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Umami taste dysfunction in patients receiving radiotherapy for head and neck cancer

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Summary Taste loss is a major cause of morbidity in patients undergoing head and neck irradiation. Previous studies have reported the alteration of the four basic tastes in patients with head and neck cancer during radiotherapy. However, only a few studies have been conducted on the effects of irradiation on the function of *umami* taste, a novel and basic taste recently recognized. In a prospective study, 52 patients undergoing radical head and neck irradiation were assessed for taste loss. Taste ability was measured by the taste threshold for *umami* quality using the whole-mouth taste method in patients before, during, and immediately after radiotherapy. *Umami* taste declined of the 3rd week after the start of radiotherapy and improved of the 8th week.

Introduction

Taste dysfunction is one of the most frequent complaints of patients undergoing radiation therapy (RT) for head and neck cancer. Complaints of taste disorders have been reported in 75% of patients with head and neck cancer undergoing radiation, and 93% of these patients complain of long-term xerostomia.[1] Many patients undergoing dose-intensive radiation experience reduced taste (ageusia) or altered taste (dysgeusia), which may have a significant impact on quality of life (QOL). Patients with taste disturbance experienced greater weight loss than those who did not report a change in taste.[2] On the other hand, patients with taste loss had a worse outcome than those did not lose their sense of taste and were able to maintain their food intake and nutritional support.[3] To design a diet that maximizes

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on the remaining taste abilities might result in the most palatable diet to the patients with taste loss and thus, better outcome and QOL might be expected. This would require individual diet management and especially, depend on a well understanding of the changes of the five basic tastes.

In addition to sweet, salty, bitter, and sour, a novel taste that is referred to by the Japanese word *umami* has come to be recognized as a ''fifth taste''.[4–7] *Umami* taste is found in a diversity of foods like fish, meat, milk, tomato, and some vegetables,[5] and considered to have an important role in the determination of food palatability as well as the intake of food.[8] In Japan, palatable and flavor enhancing taste is given a descriptor word *umami*, which means delicious. In 1908 Ikeda[9] extracted the glutamic acid from seafood and firstly put forward the conception of independent *umami* taste. Unfortunately, *umami* was not internationally accepted as a basic taste because it was supposed that *umami* could be duplicated with appropriate combinations of the other four basic tastes. However, Ikeda's pioneering opinion can be much supported by recent researches. According to the excellent review of taste that was recently published,[10] *umami* is considered to be one of the five basic tastes.

The relationship between changes in the taste recognition threshold for the new taste *umami* and the timing of radiation were analyzed.

Materials and methods

The subjects were 52 patients who underwent RT for their head and neck cancers at the Tokyo University Hospital from April 2002 to August 2007. None of the patients was treated with surgery prior to RT. The malignancies were distributed among the 52 patients as follows: nasopharyngeal cancer, 5; oropharyngeal and hypopharyngeal cancer, 1; oropharyngeal cancer, 17; hypopharyngeal cancer, 20; and the other head and neck cancers, 9. The mean age was 64 years (range, 29–89 years). There were 46 men and six women. Most patients were in good general condition {the 90% rate of Karnofsky performance status was 69% (36/52)}. In most patients (48/52), the RT was administered as a dose of 2 Gy once a day, five times each week. The total RT period ranged from 38 to 62 days (median: 47 days). Conventional radiation technique was used in this study. Only photon energy was used. Off-cord reductions were performed at 40 Gy in 20 fractions. The anterior oral tongue was deflected from the radiation volume after off-cord reduction. Concurrent chemotherapy was allowed in this study. Thirty-three subjects (63%) underwent chemotherapy combined with RT.

The cancers were limited to the head and neck area. Patients who had only a part of tongue within the radiation field were excluded from the study.

LINAC (6 MV in most cases) was used as a radiation source. In most cases, from the start to 40 Gy in 20 fractions, the radiation method was in three fields (their gantry angles were 0, 80, and 280° and beam weight was 1:1:1) in order to include the bilateral whole neck lymph nodes within radiation field. The radiation treatment of the nasopharyngeal and hypopharyngeal cancer also included the oral tongue within the volume of tissue radiated. That is why all patients received radiation dose of at least 11.4 Gy to the anterior tongue. After that, up to 60 Gy in 30 fractions, two shrinking and right and left opposing fields were used. In addition, the radiation field to the tumor bed was reduced. Most patients received a total radiation dose of 72 Gy in 36 fractions (mean: 68.4 Gy, range of dose: 36–72 Gy). The determination of the radiation fields was confirmed with linacgraphy. The planning was based on a three-dimension CT in all patients.

No tumor ablative procedures, or alteration of altering salivary beds, were performed in this study. No patients were taking Salagen or amifostine. None of the enrolled subjects had total or partial glossectomies.

All subjects gave written informed consent before entry into the study. The subjects had no intercurrent illnesses that affected salivary function (i.e., Sjögren's syndrome, human immunodeficiency virus [HIV]). No concurrent medicines altering the taste of the subjects were administered.

The taste recognition threshold for *umami* was measured using the whole-mouth taste method. Test solutions of monosodium glutamate (MSG; 25, 50, 75, or 100 mM) were prepared, and the subjects were tested with 10 mL of each concentration for a recognition threshold. First, the subject was asked to rinse mouth with distilled water and perceive the *umami* taste of the distilled water. Then, using a polyethylene pipette, 10 mL solution of the lowest concentration of one taste was circularly dropped into the mouth of the subject. The subject was instructed to identify the taste and then spat out the solution. When a wrong response was made, the next higher concentration would be applied. The lowest concentration that the subject continuously recognized the stimuli for two times was defined as the recognition threshold.

These taste recognition threshold measurements were performed once before RT and weekly thereafter from the first week to 10–12 weeks after the start of RT. At the same time, the subjects were questioned about xerostomia and mucositis by the radiation oncologists weekly.

Xerostomia or mouth dryness was classified into grade 0, normal; grade 1, mild and slight dryness of mouth, or symptomatic (dry or thick saliva) without significant dietary alteration; grade 2, moderate dryness of mouth, or symptomatic and significant oral intake alteration (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); and grade 3, complete dryness of mouth, or symptoms leading to inability to adequately aliment orally; IV fluids, tube feedings, or TPN indicated. Stomatitis due to radiation was classified into grade 1, erythema of the mucosa or minimal symptoms, normal diet; grade 2, patchy ulcerations or symptomatic but can eat and swallow modified diet; grade 3, confluent ulcerations or bleeding with minor trauma or symptomatic and unable to adequately aliment or hydrate orally; and grade 4, tissue necrosis, significant spontaneous bleeding, or symptoms associated with life-threatening consequences.

Results

Patients

The mean and median total doses of RT for tip of the tongue were 13.5 Gy and 13.3 Gy (range, 11.4–14.8 Gy) and for the