

Salivary pH changes post-nasopharyngeal carcinoma radiotherapy using linac X-ray



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Abstract

Objective: The purpose of this study is to obtain an illustration of saliva pH in patients undergoing radiotherapy with linear accelerator (linac) X-ray radiation for nasopharyngeal carcinoma. Radiation therapy for nasopharyngeal carcinoma frequently causes severe salivary gland dysfunction. The salivary gland dysfunction is possibly influenced by saliva pH.

Material and Methods: The study was a simple descriptive. This study was conducted on 7 males and 2 females undergoing

radiation therapy with LinacX-ray for nasopharyngeal carcinoma. The measurement of saliva pH was done using an electrode pH meter.

Results: This study shows that the range of saliva pH in 9 patients undergoing radiation therapy is 5.34 to 6.19.

Conclusion: The saliva pH in 9 patients undergoing radiation therapy with linac X-ray radiation for nasopharyngeal carcinoma at Dr. Hasan Sadikin Hospital is lower than its normal value.

Keywords: Saliva pH, Nasopharyngeal carcinoma, Linac X-ray radiation

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Introduction

Nasopharyngeal carcinoma is a carcinoma that appears in the nasopharyngeal area (the area above the throat and behind the nose) which shows evidence of mild microscopic squamous cellular or ultrastructural diffusion. The prevalence of nasopharyngeal carcinoma in Indonesia reaches 5.6%.¹ Nasopharyngeal carcinoma is the highest malignancy in the neck area of the field of Ear, Nose and Throat (ENT) diseases. The incidence of nasopharyngeal carcinoma is quite high in Indonesia with approximately 4.7 new cases per year per 100,000 population. The incidence rate of nasopharynx carcinoma is more in men than women with a ratio of 2-3 men compared to 1 woman.²

The main treatment for nasopharyngeal carcinoma is radiation.³ This is because tumour cells in nasopharyngeal carcinoma are radiosensitive.⁴ Radiation therapy is a method of treating malignant diseases using ionizing rays. Radiotherapy is used as a primary treatment, surgical support, surgical treatment combined with chemotherapy, or as a palliative therapy. The determination of radiotherapy is based on the histopathology of tumour nasal cells, the stage and extent of the spread, the patient's health condition, and the availability of facilities and infrastructure.⁵⁻⁷

Currently, radiotherapy has been accepted as one of the most important types of therapy for this disease, in addition to surgery and chemotherapy. This method began to be used as one type of treatment of malignant tumours not long after the discovery of X-rays by W.C. Roentgen at the end

of the nineteenth century.⁷ The basic principle of radiation therapy is to cause as much damage as possible in the tumour tissue and as little damage as possible in the normal tissues around the tumour.⁸ Radiation therapy works by causing enough genetic damage to kill cells directly or by inducing cellular suicide (apoptosis).⁹

Linear accelerator (linac) was first introduced by R. Wideroe in Switzerland in 1929.⁵ Linac began to be used for medical purposes at the Radiation Research Center of the Hammersmith Medical Research Council London in 1953.¹⁰ Linac is a cyclic accelerator that can accelerate electrons to produce a kinetic energy between 4-25 MeV using a microwave radiofrequency (RF) which has a frequency range between 10³ MHz to 10⁴ MHz. Some Linac work on a frequency of 2856 MHz.¹¹

Treatment of nasopharyngeal carcinoma using Linac can be used to accelerate particles to above 1 MeV. Radiotherapy can also be executed using high-energy electrons. X-ray sources from an electron Linac beam can act as a rapid particle radiation source which can be utilized for tumour radiotherapy.⁵

The use of radiotherapy for the nasopharynx and surrounding tissues can lead to biological effects, especially on cells and tissues in the area. This condition affects the oral environment beginning with changes in the mucosa, minor salivary trajectory, and especially the major salivary glands located in the irradiation field.²

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These changes may occur because the components of the salivary glands, formed from the parenchyma tissue, are more radiosensitive resulting in an acute inflammatory response at the onset of radiotherapy, especially in the amino acid which results in salivary gland atrophy.² The inflammatory response will be chronic after several months of radiotherapy. Inability to repair mitochondrial dysfunction and the onset of cell membrane defects will lead to irreversible lesions.¹²

As a result of this damage, the resulting salivary secretions will be very small. The previous research demonstrated that the effect of radiotherapy treatment of nasopharyngeal carcinoma influenced the volume and flow of saliva. This resulted in increased Na^+ , Cl^- , Ca^{2+} , and protein concentrations. The buffer capacity also decreases due to the low concentration of HCO_3^- in the xerostomic state.^{13,14} The aim of this study is to determine the salivary pH after radiation therapy.

