ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 07, pp.54129-54134, July, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

COMPARISON OF EFFECTS OF SODIUM BICARBONATE AND NORMAL SALINE MOUTHWASH FOR MANAGEMENT OF RADIATION INDUCED MUCOSITIS IN PATIENTS UNDERGOING RADIATION FOR OROPHARYNGEAL CANCER

[1]Dr. Arunkumar, C., [2]Dr. Srinivasan, V., *[3]Dr. Balaji, N. and [4]Dr. Indumathi, G.

[1]Assistant Dental Surgeon, Department of Oral Oncology, Govt Aringer Anna Memorial Cancer Hospital, Kanchipuram-631552
[2]Professor, Department of Radiation oncology, Govt Aringer Anna memorial cancer hospital, Kanchipuram- 631552
[3]Reader, Department of Oral Medicine & Radiology, Tagore Dental College & Hospital, Rathinamangalam, Chennai-600127
[4]Assistant professor of Dental surgery, Government Kasturba Gandhi Hospital for Women and children, Triplicane, Chennai- 600014

ARTICLE INFO

Article History:
Received 21st April, 2017
Received in revised form
07th May, 2017
Accepted 25th June, 2017
Published online 26th July, 2017

Key words:

Oral carcinoma, Radiation, Sodium bicarbonate.

ABSTRACT

Background: Oral Carcinoma is the 6th most common carcinoma worldwide and Radiotherapy is the one among the treatment option. Oral care is the most important option to combat complication due to radiation, in oral cancer. Sodium bicarbonate mouth rinse is better than normal saline in relieving side effects.
Aim: To compare the effects of sodium bicarbonate and normal saline in reducing radiation induced side effects
Methods: A total of 73 patients undergoing radiation for head and neck cancer were selected. Among them, 36 patients (Including 19 males and 17 Females) were allowed to gargle with normal saline and remaining 37 patient (Including 20 Males and 17 Females) were given sodium bi carbonate for mouth gargles. They were looked for radiation induced side effects in 2 weeks period and 4week period. The data were recorded and analyzed.
Results: Results were analysed with spss version 16 software and statistical test used: chi square and fisher exact test
Conclusion: Sodium bicorbonate mouthwash during radiation therapy for oral cancer is better than saline mouthwash in reducing severity of radiation induced mucositis.

Citation: Dr. Arunkumar, C., Dr. Srinivasan, V., Dr. Balaji, N. and Dr. Indumathi, G. 2017. "Comparison of effects of sodium bicarbonate and normal saline mouthwash for management of radiation induced mucositis in patients undergoing radiation for oropharyngeal cancer", *International Journal of Current Research*, 9, (07), 54129-54134.

INTRODUCTION

Cancer is one of the major threats to public health in the developed world and increasingly in the developing countries. In developed countries, cancer is the second most common cause of death (Petersen, 2005) Oropharyngeal cancer is more common in developing countries (Stewart, 2003 and Petersen, 2003). Cancer patients commonly suffer from oral complications during and following cancer therapy. These include oral/pharyngeal mucositis (OM), oral infection, pain, bleeding, and hyposalivation. In addition, rampant dental caries may develop in patients treated with radiation in the head and neck region (H&N RT) (Joel, 2004).

Corresponding author: **Dr. Balaji, N.**
Reader, Department of Oral Medicine & Radiology, Tagore Dental College & Hospital, Rathinamangalam, Chennai-600127

Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer (Ridge, 2008). Mucositis can occur anywhere along the gastrointestinal (GI) tract, but oral mucositis refers to the particular inflammation and ulceration that occurs in the mouth. Oral mucositis is a common and often debilitating complication of cancer treatment (Sonis, 1998). The pathogenesis of OM is complex, involving cells of connective tissue and epithelium (Sonis, 1998). Bacterial colonization of mucosal lesions and exposure of submucosal tissues to lipopolysaccharide may contribute to the severity of mucositis. It is important to further identify the sequence of the cellular and tissue events involved because this may provide a key to adequate prevention and treatment (Joel, 2004). Consequently, treatment of mucositis is still limited to reduction of its severity. Oral care programs, relief of pain and discomfort,

