



Reduction of Salivary Gland Damage During Radioiodine Therapy for Differentiated Thyroid Cancers

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Radioiodine therapy is one of the major therapeutic modalities in the management of differentiated thyroid cancers (DTCs), and it has been successfully applied in the clinical setting for eight decades. The uptake of radioiodine in DTCs relies on the expression of sodium iodide symporter (NIS), and accumulation of radioiodine induces lethal radiation harm to the lesions through the emission of beta rays [1, 2]. Salivary glands also express NIS; therefore, they naturally take up radioiodine. Because of the underlying nature of the salivary glands, there is a high prevalence of radioiodine-induced dysfunction followed by damage to the salivary glands. Symptoms of salivary gland dysfunction, including pain, swelling, altered taste, dry mouth, and swallowing/speaking difficulties, are the most serious and common complaints of patients who have undergone radioiodine therapy, and some of these symptoms are lifelong and negatively affect the patient's quality of life [3]. The risk of adverse effect may force strict indications for radioiodine therapy in patients with DTC. Prevention or reduction of radioiodine therapy-induced damage to the salivary glands could increase the active use of effective radioiodine therapy by reducing both patients' and physicians' reluctance to the therapy.

Reducing the accumulation of therapeutic radioiodine in the salivary glands mitigates damage to the glands and can be feasibly assessed on imaging using a gamma camera. Therefore, nuclear medicine technology is one of the most important technologies in researches on salivary gland protection [4]. Although nuclear imaging has not been frequently used to assess radioiodine accumulation in the salivary glands, the application of this technology can provide important

information (e.g., kinetic information on radioiodine in the salivary glands) that can assist in the development of strategies for reducing salivary damage [5].

To protect patients from salivary gland damage during radioiodine therapy, various interventions including sialogogues and sufficient water intake have been widely applied. Sialogogues increase salivation and reduce the concentration of radioiodine in the salivary glands, and adequate water intake alleviates dehydration, which decreases salivary lavage [6].

Pilocarpine and amifostine have been used in an attempt to prevent salivary damage; however, the application of these agents is not recommended by various guidelines, mainly because of their limited and debated level of effectiveness as well as their adverse pharmacologic effects [7, 8]. In addition, pharmacologic intervention may reduce the therapeutic effect of radioiodine on DTC lesions.

External massage to the salivary glands has been recommended to expel radioiodine-containing saliva from the glands. Clinical trials of external massage reported reduced accumulation of radionuclides (Tc-99m or I-123) in the salivary glands and low incidence of salivary gland damage after I-131 therapy [9–11]. Conversely, nonpharmacologic interventions show no systemic effects and do not influence the therapeutic effect of radioiodine on DTC lesions.

Extensive preclinical and clinical research have been conducted on methods to protect the salivary glands during radioiodine therapy. However, prevention of salivary gland damage remains an unmet need in the field of radioiodine therapy, and damage mitigation is desperately warranted to improve the quality of life of patients with DTC who require radioiodine therapy. The development of an optimal protocol to protect the salivary glands during radioiodine therapy may reduce both patients' and physicians' reluctance to use this therapy and broaden the indications for effective radioiodine therapy in patients with DTC.

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Compliance with Ethical Standards

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