Material and Methods

The study was conducted after the approval of the ethics committee. Radiopharynx carcinoma radiation therapy using Linac X-ray was performed on 7 male patients and 2 female patients at Dr. Hasan Sadikin Hospital. The research was descriptive research aimed to determine the salivary pH value after radiation using Linac X-ray plane. The sampling technique uses incidental sampling. More specifically, data was obtained from the sample by an incidental or accidental way, not using a specific plan.¹⁵

The research procedure required the following tools and materials: 10 mL glass beaker, pH meter electrode, stopwatch or watch, informed consent, aquades, patient saliva, pH 4 and 7 buffered

solutions for calibration, questionnaire, and sample status data sheet. Patients were asked to fill in informed consent as a sign of approval to be the subject of research. Prior to the study, patients were instructed not to take any action that could trigger salivary flow stimulation such as eating, chewing, brushing teeth or gargling with mouthwash within at least 1 hour.¹⁶ Patients were asked to sit their body position perpendicular to the floor. They were then invited to rinse their mouth with the intention of removing any remaining food that is still attached in the oral cavity. Patients were allowed to swallow once, to remove the rest of the mouthwash, and then were asked not to swallow saliva and hold it in the oral cavity without stimulation. The patients were asked to spit out the saliva every 1 minute into the glass beaker.

Results

A study of a sample of 9 people with nasopharyngeal carcinoma undergoing Linac X-ray radiation therapy was performed by measuring salivary pH. The results consisted of salivary pH, age, sex, and sample medical record data [table 1](#).

[Table 1](#) the highest value of saliva sample pH was 6.19 (patient 5) and the lowest value was 5.34 (patient 9). The amount of irradiation varies greatly with the lowest being 2 times (patient 1) and the highest being 28 times (patient 9). The number of samples of men (7 patients) was greater than women (2 patients). The sample age varied greatly where 7 patients were over 40 years old and 2 patients were under 40 years old. There were 3 patients using 4 radiation fields and 6 patients using 3 irradiation fields.

Medical record data on radiation field area and fraction dose on each sample are shown in [table 2](#).

Table 1 Characteristics of patients with nasopharynx carcinoma undergoing Linac X-Ray radiation therapy

Patient	Age (Years)	Gender	Lots of Radiation	Number of Fields	Salivary pH
1	55	F	2x	3	5.97
2	23	M	4x	4	5.93
3	50	M	6x	3	5.41
4	44	M	10x	3	5.80
5	65	M	16x	3	6.19
6	58	M	17x	3	5.78
7	48	F	20x	4	5.67
8	30	M	27x	3	6.11
9	41	M	28x	4	5.34

Table 2 Radiation plan for patients with nasopharynx carcinoma using Linac X-Ray Radiation Therapy

Patient	Radiation Plan					
	FieldI/II		FieldIII		FieldIV	
	Size (cm ²)	Dose (cGy)	Size (cm ²)	Dose (cGy)	Size (cm ²)	Dose (cGy)
1	13.7 x 10.3	½ x 200	-	-	15.8 x 10.1	200
2	17.5 x 8.7	⅓ x 200	12.7 x 17.5	⅓ x 200	18.3 x 10.8	200
3	19.0 x 11.0	½ x 200	-	-	16.8 x 9.6	200
4	9.80 x 16.6	½ x 200	-	-	16.0 x 9.0	200
5	10.8 x 18.2	½ x 200	-	-	18.9 x 10.2	200
6	11.8 x 17.3	½ x 200	-	-	18.1 x 8.1	200
7	18.8 x 10.2	⅓ x 200	12.7 x 18.8	⅓ x 200	16.9 x 7.2	200
8	17.1 x 14.3	½ x 200	-	-	19.1 x 9.9	200
9	11.6 x 16.2	⅓ x 200	11.5 x 16.2	⅓ x 200	18.0 x 11.9	200

Discussion

Radiation in the head and neck area, especially the nasopharynx, will cause exposure to radiation in the oral mucosa and parotid gland. Side effects on the oral cavity in the soft tissues resulting from this radiation can be erythrocyte in the early stages and can develop into mucositis. Hard tissues, such as teeth, can also be affected resulting in necrosis of the dental pulp and jawbone. All of these processes are initiated by changes in vascularization, the immune system and the volume of saliva.³

