Topical Fluorides for Head and Neck Cancer Patients Subjected to Surgical Resection and Radiation Therapy in Resource Restraint Settings

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ABSTRACT

Patients undergoing surgical resection and ionizing radiations for the treatment of head and cancer may lead a challenging life even after the cure of the disease; because these procedures can adversely affect the oral mucosa, salivary gland, bone, masticatory musculature, and the dentition. Especially, if major salivary glands are exposed to high dose radiation, an irreversible xerostomia may occur that can lead to rampant dental caries. Treatment of these complications demands high cost and time; and is often unaffordable for the patients in the resource constraint setting rendering them to compromise on their quality of life. The healthcare providers should work together in a team to prevent or manage these complications and improve the lives of the patients. This review paper focuses on the significance of low cost fluoride treatment for salvaging the dentition among patients who have had developed head and neck carcinoma and later got subjected to surgical resection and radiation therapy.

Key Words: Head and neck carcinoma, Salivary glands, Surgical resection, Radiation therapy, Xerostomia, Fluoride therapy.

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INTRODUCTION

Carcinomas of the oral cavity, nasal cavity, paranasal sinuses, salivary glands, larynx, pharynx and hypopharynx are cumulatively termed as head and neck cancers.¹ The incidence of oral cancer is the highest (40% of all cancers) in India and parts of South Asia (including Pakistan and Bangladesh); whereas, in Western countries the incidence is around 3% of all new cancers.² The management of oral cancer depends on the size of the lesion, invasion of the malignant tissue into the neighbouring structures and metastasis to the lymph node and beyond.³ Treatment options available are surgery, radiotherapy, and chemotherapy.⁴ The management could either be curative or palliative, depending upon staging and grading of the cancer.

The objective of the curative treatment is to completely eradicate the disease with minimum morbidity, while palliative treatment is focused at managing the symptoms of the patient. The aim of the latter is to improve the quality of patient's life without actually curing the primary disease.⁵ Dentists have an important role in

screening the head & neck cancer patient at an early stage. Patients who present with leukoplakia, especially speckled leukoplakia on buccal mucosa, gingivae, palate or floor of mouth, should be investigated thoroughly and referred to the specialist without any delay.

The management of head and neck cancer is a challenging task. Consultants belonging to otolaryngology, oral maxillofacial surgery, plastic surgery, radiation oncology, medical oncology, histopathology, nutrition, speech therapy, and prosthodontics have to work as a multi-disciplinary team to get predictable outcomes. The oral cavity of head and neck cancer patients should be thoroughly examined before sending the patient for surgery or radiation therapy. The teeth with hopeless or doubtful prognosis must be removed; correction should be made in the ill-fitting dentures that can potentially cause discomfort or ulceration; the elimination of roughened cusps by smoothing of the jagged ends; and irregular margins of restorations should be carried out. A thorough scaling and polishing of remaining teeth with reinforcement of oral hygiene instructions is of paramount importance. These steps are needed as they not only lessen the risk and severity of oral complications after radiotherapy,⁶ but also improve the quality of life.

As mentioned earlier, surgical excision and radiotherapy are the main treatment options for head and neck cancer

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management, each modality has its own pros and cons. Surgery involves resection of the affected tissue which may be an important functional unit such as lips, tongue or mandible. Radiation therapy may produce immediate morbidity or long-term problems. Adverse effects of radiotherapy are related to the radiation dose, extent of irradiated tissues and type of ionizing radiations. Temporary side-effects include mucosal ulcers/ mucositis, pain, taste alterations, candidiasis, dermatitis and erythema.⁷ Permanent side-effects include xerostomia, caries at cervix of teeth, osteoradio-necrosis, telangiectasia, and focal hyperpigmentation.^{7,8} Radiation dose in the range 66-70 Grays (Gy) is usually given to the head & neck cancer patients. This dose can lead to permanent hypo-salivation (reduced salivary flow) and can cause changes in the oral micro flora.⁹

