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Does the use of recombinant TSH in preparation for I-131 scintigraphy scan affect hearing function?

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Abstract

Objective: The objective of this study was to examine the effect of hypothyroidism on hearing function in patients surgically treated for differentiated thyroid cancer and subsequently experienced hypothyroidism during preparation for follow up I-131 scintigraphy scan by either recombinant human thyroid stimulating hormone (rhTSH) treatment or thyroid hormone withdrawal (THW).
Methods: A total of 55 patients undergoing I-131 scintigraphy scan following surgeries for differentiated thyroid cancer were included in the study, including 25 patients prepared by administration of recombinant TSH (rhTSH Group) and 30 patients by thyroid hormone withdrawal (THW Group).
Results: Air conduction thresholds at 1, 2 and 4 kHz for both ears were higher during hypothyroid period than during euthyroid period for patients in the THW group ($p < 0.05$) but not for patients in the rhTSH group.
Conclusion: Sensorineural hearing loss was detected, especially at low frequencies, in patients with DTC after surgical treatment whose hormone replacement therapy was withdrawn but not in those receiving rhTSH. It is therefore preferred to use rhTSH when preparing for I-131 scintigraphy scan in patients at risk for hearing loss.

Keywords: Hearing loss; Recombinant TSH; Thyroid hormone withdrawal; Radioiodine

1. Introduction

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy and its prevalence is increasing worldwide (McNally et al., 2012; Nixon, 2015). The mainstay of therapy for DTC is surgery and the initial surgical approach is total or nearly total thyroidectomy with or without lymph node dissection (Nixon, 2015; Chen et al., 2008). Thyroid hormone replacement therapy is initiated in all patients after total thyroidectomy and used throughout their lives.

In patients with DTC, postoperative ablation therapy with high-dose I-131 (radioactive iodine, RAI) is administered to both ablate residual thyroid tissue and treat unrecognized micrometastases. Whole body scintigraphy is conducted on the 8th–9th days following high-dose I-131 treatment, and low-dose I-131 whole body scintigraphy is repeated at the follow-up in the 8th–12th months after high-dose I-131 treatment. I-131 scintigraphy has a higher sensitivity than morphologically based imaging modalities in detecting residual and metastatic DTC (Buck et al., 2008; Al Balooshi and Vinjamuri, 2015).

Certain patient preparation is needed in order to increase I-131 uptake by tumor tissue both before high-dose ablation therapy and

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before low-dose I-131 scintigraphic scanning during follow-up. For optimal sensitivity, I-131 imaging requires stimulation of thyroid tissue by elevated TSH levels. This can be achieved either with thyroid hormone withdrawal (THW) for 4 weeks to achieve a TSH level ≥30 uU/mL, or with stimulation by recombinant human TSH (rhTSH) (American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid CancerCooper et al., 2009; Verburg et al., 2011). Foods, drinks and drugs that may interfere with iodine uptake by thyroid cells are also routinely limited. In patients undergoing thyroid hormone withdrawal, symptoms such as depression, dysmnesia, concentration difficulty, fatigue, dry hair and skin, facial and eye swelling, cold intolerance, weight gain, constipation, and increased signs of menstrual cycle may be observed during hypothyroid period (Dietlein et al., 2005). Recombinant TSH is well tolerated due to its short half-life. Hypothyroidism symptoms can be avoided or progress more mildly in these patients, although side effects like minimal nausea, headache, and fatigue may occur (Klubo-Gwiezdzinska et al., 2012).

According to American Thyroid Association Management Guidelines, in patients with low and intermediate risk DTC without extensive lymph node involvement (i.e. T1-T3, N0/Nx/N1a, M0), in whom radioiodine remnant ablation or adjuvant therapy is planned, preparation with rhTSH stimulation is an acceptable alternative to thyroid hormone withdrawal for achieving remnant ablation, based on evidence of superior short-term quality of life, non-inferiority of remnant ablation efficacy, and multiple consistent observations suggesting no significant difference in long-term outcomes (Haugen et al., 2016).