Radiation exposure to major salivary glands is unavoidable during radiotherapy for malignant treatment in the oral and oropharyngeal areas. The components of the salivary glands, that are formed from the parenchyma tissue, are more radiosensitive. This may lead to an acute inflammatory response after radiotherapy, especially in amino acid that results in salivary gland atrophy.²

Patient 1 received radiation 2 times and had a salivary pH of 5.97, while the patient 9 received irradiation 28 times and had salivary pH of 5.34. In this case, the salivary pH is directly proportional to the amount of irradiation received. Patient 2 received irradiation 4 times resulting in a salivary pH of 5.93, while patient 8 received irradiation 27 times and had a salivary pH of 6.11. This shows that a decrease in saliva pH is not in line with the number of radiation doses received by healthy tissue around the cancer. In these circumstances, it seems that there are other factors that are not controlled such as diet, age and nutritional intake.

The number of irradiation fields does not seem to make a marked difference as seen in patients 1, 2, 4, 6, 7 and 9. These circumstances may be due to the dose being divided according to the number of irradiation fields. The patients low salivary pH may be caused by damage to patients salivary gland before

undergoing radiation therapy. It is possible that low body resistance leads to a sensitive response to radiation. Patient 5 that received irradiation 16 times has a salivary pH of 6.19. This value is higher than the salivary pH of other patients receiving less irradiation. This is probably due to a good immune system. Based on the questionnaire filled in by the patient, it is known that patient 5 consumes milk powder twice a day. The high pH may also be due to patient 5 consuming Lycalvit. Lycalvit is used as a therapy for a vitamin deficiency and prophylaxis. Robbins et al.¹² stated that vitamin intake plays a role in tissue healing rates. The amount of protein and mineral intake will help the process of repairing normal tissue damaged by irradiation. Based on the questionnaire, it is also known that patient 5 uses a mouthwash containing menthol. Menthol can stimulate salivary secretion. An increase in salivary secretion will be followed by an increase in salivary pH.¹⁸ Patient 8 underwent irradiation 27 times and had a salivary pH of 6.11. This value is higher than the salivary pH of patient 6 who received irradiation 20 times and had a salivary pH of 5.78. One possible occurrence of this condition is due to the age factor of the patient. Age factor affects the regeneration of salivary glands. Younger patients will undergo tissue repair easier than older patients. The intake of vitamins consumed by the patient is thought to help the process of repairing normal tissue damaged by radiation therapy.

This study shows the salivary pH of patients with nasopharyngeal carcinoma undergoing Linac X-ray radiation therapy at Dr Hasan Sadikin Hospital is in the range of 5.34 to 6.19. The normal salivary pH range in the literature varies. Bradley said salivary pH varied between 6.7 to 8.0 in maximal salivary secretion, whereas the normal state of salivary pH

was in the range of 6.8 to 7.0.¹⁷ The results showed that salivary pH decreased when compared with normal salivary pH. The results of this study are in accordance with the theory that exposure of the salivary glands to irradiation resulted in a decreased salivary pH.¹⁸

Decreased salivary pH is caused by hypoxia that results from oxidative phosphorylation by mitochondria which causes the formation of ATP to be slow or stalled. Loss of ATP has an impact on the system in the cell, especially the activity of ATPase. A reduction of ATPase activity results in the failure of the Na⁺ pump causing intracellular Na⁺ accumulation and K⁺ diffusion out of the cell. This situation water to enter the cell via osmosis resulting in acute cell swelling. The decrease in cell ATP stimulates the enzyme phosphofructokinase resulting in anaerobic glycolysis to maintain the source of cell energy by the formation of ATP from glycogen. Through this process, glycogen is quickly exhausted. Glycolysis causes the accumulation of lactic acid and organic phosphate from the hydrolysis of phosphate esters and therefore, lowers the intracellular pH. The decrease in pH causes injury to the lysosomes that results in leakage of enzymes into the cytoplasm, thus activating hydrolysed acid and enzymatic digestion of cell components. The inflammatory response will be chronic after several months of radiotherapy. The inability to repair mitochondrial dysfunction and the onset of cell membrane disturbances leads to irreversible lesions. The loss of volume adjustment, increased permeability and membrane defects occur in the early stages of irreversible lesions. Membrane damage also causes the Ca²⁺ efflux out of the cell.¹² The amount and severity of salivary glandular tissue damage depends on the dose and duration of transmission. The salivary glands then develop fibrosis and vascularization disorders.^{13,17,19}

Conclusion

Patients with nasopharyngeal carcinoma undergoing Linac X-ray radiation therapy at Dr Hasan Sadikin Hospital observed a decreased salivary pH.

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Conflict of Interest

The authors report no conflict of interest.

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