early diagnosis and treatment of concomitant secondary mucosal infections and/or strategies to eliminate micro-organisms, that are thought to promote or aggravate mucositis, are all engaged in its treatment. MASCC (Multinational Association of Supportive Care in Cancer Guidelines, 2005). and NCCN (Dosia Antonadou, 2002), guidelines and a National Cancer Institute report recommend "basic oral care" as a standard practice to prevent infections and potentially help alleviate mucosal symptoms (Keefe, 2007 and Sonis, 2004). Benzydamine is a topical nonsteroidal agent that is currently available in Canada and the European Union as different preparations. Benzydamine has anti-inflammatory, analgesic/ anesthetic, and antimicrobial effects that have been shown in clinical trials (Epstein, 1986). Antimicrobial and antiseptic agents have also been evaluated for their value to prevent mucositis. The use of oral antiseptics has not been fruitful. Chlorhexidine has been shown to be ineffective or even detrimental to HN RT patients, so it is not recommended (Trotti, 2004). Many agents of differing mechanisms of action have been used in the prevention and treatment of oral mucositis induced by anticancer therapies. Currently, no intervention is completely successful at preventing or treating oral mucositis. The several solutions, drugs and methods used and studied in the prophylaxis and therapy of chemotherapy or radiotherapy-induced oral mucositis reflects the need of new, more efficient tools in the management of this complication (Demarosi, 2002).

MATERIALS AND METHODS

This study was conducted in Aringer Anna memorial cancer hospital and research institute at Kanchipuram, Tamilnadu from Jan 2016 to December 2016 after getting approved by the Institutional Ethical committee. Informed consent was obtained from the patients taken up for the study. The sample size comprised of 73 patients, of both genders within age groups of 18 years to 70 years, diagnosed with oral malignancy clinically and histopathologically. The patients were selected based on inclusion and exclusion criterias. Of the 73 patients, the group comprised of 39 males and 34 females within ages of 18 to 70. The minimum age of female was 30 years of age and the maximum age was 65 years. The minimum age of male was 34 and the maximum age was 70 years. Clinical examination of the oral cavity and the surrounding structures were done and the clinical findings recorded in a structured proforma designed for the study. Preliminary laboratory investigations including complete blood investigations like Total count, differential counts of WBC's, RBC count, hemoglobin level, bleeding and clotting times, the peripheral smear etc were done. Patients were referred to the ICTC for test for HIV. All the findings were recorded in the structured proforma designed for the study. The staging of the malignancy was done based on the TNM staging system. The patients were given habit counselling regarding stopping of the habit of Tobacco usage both in smoking and chewing form. The patients were motivated for cessation of the habit. The patients were advised on basic oral hygiene and Oral prophylaxis was done. Conservative management with restorations were done for amenable teeth. Extractions of necessary teeth with poor prognosis with poor periodontal condition and in the field of radiation were done. The patients were then referred to the Dept of Radiation Oncology, Aringer Anna memorial cancer hospital and reseach institute at kanchipuram, Tamilnadu for Radiotherapy.

Armamentarium (Study materials) used in our study are:

- Sodium bicarbonate
- Normal saline

Patients were divided into two groups by simple random sampling.

Group A: Sodium bicarbonate group (36 patients)
Group B: Normal saline group (37 patients)

Group A: Patients were instructed to swish sodium bicorbonate mouthwash for 3 minutes and spit out 10 minutes before and after Radiotherapy.

Group B: Patients were instructed to swish normal saline mouthwash for 5 minutes and spit out 10 minutes before and after Radiotherapy.

Mouthwashes were started from day 1 of radiotherapy

Assesment: Patients were assesed at every 1000cgy equivalent dose of radiotherapy, by a blinded observer. Assessment were based on objective and subjective criteria using WHO mucositis scale assessment. Sites examined for mucositis are upper and lower lips, buccal Mucosa, lateral border of tongue, floor of the mouth , soft and hard palate.

WHO MUCOSITIS GRADING (WHO, 2008):

Mucositis

I-Oral soreness, erythema
II-Oral erythema ulcers, solid diet possible
III-Oral ulcers, liquid diet only
IV -Oral alimentation impossible

Oral cavity were assessed with WHO oral mucositis scale for both the groups (Group A & Group B). Sodium bicorbonate and normal saline mouthwashes were provided twice a day to the group A&B respectively for one week and the effectiveness were assessed after second and fourth week in both the group for one month.

RESULTS

Onset (Mucositis): The present study revealed that patients in Group A (sodium bicarbonate group) had a delayed onset of mucositis, compared to Group B (normal saline group).