The relationship between hypothyroidism and hearing loss has been known for many years. In various studies investigating the relationship between hypothyroidism and hearing loss in DTC patients in the literature, it is observed that acute hypothyroidism may cause an increase in hearing thresholds and subclinical cochlear damage (Psaltakos et al., 2013; Hasbek et al., 2014). We could not find any study investigating the effect of rhTSH usage on hearing in the literature. Therefore, the aim of the present study was to examine the effect of hypothyroidism on hearing function in patients who experienced hypothyroidism while receiving rhTSH, as well as thyroid hormone withdrawal, in preparation for I-131 scintigraphy scan, using pure tone audiometry, otoacoustic emissions and tympanometry.

2. Materials and methods

Study subjects were patients who had undergone total/nearly total thyroidectomy between January and December 2014 for differentiated thyroid carcinoma followed by ablation therapy with high-dose I-131, and were referred to the Nuclear Medicine Department in the 8th−12th months with the request for routine whole body low-dose I-131 scintigraphy scan. A total of 55 patients were recruited, including 25 patients who experienced hypothyroidism following administration of recombinant TSH (rhTSH Group) and 30 patients who developed hypothyroidism following thyroid hormone therapy withdrawal for 4 weeks (THW Group). Audiological tests were conducted during both hypothyroid and euthyroid periods in both groups of patients and results were compared.

TSH stimulation before oral administration of I-131 for patients in the THW Group was achieved by discontinuing thyroxine (LT4) intake for 4 weeks, or by IM injection of rhTSH (0.9 mg/day for 2 days) for patients in the rhTSH group. Patients on rhTSH did not discontinue thyroxine therapy. The authors did not have a primary role in selecting the patients into these two groups, but patient treatment strategies were determined by specialists in the Endocrine and Metabolism Department, while scintigraphy scan was prepared by the same physician (ZH) from the Nuclear Medicine Department. Therefore, there were no healthy control subjects in the study and only patients' euthyroid and hypothyroid data were compared in both rhTSH and THW groups.

Serum thyroglobulin (Tg), anti-thyroglobulin antibody (anti-TgAb), free T3 (fT3), free T4 (fT4) and thyroid stimulating hormone (TSH) levels were recorded before whole body scintigraphy scan in all patients. The reference range of fT4, fT3, and TSH was 0.7−1.48 ng/dL, 1.71−3.71 pg/mL and 0.35−4.94 mIU/mL, respectively.

Hearing tests included pure tone audiometry, otoacoustic emissions and tympanometry performed by the same tester at the ENT clinic who was unaware of the thyroid hormone state of the patient during both hypothyroid and euthyroid periods. Detailed anamnesis information, thyroid function test results, otoscopic examination notes, audiograms and otoacoustic emission findings were recorded in the patient follow-up forms.

Air and bone conduction thresholds at 0.25, 0.5, 1, 2, 4, 6, 8, 12 and 16 kHz were measured using a clinical audiometer (INTERACOUSTICS AC 40 Clinical Audiometer, Assen, Denmark) which was calibrated according to ISO standards. Masking was provided to the opposite ear. Transient evoked otoacoustic emissions (TEOAE) testing and analysis were performed using a commercially available device (Maico, ERO Scan Analyzer, GmbH Salzufer, 13/14, 10587, Berlin GE), which was calibrated before being used, and disposable probe tips inserted into the ear canal. Clicks (0.7−4 kHz, 83 ± 3 dB/SPL) were used as stimuli and responses at less than 6 dB above noise floor signified no otoacoustic emissions. Based on whether TEOAEs were determined to be present, the ear was marked as “PASS” or “REFER”. Testing was repeated in ears marked as “REFER” for verification. Results were recorded in individual frequency bands (bandwidth = 1.5−4 kHz) at 1.5, 2, 2.5, 3, 3.5 and 4 kHz.

Exclusion criteria were as follows: history of ear surgery, ear or head trauma, acute or chronic otitis media, syphilis, other malignancy, upper respiratory tract infection, intake of ototoxic drugs or employment in a noisy environment, diseases potentially associated with hearing loss such as hypertension, liver failure, and renal failure, receiving radiotherapy or chemotherapy treatment in the last month, vascular diseases, congenital cochlear malformation, neurologic disease (causing a loss of hearing), and TSH level of <30 mIU/mL before whole body scintigraphy scan. Moreover, patients who did not agree to participate in hearing tests, had ear infection

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