Radiation-induced hypo-salivation restricts the oral functions such as speech, chewing and swallowing. Patients who underwent radiation therapy have a change in lifestyle. Their diet changes significantly. They need to take more water to manage xerostomia. Frequent intake of soft food items, especially the ones that are carbohydrate-rich, leads to increase in the caries susceptibility. With low quality and quantity of saliva, these patients develop a relatively rapidly progressive dental caries called radiation-induced rampant caries.¹⁰ Other habits such as alcohol and smoking along with poor oral hygiene practices further exacerbate the radiation-induced caries. Therefore, dental caries prevention among radiation-induced xerostomia patients is different than non-cancer patients.

The present review deals with the studies suggesting an appropriate fluoride therapy for salvaging the dentition of the radiation induced xerostomia patients.

Radiation and Oral Cavity:

Ionizing radiations damage the healthy tissues that are present in the field of radiation. Damage to major salivary glands leads to hypo-salivation. A reduced salivary flow is accompanied with biochemical changes in saliva (reduced buffering capacity), increased viscosity, variable electrolyte concentration, and change in antimicrobial resistance of the saliva.^{9,11} The sensation of taste also gets altered due to change in the physiology of taste-buds located on oral mucosa. All of this lead to various problems, of which radiation caries is the most debilitating irreversible complication for the dentition. The radiation-induced dental caries becomes evident in only a few months' time period. It may involve the most caries-resistant areas, e.g. labial areas, cervical areas, and anterior mandibular teeth due to hampered flow of saliva, produces a brownish-black discoloration of tooth. This is accompanied by increased brittleness of tooth surface to an extent that eventually complete decoronation of the tooth crown takes place.¹²

Table I: Forms of fluoride.

Fluoridated toothpastes (>1500 ppm Fluoride content)
Fluoride gels
Swish and swallow tablets
Fluoridated mouth rinses
Fluoride lozenges
Fluoride-vitamin supplements
Fluoride drops
Fluoride varnishes

**ppm refers to part per millions*

Role of Fluorides:

In 1930s and 1940s, Dean reported that caries experience drop sharply as the fluoride concentration in the drinking water rose from negligible to 1.0 ppm.¹³ In USA, the authorities advocate that drinking water in community should ideally have fluoride in a range of 0.7-1.2 ppm (depending on the climate). Apart from water fluoridation, many topical fluoride supplements have been available in developed part of the world for over 80 years (Table I). The fluoride drops, tablets, swish and swallow type lozenges etc. typically have 0.25 to 1 mg fluoride. Additionally, a 50% drop in dental caries incidence among primary teeth was reported as early as 1942, with the help of topical application of solution of potassium fluoride (KF).¹⁴ Within a few years, Knutson technique was developed in which 2% solution of sodium fluoride (NaF) was applied topically in a series of four treatments over a period of several days, following an initial dental prophylaxis. Later in 1950's, annual application of 8% stannous fluoride (SnF₂) was advocated as having benefits comparable to NaF. However, an unpleasant taste and dental staining soon made SnF₂ unpopular among dental professionals.

Professionally applied fluorides are highly concentrated compounds that require careful technique and attention to the amounts.¹⁵ Commonly prescribed examples of such preparations are acidulated phosphate-fluoride (APF) gels and varnishes. APF is the most widely used fluoride compound for professional application and has a pH of about 3.0.¹⁶ It has been demonstrated that uptake of topical fluoride in enamel was significantly higher in an acidic environment.¹⁶ Fluoride varnishes are adhesive and have the ability to have high concentration of fluoride and having benefit of keeping high fluoride content in close contact with the tooth for extended period of time.