At 2 Weeks (Mucositis): When comparing grade II mucositis affecting more than 3 sites in male group, 66.7% were normal saline users and 33.3% were on sodium bicarbonates mouth rinse. Patients affected with grade III mucositis, in less than 3 sites, (100%) all were normal saline user in males. Where as in female patients, patient with grade III mucositis were all on saline mouth wash and sodium bicarbonate user were all free of grade III(Tables 1&2).

At 4 Weeks (Mucositis): In males, when comparing grade III mucositis affecting less then 3 sites, 42.3% were normal saline users and 57.% were bicarbonates users .Grade III mucositis more than 3 sites, 83.3% were on normal saline and 16.7% were on bicarbonate mouth rinse (Table 3) &(Graph 1).

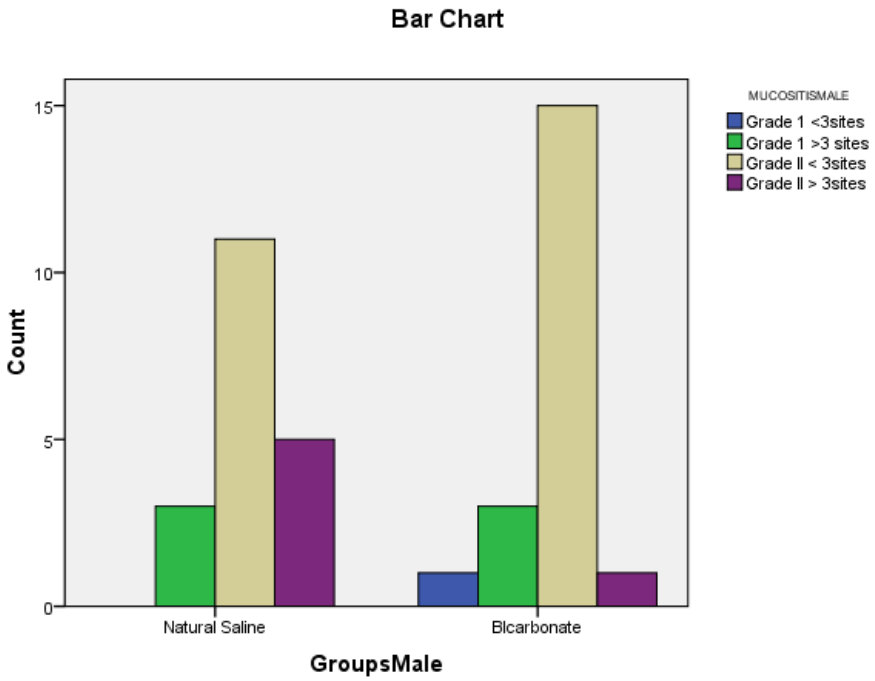
Table 1. Distribution of different grades in males groups a&b

End of 2nd week of radiotherapy:

			MUCOSITISMALE					Total
			Grade 1 <3sites	Grade 1 >3 sites	Grade II < 3sites	Grade II > 3sites	Grade III < 3 sites	
GroupsMale	Normal Saline	Count	2	2	10	2	3	19
		% within GroupsMale	10.5%	10.5%	52.6%	10.5%	15.8%	100.0%
		% within MUCOSITISMALE	50.0%	100.0%	37.0%	66.7%	100.0%	48.7%
	BIcarbonate	Count	2	0	17	1	0	20
		% within GroupsMale	10.0%	.0%	85.0%	5.0%	.0%	100.0%
		% within MUCOSITISMALE	50.0%	.0%	63.0%	33.3%	.0%	51.3%
Total		Count	4	2	27	3	3	39
		% within GroupsMale	10.3%	5.1%	69.2%	7.7%	7.7%	100.0%
		% within MUCOSITISMALE	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	7.127[a]	4	.129
Likelihood Ratio	9.081	4	.059
Linear-by-Linear Association	.732	1	.392
N of Valid Cases	39		

a. 8 cells (80.0%) have expected count less than 5. The minimum expected count is .97.



Graph 1. Distribution of grades in males at the end of 4 weeks of radiotherapy

In females, on comparison of grade III mucosites affecting less then 3 sites, 38.5% were normal saline user 61.5% were bicarbonate user. Grade III mucosites more than 3 sites, 92.3% were normal saline user and 7.7% were sodium bicarbonate user (Table 4) & (Graph 2). The results revealed that comparing sodium bicarbonate and normal saline, sodium bicarbonate delays the onset of mucositis, compared to normal saline, and the severity of grades is less with sodium bicarbonate mouthwash compared with normal saline mouthwash.

