Review Article

Seeking Optimal Management for Radioactive Iodine Therapy-induced Adverse Effects

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ABSTRACT

Radioactive iodine therapy (RAIT) is one of the important treatment modalities in the management of differentiated thyroid cancer (DTC). RAIT with iodine-131 has long been used in the management of DTC for the ablation of residual thyroid or treatment of its metastases. Despite being reasonably safe, radioiodine therapy is not always without side effects. Even relatively low administered activities of RAIT used for remnant ablation have been associated with the more clinically significant side effects of sialadenitis, xerostomia, salivary gland pain and swelling, dry eyes, excessive tearing, or alterations in taste in as many as 25% of patients. Given that there is a lack of comprehensive management of these RAIT-induced adverse effects, this paper explores the use of other nonpharmacological measures and their effectiveness as interventions to minimize salivary gland damage.

Key words: Nonpharmacological, radioiodine, salivary gland side effects

Introduction

Differentiated thyroid cancer (DTC) is defined as a carcinoma deriving from the follicular epithelium and retaining basic biological characteristics of healthy thyroid tissue.[1] The incidence of thyroid cancer has been increasing in many countries over the past 30 years while mortality has been slowly decreasing.[2] DTC, namely papillary and follicular thyroid carcinoma, accounts for over 90% of all thyroid cancers.[3] The number of DTC survivors within Europe accounts for approximately 250,000,[4] meaning that the DTC management has significant patient quality of life and pharmacoeconomic implications that need to be considered.[1] The guidelines

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for the treatment of DTC involve thyroidectomy with suppression of thyroid-stimulating hormone using levothyroxine.[5,6] Radioactive iodine is often administered postoperatively to ablate remaining thyroid tissue, eliminate any suspected micrometastases, or eliminate recurrent disease.[5,6] Radioactive iodine therapy (RAIT) is defined as the systemic administration of 131-sodium or potassium iodide (^{131}I) for selective irradiation of thyroid remnants, microscopic DTC or other nonresectable or incompletely resectable DTC, or both purposes.[1] Iodine-131 (I-131) is a beta-emitting radionuclide with a maximum energy of 0.61 MeV, an average energy of 0.192 MeV, and a range in tissue of 0.8 mm.[7]

Radioactive Iodine Therapy-induced Adverse Effects

RAIT is frequently used in the treatment of thyroid disorders such as thyroid carcinoma or thyrotoxicosis and is generally well tolerated if appropriate single and cumulative activities are used and precautions employed. However, the RAIT procedure does have a number of potential early and late adverse effects because of its concentration in the salivary glands by the striated ducts that can cause glandular damage and consequent salivary dysfunction.[8] These include a range of uncomfortable symptoms such as pain or swelling in the neck and parotid region, sialadenitis, dryness of mouth, altered taste, and difficulty in swallowing.[9]

Pharmacological Interventions for Managing Radioactive Iodine Therapy-induced Adverse Effects

The management of RAIT-induced adverse effects through conventional pharmacological interventions has proven to be lacking. Patients continue to experience various levels of adverse effects not only during RAIT but also long after the completion of the treatment. Furthermore, it is not infrequent that many patients to experience pharmacological-induced secondary side effects caused by medications such as pilocarpine and amifostine. The main barriers limiting the applicability of amifostine have been the logistics of its use and its toxicity.[10] Similarly, for pilocarpine, the side effect rate is high (usually the result of generalized parasympathomimetic stimulation), and side effects tend to be the main reason for withdrawal.[11,12] These side effects include sweating, wheezing, abdominal cramps, lacrimation, nausea, vomiting, diarrhea, dizziness, headache, palpitations, asthenia, chills, increased urinary frequency, and rhinitis. These can lead not only to patients' poor adherence to the pharmacological treatment but also to RAIT.[13] Furthermore, patients are reluctant to take these medications who creates an additional burden as a result of polypharmacy that they already experience.[14] Additional barrier to the pharmacological treatments is the financial toxicity that many patients might face as a result of the expensive treatments they need to undertake.[15]