It's interesting to note that the United States' Food and Drug Administration (FDA) considers fluoride varnish as a medical device that can be used as a root desensitiser (to manage dentinal hypersensitivity) and cavity liner (a base under deep dental restoration) but not as an anti-caries drug/product.¹⁷ The mainstay of fluoride delivery to general public is via common dentifrices, which contain fluoride in the form of NaF, SnF₂ or sodium monofluorophosphate (NaMFP) in a concentration range of 1000 to

Table II: Forms of topical fluorides available for head & neck cancer patients subjected to radiation therapy.

Fluoride form	Recommended percentage	Over the counter / commercial products*	Advantages	Disadvantages
Sodium Fluoride (NaF)	1.1% 0.05%- daily 0.2%- weekly	Duraphat paste, Prevident gel, Fluorocare rinses	Pleasant taste, neutral pH	Might cause gingival irritation
Stannous Fluoride (SnF ₂)	0.4%	Gel Kam, Topex Take Home Care	Arrests incipient lesions, antimicrobial,	Metallic taste, staining of the teeth
Acidulated Phosphate Fluoride (APF)	1.23%	Phos Fluor rinses	Arrests root caries	Might damage glass ionomer based restorations, requires low pH to be effective, cause staining
Non-Fluoride: Casein phosphopeptide amorphous calcium phosphate (CPP-ACP)**	variable	Tooth Mousse, ReCaldent gum, MI paste, MI paste plus, MI paste One	Reducing demineralisation and promoting remineralisation	Not known

*Made by Colgate-Palmolive Limited; **Made by GC America.

1500 ppm.^{16,17} Tooth brushing with fluoride toothpastes boosts the salivary fluoride concentration by 100-folds but it quickly drops down to baseline level within a couple of hours. Mouth rinses, available for daily use, contain 0.05% NaF and for weekly use, contain 0.2% Na. All these formulations have caused a decline in caries incidence in USA (Table II).

Water fluoridation, dentifrices and mouthwashes are sufficient for the general population but their concentration is inadequate for the patients with high risk features such as those affected with radiation-induced caries.¹⁸ It has been reported that the patients who adhere to the same (pre-radiation therapy) oral hygiene practices in their post-radiation therapy period, are likely to experience 50 times more carious tooth surfaces compared to pre-radiation therapy period.¹⁹ This study also revealed that patients who underwent radiation therapy, later used 1.1% NaF gel (5000 ppm) topically for 5 minutes per day in a custom tray (in addition to standard fluoride dentifrice) exhibited 92% less caries experience than controls.¹⁹

The 1% NaF or 0.4% SnF₂ gel in a custom tray has now become a commonly prescribed treatment against post-radiation caries. This procedure demands high compliance (about 70%) for its potential effectiveness. This is important as radiation caries may develop rapidly and get quite severe, if patients fail to apply these gels as prescribed; or become negligent in maintaining their oral hygiene on regular basis. Fluoride varnishes are effective on occlusal surfaces but gels are supposed to offer protective anti-caries effects on smooth surfaces as well.

Adverse Aspects:

Multiple studies reveal that time-consuming application, discomfort, lack of interest, inadequate dental follow-ups, and lack of reinforcement are the factors resulting in less than ideal compliance.²⁰ On the other side, continuous use of high concentration fluoride can have adverse effects as well. The nephrotoxicity is the most important concern as daily use of fluoride in high concentrations can raise its level in the plasma.

A possible solution to deal with the compliance problem has been proposed. It can elevate the intra-oral fluoride levels by providing continuous low dose for months. Intra Fluoride Release System (IFRS) can be worn continually which releases fluoride at pre-determined rates of 0.02 to 1.0mg per day for up to 4 or 6 months.¹⁶ The IFRS has two components, first is the tablet that releases fluoride in a sustained manner, referred to as an intra-oral fluoride-releasing device (IFRD) and second is the retainer that keeps and protects the IFRD intra-orally. It is a reservoir type device with a central core containing the active ingredient, *i.e.* sodium fluoride (NaF) in copolymer matrix.²¹ When the matrix becomes hydrated, small quantities of granulated NaF are diluted and thus released into the oral environment. The consumed IFRD can be replenished by a new supply of fluoride preparation at given intervals.