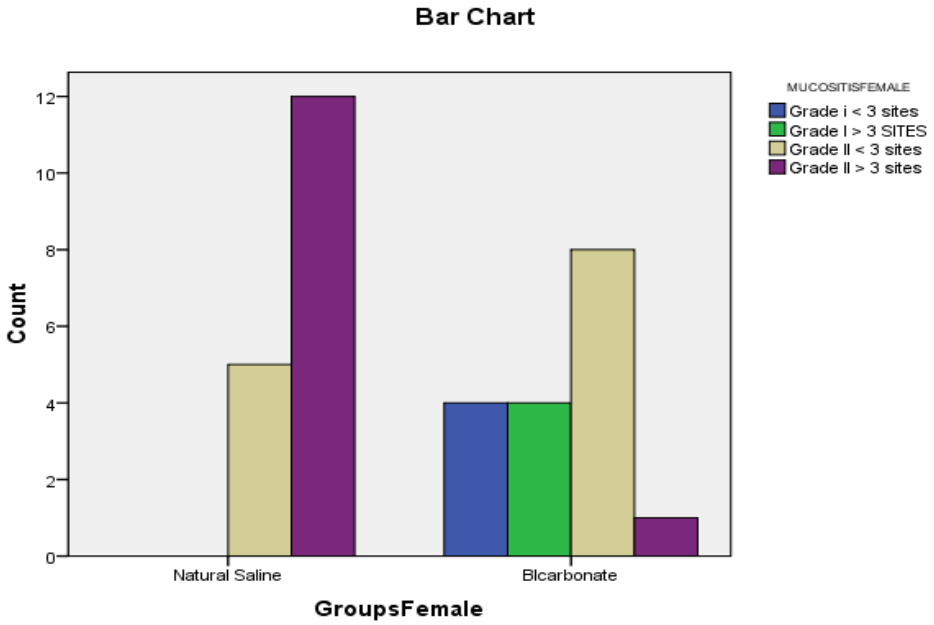
DISCUSSION

Oral complications arise from radiation injury to the Oral mucosa and tongue, salivary glands, oral musculature and alveolar bone. Radiation-induced mucositis is a normal accompaniment of radical radiotherapy to the head and neck region. Normally, the oral mucosa has a relatively high cell turnover rate. Exposure to ionizing radiation leads to mucosal erythema, small whitish patches [16] and ultimately results in confluent mucositis. In the later phases, oral ulceration and bleeding become a dose-limiting toxicity. Mucositis is a result of imbalance between cell loss and cell proliferation.

Table 2. Distribution of different grades of mucositisin females groups a&b end of 2nd week of radiotherapy:

Crosstab								
			MUCOSITISFEMALE					Total
			Grade i < 3 sites	Grade I > 3 SITES	Grade II < 3 sites	Grade II > 3 sites	Grade III < 3 sites	Grade III >3 sites	
Groups Female	Natural Saline	Count	1	0	11	1	3	1	17
		% within GroupsFemale	5.9%	.0%	64.7%	5.9%	17.6%	5.9%	100.0%
		% within MUCOSITISFEMALE	50.0%	.0%	45.8%	100.0%	100.0%	100.0%	50.0%
	BIcarbonate	Count	1	3	13	0	0	0	17
		% within GroupsFemale	5.9%	17.6%	76.5%	.0%	.0%	.0%	100.0%
		% within MUCOSITISFEMALE	50.0%	100.0%	54.2%	.0%	.0%	.0%	50.0%
Total		Count	2	3	24	1	3	1	34
		% within GroupsFemale	5.9%	8.8%	70.6%	2.9%	8.8%	2.9%	100.0%
		% within MUCOSITISFEMALE	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.167[a]	5	.147
Likelihood Ratio	11.257	5	.047
Linear-by-Linear Association	5.011	1	.025
N of Valid Cases	34		



Graph 2. Distribution of grades in females at the end of 4 weeks of radiotherapy

Table 3 : Distribution of different grades of mucositis in males groups a&b end of 4th week of radiotherapy:

