\_Managment\\_Tool\\_v3\\_1.pdf](http://ccacont.ca/Upload/esc/General/Palliative__Care_Managment_Tool_v3_1.pdf). (Accessed June 19, 2007).
12. Anon. Slang terms and jargon can cause medication errors. *Drugs & Therapy Bulletin*. Shands at the University of Florida. November/December 2005;19(10):1-3. <http://www.shands.org/professionals/drugInfo/bulletins/1005.pdf>. (Accessed June 19, 2007).
13. Bulletin Board of Oral Pathology. University at buffalo. <http://listserv.buffalo.edu/cgi-bin/wa?A2=ind0704&L=bboplist&T=0&P=11645>-. (Accessed June 19, 2007).
14. North Carolina Board of Pharmacy. [http://www.ncbop.org/faqs/Pharmacist/faq\\_DukesMagicMouthwash.htm](http://www.ncbop.org/faqs/Pharmacist/faq_DukesMagicMouthwash.htm). (Accessed June 19, 2007).
15. Hodgins C, Mosley M, Pola-Strowd M. Recommendations for the diagnosis and management of recurrent

- aphthous stomatitis. National Guideline Clearinghouse. [http://www.guideline.gov/summary/summary.aspx?ss=15&doc\\_id=4368&nbr=3290](http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=4368&nbr=3290).
16. Kazemian A, Kamian S, Aghili M, Hashemi FA, Haddad P. Benzylamine for prophylaxis of radiation-induced oral mucositis in head and neck cancers: a double-blind placebo-controlled randomized clinical trial. *Eur J Cancer Care (Engl)*. 2009 Mar;18(2):174-8. doi: 10.1111/j.1365-2354.2008.00943.x.
  17. Epstein JB, Silverman S Jr, Paggiarino DA, Crockett S, Schubert MM, Senzer NN, Lockhart PB, Gallagher MJ, Peterson DE, Leveque FG. Benzylamine HCl for prophylaxis of radiation-induced oral mucositis: results from a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Cancer*. 2001 Aug 15;92(4):875-85.
  18. Kuk JS, Parpia S, Sagar SM, Tsakiridis T, Kim D, Hodson DJ, Zywine C, Wright JR. A randomized phase III trial of magic mouthwash and sucralfate versus benzylamine hydrochloride for prophylaxis of radiation-induced oral mucositis in head and neck cancer. *Journal of Clinical Oncology*. 2011 May 20;29(15\_suppl):5521
  19. Trotti A, Bellm LA, Epstein JB, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. *Radiother Oncol* 2003 Mar;66(3):253-62.
  20. Sonis ST. The pathobiology of mucositis. *Nat Rev Cancer* 2004;4(4):277-84.
  21. McCarthy GM, Awde JD, Ghandi H, Vincent M, Kocha WI. Risk factors associated with mucositis in cancer patients receiving 5-fluorouracil. *Oral Oncol* 1998 Nov;34(6):484-490.
  22. Zalcberg J, Kerr D, Seymour L, Palmer M. Haematological and nonhaematological toxicity after 5-fluorouracil and leucovorin in patients with advanced colorectal cancer is significantly associated with gender, increasing age and cycle number. Tomudex International Study Group. *Eur J Cancer* Nov;1998 34(12):1871-1875.
  23. Sandoval RL, Koga DH, Buloto LS, Suzuki R, Dib LL. Management of chemo- and radiotherapy induced oral mucositis with low-energy laser: initial results of AC Camargo Hospital. *Journal of applied oral science*. 2003 Dec;11(4):337-41.
  24. Bensadoun RJ, Franquin JC, Ciais G, Darcourt V, Schubert MM, Viot M, et al. Low-energy He/Ne laser in the prevention of radiation-induced mucositis. A multicenter phase III randomized study in patients with head and neck cancer. *Support Care Cancer* 1999; 7(4): 244-52.
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