Mirth *et al.* have reported elevated level of fluoride in the saliva without major elevation in serum or urine.²² Meyerowitz compared the anti-caries effectiveness of an IFRS with a regimen of a 1.1% NaF gel among patients with head and neck cancer and radiation therapy.²¹ The subjects were given IFRS for six months. The study results showed several advantages of IFRS device over the daily fluoride use. Moreover, IFRS was well tolerated with improved satisfaction levels. It appeared that such devices could be of immense clinical benefits in head and neck cancer patients. However, more randomised clinical trials are needed to confirm their efficacy.

Many complications are associated with surgical resection and radiotherapy. Early complications are mucositis, loss of taste, hypo salivation, and late complications include radiation caries and osteoradionecrosis.²³ Radiation caries occur as a result of hypo-salivation when major salivary glands are exposed to high-dose ionizing radiations. Lifestyle modification and implication of oral hygiene instructions are important along with appropriate treatment to deal with these complications.

Dental care is required to deal with such complications including caries excavation, followed by restorative

procedures (such as permanent fillings), prosthodontics procedures (related to fixed, removable and implant supported prosthesis), endodontic procedures (root canal procedures) or dental surgery procedures (such as tooth extractions, dental implant placement, periodontal surgeries) etc.²⁴ Treatment of these complications not only demands patient's compliance and time but also adds to the financial burden.

Another chemical that is effective in prevention of dental caries is casein phosphopeptides-amorphous calcium phosphate (CPP-ACP). It is a bioactive agent comprising of two component parts: casein phosphopeptides (CPP) and amorphous calcium phosphate (ACP). CPP is derived from milk protein casein and has an ability to increase the level of calcium phosphate in dental plaque. CPP-ACP buffers the free calcium and phosphate ion, thereby reducing demineralisation of tooth enamel and promoting remineralisation. The free calcium and phosphate ions move out of the CPP, enter the enamel rods and reform onto apatite crystals. Studies have shown that CPP-ACP inhibits cariogenic activity.²⁵

Although, it is a non-fluoride agent but CPP-ACP is effective against white spot lesions, hypomineralised enamel, mild fluorosis, tooth sensitivity and erosion, and prevents plaque accumulation around brackets and other orthodontic appliances. A variant of CPP-ACP known as biomimetic self-assembling peptide (P11-4) has shown significantly high remineralising efficacy compared to topical fluorides and CPP-ACPF exhibiting its potential as a non-invasive enamel regenerative material.²⁶ These compounds have been recommended to be commercially added to foods, soft drinks and chewing gum, as well as in toothpastes and mouthwashes to control dental caries.

Preventive and curative options are numerous but selecting the intervention that strikes the balances between clinical effectiveness and cost effectiveness is crucial in the resource restraint settings of developing countries. Fluoride therapy is the low cost management option with respect to avoiding high cost late complications.²⁷ The use of interventions that can notably reduce the rate of dental caries and related complications in radiation-induced xerostomia patients would not only reduce the number of patients requiring treatment but would also alleviate the cost burden.

CONCLUSION

Topical fluoride therapy has proven to be a cost-effective intervention against dental caries and related complications among radiation-induced xerostomia patients. Many fluoride sources are available to prevent caries including water fluoridation, mouth-washes and dentifrices but high concentration fluoride is needed for the prevention of post-radiation caries. At present, 1.1% neutral NaF gel in customised tray is the widely

prescribed treatment; but various fluoridation medications and devices are now available to improve the patient compliance, thus providing greater post-radiation caries protection to the high risk subjects.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

AS: Wrote the draft and did the literature search.

FRK: Conceived the idea and critically appraised the paper.

ST: Contributed in compiling the data stated in the tables.

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