Crosstab							
			MUCOSITISMALE				Total
			Grade 1 <3sites	Grade 1 >3 sites	Grade II < 3sites	Grade II > 3sites	
GroupsMale	Natural Saline	Count	0	3	11	5	19
		% within GroupsMale	.0%	15.8%	57.9%	26.3%	100.0%
		% within MUCOSITISMALE	.0%	50.0%	42.3%	83.3%	48.7%
	BIcarbonate	Count	1	3	15	1	20
		% within GroupsMale	5.0%	15.0%	75.0%	5.0%	100.0%
		% within MUCOSITISMALE	100.0%	50.0%	57.7%	16.7%	51.3%
Total		Count	1	6	26	6	39
		% within GroupsMale	2.6%	15.4%	66.7%	15.4%	100.0%
		% within MUCOSITISMALE	100.0%	100.0%	100.0%	100.0%	100.0%

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.259[a]	3	.235
Likelihood Ratio	4.890	3	.180
Linear-by-Linear Association	2.170	1	.141
N of Valid Cases	39		

Table 4. Distribution of different grades of mucositis in females groups a&b end of 4th week of radiotherapy:

Crosstab							
			MUCOSITISFEMALE				Total
			Grade i < 3 sites	Grade I > 3 SITES	Grade II < 3 sites	Grade II > 3 sites	
GroupsFemale	Natural Saline	Count	0	0	5	12	17
		% within GroupsFemale	.0%	.0%	29.4%	70.6%	100.0%
		% within MUCOSITISFEMALE	.0%	.0%	38.5%	92.3%	50.0%
	BIcarbonate	Count	4	4	8	1	17
		% within GroupsFemale	23.5%	23.5%	47.1%	5.9%	100.0%
		% within MUCOSITISFEMALE	100.0%	100.0%	61.5%	7.7%	50.0%
Total		Count	4	4	13	13	34
		% within GroupsFemale	11.8%	11.8%	38.2%	38.2%	100.0%
		% within MUCOSITISFEMALE	100.0%	100.0%	100.0%	100.0%	100.0%

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	18.000[a]	3	.000
Likelihood Ratio	22.760	3	.000
Linear-by-Linear Association	15.573	1	.000
N of Valid Cases	34		

The intensity of mucositis can be altered by new fractionation schedules, concurrent chemo-radiotherapy and co-morbid medical conditions. Bacterial colonization in the oralmucosa can aggravate the preexisting mucositis. Endotoxins released from the gram-negative bacilli are potent mediators of the inflammatory process in the oral mucosa. oropharyngeal flora too contributes to the radiation-induced mucositis (Bernhoft, 1985 and Miller, 1981). In the present study, 73 patients were selected for the study. There were 39 (53.42%) males and 34 (46.58%) females. The minimum age of male was 34 years and the maximum age was 70 years. The minimum age of female was 30 years and the maximum age was 65 years. These patients were planned for radiotherapy. Cobalt- 60 equipment was used for radiation treatment.

The 73 patients were randomly divided into two groups.

Group A (n=36):thirty six patients in Group A were instructed to rinse with normal saline,15 minutes before,15 minutes after radiotherapy and spit out.

Group B (n=37):thirty seven patients in Group B were instructed to rinse with sodium bicarbonate solution,15 minutes before,15 minutes after radiotherapy and spit out.

The onset of Grade I (WHO Mucositis Grading) was clinically observed in all the 2 groups, and severity is clinically observed by the days of onset of grades II, III,& IV in the 2 groups and also the number of patients with more severe clinical and functional grades of III & IV. The results revealed that comparing sodium bicarbonate and normal saline, sodium bicarbonate delays the onset of mucositis, compared to normal saline, and the severity of all the grades of mucositis is less with sodium bicarbonate mouthwash compared with normal saline mouthwash. There are many different modalities for management of mucositis such as using transforming growth factor ß3 (Wymenga, 1999), keratinocyte growth factor (Dorr, 2001), chemical protection of mucosa such as amifostine (Schonekas, 1999), G-CSF (Mascarin, 1999), anti inflammatory agents (Epstein, 1989) and local antibiotic lozenges (Okuno, 1997). These treatments are not easy to use and produce differing results.

Sodium bicarbonate is a cheaper, easily available agent, particularly in our present Indian scenario.

Conclusion

Sodium bicorbonate mouthwash during radiation therapy for oral cancer is better than saline mouthwash in reducing severity of radiation induced mucositis.

REFERENCES

Bernhoft CH, Skaug N. 1985. Oral findings in irradiated edentulous patients. Int J oral Surg 14:416

Biswa Mohan Biswal, Ahmad Zakaria,Nik Min Ahmad.Topical application of honey in the management of radiation mucositis; Support Care Cancer(2003) 11:242-248.