Nonpharmacological Interventions for Managing Radioactive Iodine Therapy-induced Adverse Effects

Preceding studies have mainly emphasized on the use of various sialogogues as nonpharmacological means to better manage the treatment-induced adverse effects. The studies provided evidence on the varying level of effectiveness of these nonpharmacological interventions. Sialogogues such as lemon candy, Vitamin E, lemon juice, and lemon slice can reduce the damage caused to the salivary glands by increasing salivary secretion and hence help the excretion of the radioiodine. Other nonpharmacological interventions include the use of Vitamin C and chewing gum. Parotid gland (PG) massage is also used to manage radioisotope accumulation in the salivary gland.

A study by Liu *et al*.[16] explored the effectiveness of Vitamin C (lozenge containing 100 mg of Vitamin C) as a sialogogue in decreasing ^{131}I absorption by the salivary glands. Salivary gland scintigraphy was used to assess the damage induced to the glands by the ^{131}I at several time points. The results showed that Vitamin C had a limited effect in decreasing ^{131}I absorption by the salivary glands.

Hong *et al*.[17] in a prospective study with 44 patients who underwent total thyroidectomy and ^{131}I ablation explored the effect of PG massage for removal of radioiodine from the PG. Three serial salivary gland scans were performed 2 h after administration of ^{123}I. PG massage reduced the radioiodine accumulation in PG and can, therefore, be applied to thyroidectomized thyroid cancer patients who received high-dose radioiodine therapy to reduce PG dysfunction.

Fallahi *et al*.[18] in a double-blind, randomized controlled trial tested the effectiveness of Vitamin E (800 IU of Vitamin E orally) in preventing salivary gland damage caused by ^{131}I therapy in DTC patients following thyroidectomy. Salivary gland scintigraphy was performed on the day of administration of ^{131}I and 6 months later. The results showed that Vitamin E was effective in reducing salivary gland damage.

The effectiveness of lemon juice was tested in a pilot study[19] in nine patients awaiting ^{131}I ablation. The patients underwent two salivary gland scintigraphies; the first just

after drinking lemon juice and the second without lemon juice, after administration of ^{123}I. Based on the results, a lower percentage of radiation absorption was observed in patients who received the lemon juice.

Chewing gum's effect in reducing salivary gland damage induced by ^{131}I was tested in a prospective study[20] with ten patients awaiting radioiodine therapy following total thyroidectomy. The results showed that chewing tasteless gum immediately after administrating ^{124}I did not significantly reduce the absorbed dose to the salivary glands.

Nakada *et al*.[21] explored the effect of lemon candy prospectively and longitudinally in two groups of patients with postsurgical DTC with varying regimens for sucking lemon candy. The onset of salivary side effects was monitored during hospital admission and regular follow-up on the basis of interviews with patients, a visual analog scale, and salivary gland scintigraphy using ^{99m}Tc-pertechnetate. Based on the results, the authors concluded that lemon candy can have positive effects on reducing salivary glands damaged when administered 24 h after radioiodine therapy.

Nakayama *et al*.[22] investigated the effects of aromatherapy in decreasing salivary gland damage in 71 patients with DTC undergoing RAIT. Patients in the aromatherapy group inhaled a blend of 1.0 mL of lemon and 0.5 mL of ginger essential oils. Patients in the control group inhaled distilled water as placebo for 10 min during admission. The results showed an amelioration of salivary gland function in the aromatherapy group, suggesting the efficacy of aromatherapy in the prevention of treatment-related salivary gland disorder.