Demarosi F, Bez Carrassi APrevention and treatment of chemo- and radiotherapy-induced oral mucositis Minerva Stomatol. 2002 May;51(5):173-86.

Dorr W, Noack R, Spekl K, Forrell CL. Modification of oral mucositis by keratinocyte growth factor: single radiation exposure. Int Radiat Biol. 2001; 77:341-347.

Dosia Antonadou *et al*. Prophylactic use of amifostine to prevent radiochemotherapy-induced mucositis and xerostomia in head-and-neck cancer. International Journal of Radiation Oncology, Bioloigy,P hysics. Volume 52, Issue 3 , Pages 739-747, 1 March 2002.

Epstein JB, Stevenson-Moore P, Jackson S, Mohamed JH, Spinelli JJ. Prevention of oral mucositis in radiation therapy: a controlled study with Benzydamine hydrochloride rinse. Int J Radiat Oncol Biol Phys. 1989; 16:1571-5.

Epstein JB, Stevenson-Moore P: Benzydamine hydrochloride in prevention and management of pain in oral mucositis associated with radiation therapy. Oral Surg Oral Med Oral Pathol 62:145-148, 1986

Joel B Epstein, Judith E Raber-Durlacher.Topical Agents for the Management of Oral Complications in Cancer Patients. Business brieging: usoncology review 2004.

Keefe DM, Schubert MM, Elting LS, *et al*: Updated clinical practice guidelines for the prevention and treatment of mucositis. Cancer 109: 820-831, 2007

Mascarin M, Franchin G, Minatel E, Gobitti C, Talamini R, De Maria D, Trovò MG., The effect of granulocyte colony-stimulating factor on oral mucositis in head and neck cancer patients treated with hyperfractionated radiotherapy. Oral Oncol.1999; 35: 203-8.

Miller A B .Hoogstraten B,Staquet M, Winkler A (1981) Reporting results of cancer treatment.Cancer 47:1-12.

Multinational Association of Supportive Care in Cancer Guidelines (MASCC). Updated Guidelines for the treatment of Mucositis;A report from MASCC 2005.June 30 – July 2,2005.

Okuno SI, Foote RL, Loprinzi CL, Gulavita S, Sloan JA, Earle J, Novotny PJ, Burk M, Frank AR. A randomized trail of a nonabsorbable antibiotic lozenge given to alleviate radiation-induced mucositis. Cancer.1997; 79(11):2193-9.

Petersen PE. Strengthening the prevention of oral cancer the WHO perspective. Community Dent Oral Epidemiol. 2005; 33:397-9.

Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century- the approach of WHO Global Oral Health Programme. Community Dent Oral Epidemiol 2003; 31(supp.1):3-24.

Ridge JA, Glisson BS, Lango MN, *et al*. "Head and Neck Tumors" in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach. 11 ed. 2008.

Schonekas KG, Wagner W, Prott FJ. Amifostine a radioprotector in locally advanced head and neck tumors. Strahlenther Onko.1999; l 175 [Suppl 4]:30-33.

Sonis S T, "Mucositis as a biological process: A new hypothesis for the development of chemo-therapy-induced stomatotoxiticity", Oral Oncol. (1998), 34: pp. 39–43.

Sonis ST, Elting LS, Keefe D, *et al*: Perspectives on cancer therapyinduced mucosal injury: Pathogenesis, measurement, epidemiology, and consequences for patients. Cancer 100:1995-2025, 2004.

Sonis ST. Oral Mucositis in Cancer Therapy.. J Supportive Oncology. Nov/Dec 2004; Vol 2 (Suppl 3): pp3-8.

Stewart BW, Kleihues P. World Cancer Report, 1st ed. International Agency for research on cancer, Lyon WHO 2003.

Trotti A, Garden A, Warde P, *et al*: A multinational, randomized phase III trial of iseganan HCl oral solution for reducing the severity of oral mucositis in patients receiving radiotherapy for head-and-neck malignancy. Int J Radiat Oncol Biol Phys 58:674-681, 2004

WHO Mucositis Grading (Dent Clin North Am. 2008 January; 52(1): 61).

Wymenga AN, van der Graaf WT, Hofstra LS, Spijkervet FK, Timens W, Timmer-Bosscha H, Sluiter WJ, van Buuren AH, Mulder NH, de Vries EG. Phase I study of transforming growth factor ß3 mouthwash for prevention of chemotherapy induced mucositis. Clin Cancer Res.1999; 5(6):1363-1368.

****