Thyme honey is also another sialogogue that can be effective in the management of xerostomia in this group of patients. Thyme honey was tested for its effectiveness in managing treatment-induced xerostomia in 72 head and neck cancer patients receiving radiotherapy or/and chemotherapy or/and surgery. This was a parallel randomized controlled trial with two equal arms, the experimental arm (thyme honey) and the control arm (saline). The study has demonstrated the safety and efficacy findings of thyme honey in head and neck cancer patients for the management of treatment-induced xerostomia.[23] Thyme honey is currently tested for its effectiveness as a complementary intervention for decreasing salivary gland damage due to radioiodine (^{131}I) therapy. This is a RCT with a 2 × 3 mixed between-within subjects design that will include in total, 120 participants of postsurgical DTC, who will be referred for ^{131}I therapy to ablate the remnant thyroid tissue or to treat metastatic tumor. The effectiveness of thyme honey will be prospectively studied under varying regimens of lemon candy (standard treatment) and thyme honey mouthwashes (experimental intervention).[24]

Conclusion

The incidence of thyroid cancer has been increasing in many countries, and this means that an increasing number of patients will undergo RAIT, which is associated with salivary gland damage. This damage is exacerbated by the accumulation of iodine as the number of therapies increases, especially in those cases where there is the insufficient ability of the salivary glands to excrete I^{131}. Taking preventing measures can reduce the severity of salivary gland disorders which in turn may help patients avoid therapy interruption as a result of the adverse effects. These preventing measures include both the use of pharmacological and nonpharmacological means.

Pharmacological measures used to reduce salivary gland damage although produced an increase in the saliva flow facilitating the excretion of I^{131} these were associated with significant side effects that many patients find intolerable. However, both pilocarpine and amifostine have better effects when the dose is titrated to suit individual needs. Based on the available evidence, sialogogues such as lemon candy, Vitamin E, lemon juice, and lemon slice and parotid gland massage can reduce the damage on salivary glands. A systematic review by Christou *et al*.[25] demonstrated that lemon candy appears to have the most statistically positive significant effect from all the nonpharmacological interventions reported in the literature.

This paper has highlighted the value of both pharmacological and nonpharmacological measures to reduce the RAIT-induced adverse effects. The optimal management of these adverse effects includes the use (inappropriately titrated doses) of both measures to reduce salivary gland damage.

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Conflicts of interest

There are no conflicts of interest.

References

1. Luster M, Clarke SE, Dietlein M, Lassmann M, Lind P, Oyen WJ, *et al*. Guidelines for radioiodine therapy of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging 2008;35:1941-59.
2. Pacini F, Castagna MG, Brilli L, Pentheroudakis G, Heidary N, Naik H, *et al*. Differentiated thyroid cancer: ESMO Clinical

Recommendations for diagnosis, treatment and follow-up. Ann Oncol 2009;20:143-6.
3. NCI SEER Cancer Statistics Review. Available from: http://www.seer.cancer.gov/csr/1975_2010/results_merged/sect_26_thyroid.pdf. [Last accessed on 2017 Mar 06].
4. Cancer IARC Globocan. Cancer Incidence, Mortality and Prevalence Worldwide. Lyon, France: Cancer IAfRo Globocan; 2005.
5. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, *et al*. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006;16:109-42.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Thyroid Carcinoma (Version 2). Fort Washington, PA: National Comprehensive Cancer Network; 2013.
7. Mumtaz M, Lin LS, Hui KC, Mohd Khir AS. Radioiodine I-131 for the therapy of graves' disease. Malays J Med Sci 2009;16:25-33.
8. Aframian DJ, Helcer M, Livni D, Markitziu A. Pilocarpine for the treatment of salivary glands' impairment caused by radioiodine therapy for thyroid cancer. Oral Dis 2006;12:297-300.
9. Lu L, Shan F, Li W, Lu H. Short-term side effects after radioiodine treatment in patients with differentiated thyroid cancer. Biomed Res Int 2016;2016:4376720.
10. Wu HY, Hu ZH, Jin T. Sustained-release microspheres of amifostine for improved radio-protection, patient compliance, and reduced side effects. Drug Deliv 2016;23:3704-11.
11. Nikles J, Mitchell GK, Hardy J, Agar M, Senior H, Carmont SA, *et al*. Do pilocarpine drops help dry mouth in palliative care patients: A protocol for an aggregated series of n-of-1 trials. BMC Palliat Care 2013;12:39.
12. Davies AN, Shorthose K. Parasympathomimetic drugs for the treatment of salivary gland dysfunction due to radiotherapy. Cochrane Database Syst Rev 2007;3:CD003782.
13. Rieger JM, Jha N, Lam Tang JA, Harris J, Seikaly H. Functional outcomes related to the prevention of radiation-induced xerostomia: Oral pilocarpine versus submandibular salivary gland transfer. Head Neck 2012;34:168-74.
14. Balducci L, Goetz-Parten D, Steinman MA. Polypharmacy and the management of the older cancer patient. Ann Oncol 2013;24 Suppl 7:vii36-40.
15. Zafar SY, Abernethy AP. Financial toxicity, Part I: A new name for a growing problem. Oncology (Williston Park) 2013;27:80-1, 149.
16. Liu B, Kuang A, Huang R, Zhao Z, Zeng Y, Wang J, *et al*. Influence of Vitamin C on salivary absorbed dose of 131I in thyroid cancer patients: A prospective, randomized, single-blind, controlled trial. J Nucl Med 2010;51:618-23.
17. Hong CM, Son SH, Kim CY, Kim DH, Jeong SY, Lee SW, *et al*. Radioiodine removal effect of massage on parotid glands. J Nucl Med 2013;54:1881.
18. Fallahi B, Beiki D, Abedi SM, Saghari M, Fard-Esfahani A, Akhzari F, *et al*. Does Vitamin E protect salivary glands from I-131 radiation damage in patients with thyroid cancer? Nucl Med Commun 2013;34:777-86.
19. Kulkarni K, Van Nostrand D, Atkins F, Mete M, Wexler J, Wartofsky L. Does lemon juice increase radioiodine reaccumulation within the parotid glands more than if lemon juice is not administered? Nucl Med Commun 2014;35:210-6.
20. Jentzen W, Richter M, Nagarajah J, Poeppel TD, Brandau W, Dawes C, *et al*. Chewing-gum stimulation did not reduce the absorbed dose to salivary glands during radioiodine treatment of thyroid cancer as inferred from pre-therapy (124)I PET/CT imaging. EJNMMI Phys 2014;1:100.
21. Nakada K, Ishibashi T, Takei T, Hirata K, Shinohara K, Katoh S, *et al*. Does lemon candy decrease salivary gland damage after radioiodine therapy for thyroid cancer? J Nucl Med 2005;46:261-6.
22. Nakayama M, Okizaki A, Takahashi K. A randomized controlled trial for the effectiveness of aromatherapy in decreasing salivary gland damage following radioactive iodine therapy for differentiated thyroid cancer. Biomed Res Int 2016;2016:9509810.
23. Charalambous A, Lambrinou E, Katodritis N, Vomvas D, Raftopoulos V, Georgiou M, *et al*. The effectiveness of thyme honey for the management of treatment-induced xerostomia in head and neck cancer patients: A feasibility randomized control trial. Eur J Oncol Nurs 2017;27:1-8.
24. Charalambous A, Frangos S, Talias M. A randomized controlled trial for the use of thymus honey in decreasing salivary gland damage following radioiodine therapy for thyroid cancer: Research protocol. J Adv Nurs 2014;70:1663-71.
25. Christou A, Papastavrou E, Merkouris A, Frangos S, Tamana P, Charalambous A. Clinical studies of nonpharmacological methods to minimize salivary gland damage after radioiodine therapy of differentiated thyroid carcinoma: Systematic review. Evid Based Complement Alternat Med 2016;2016:6795076.