ODÜ Tıp Dergisi / *ODU Journal of Medicine*
http://otd.odu.edu.tr

Araştırma Yazısı ***Research Study***

Odu Tıp Derg
(2015) 2: 79-82

Odu J Med
(2015) 2: 79-82

Repeated Radioiodine Treatment in Differentiated Thyroid Carcinoma Patients

Differansiye Tiroid Karsinomlu Hastalarda Tekrarlayıcı Radyoiyot Tedavisi

Ebuzer KALENDER[1], Umut ELBOĞA[1], Ertan Sahin[2], Y.Zeki ÇELEN[1], Hasan Deniz DEMİR[1], Mustafa YILMAZ[1]

[1]Gaziantep University, Department of Nuclear Medicine, Gaziantep, Turkey
[2]Namık Kemal University, Department of Nuclear Medicine, Tekirdag, Turkey

Yazının geliş tarihi / Received: 12 Mart 2014 / March 12, 2014
Düzeltme / Revised: 21 Ekim 2014 / Oct 21, 2014
Kabul tarihi / Accepted:5 Nov 2014 / Nov 5, 2014

Abstract

Aim: To evaluate the indications of repeated radioiodine treatments (RIT) in DTC patients. **Materials and Methods:** Nine hundred and forty-five patients with DTC referred for RIT after surgery were reviewed retrospectively. Seventy-seven patients who were treated with ^{131}I more than one, were selected for this study. We evaluated the indications of retreatments and also the demographic and pathological features of patients who were retreated. **Results:** Seventy-seven of the 945 patients (8.1 %) were treated more than one. Histological examination revealed papillary thyroid carcinomas in 69 patients and follicular thyroid carcinomas in 8 patients. Sixteen patients (20.8 %) were retreated for complementary ablation, 28 patients without known distant metastasis (36.4 %) were retreated empirically for high stimulated Tg levels 6 months after first RIT, 29 patients (37.6 %) were retreated for distant metastasis and 4 patients (5.2 %) were treated again for recurrence identified on the follow-up. **Conclusion:** Radioiodine is the main method for the treatment of DTC patients after surgery and its success rate is high. However, in some cases, especially in metastatic patients, repeated treatments are needed. Besides all, radioiodine maintains the fundamental position for the treatment of DTC today.

Key Words: Thyroid carcinoma, Iodine-131 treatment, retreatment.

Özet

Amaç: Diferansiye tiroid karsinomlu (DTK) hastalarda tekrarlanan radyoaktif iyot tedavisi endikasyonlarının değerlendirilmesi amaçlanmıştır. **Gereç ve Yöntem:** Ameliyat sonrası radyoaktif iyot tedavisi almak üzere refere edilen 945 DTK'lı hasta retrospektif olarak incelendi. Birden fazla ^{131}I ile tedavi alan 77 hasta bu çalışma için seçildi. Bu çalışmada yeniden tedavi alanların endikasyonları ile demografik ve patolojik özellikleri değerlendirildi. **Bulgular:** Kiniğimizde 945 hastadan 77'si(% 8.1) yeniden tedavi edilmişti. Histolojik incelemeleri sonucunda 69 hastanın papiller tiroid karsinomlu, 8 hastanın ise foliküler tiroid karsinomlu olduğu ortaya kondu. 16 hasta (% 20.8) tamamlayıcı ablasyon için yeniden tedavi edildi. 28 hasta (%36.4) ilk radyoaktif iyot tedavisinden 6 ay sonra stimüle edilmiş Tg düzeylerinin yüksek olması nedeniyle ampirik olarak yeniden tedavi edildi. 29 hasta (% 37.6) uzak metastazları nedeniyle yeniden tedavi edildi. 4 hasta (% 5.2) takipte rekürrens tesbit edimesi üzerine yeniden tedavi edildi. **Sonuç:** Radyoaktif iyot tedavisi diferansiye tiroid karsinomunda cerrahi sonrası tedavide ana yöntemdir ve başarı oranı yüksektir. Bununla beraber bazı hastalarda, özellikle de metastatik hastalarda, tekrarlayıcı tedavilere ihtiyaç duyulmaktadır. Ayrıca radyoaktif iyot tedavisi diferansiye tiroid karsinomu tedavisinde temel pozisyonunu korumaktadır.

Anahtar Kelimeler: Tiroid karsinomu, Iyot-131 tedavisi, Yeniden tedavi**.**

İletişim/*correspondence: Uzm. Dr.Umut ELBOĞA, Gaziantep Universitesi Tıp Fak., Nükleer Tıp AD Gaziantep, Turkey*
Phone : 0 535 5164132 Fax : 0 342 360 3928

Introduction

The main treatment way of differentiated thyroid carcinoma (DTC) is total or near-total thyroidectomy followed by radioiodine treatment (RIT) and suppression of thyroid-stimulating hormone (TSH) (1, 2). The use of ^{131}I has continued as a mainstay of therapy for DTC today and it has a major impact on the progressive control and cure of DTC (3). Radioiodine is used for both remnant ablation and treatment of distant metastasis in DTC patients (4). Unfortunately, the first dosage of I-131 is not always sufficient to achieve complete ablation of thyroid remnants (5, 6). Also repeated treatments may be need in patients with metastatic lesions. The aim of this retrospective study is to evaluate the indications of repeated RITs in DTC patients.

Materials and Methods

Nine hundred and forty-five patients with DTC referred to our clinic for RIT after surgery between January 2008 and January 2013 were reviewed retrospectively. Seventy-seven patients who were treated with ^{131}I more than one, were selected for this study. All patients were given RIT after total or near-total thyroidectomy. Before RIT patients did not take levothyroxine, and they had a low-iodine diet for 2 weeks (12 days before and 2 days after I-131 administration). To prevent stunning effect, diagnostic scintigraphy was not performed before the RIT. Patients were treated according to fixed dosage protocol: 75-100 mCi ^{131}I in cases without known lymph node or distant metastasis, 150 mCi ^{131}I in cases with lymph node involvement detected pre- or perioperatively and 200 mCi ^{131}I in cases of known distant metastasis. A posttreatment ^{131}I whole body scan (PWBS) was performed 5-10 days after RIT to all patients.

RIT patients were followed by periodic measurements of thyroglobulin (Tg) and diagnostic whole-body scintigraphy (DWBS) performed 6 months after RIT. Before DWBS, patients stopped taking levothyroxin for 3 weeks, and they had a low-iodine diet for 2 weeks. Just before DWBS, Tg and anti-Tg antibodies levels were measured when TSH>30 IU/ml. RIT was considered as successful when patients had Tg levels lower than 2 ng/ml under TSH stimulation and negative DWBS. But in the cases with positive anti-Tg antibodies, Tg levels were not used as a criterion for success RIT. Because in the presence of anti-Tg antibodies, levels of Tg can be mistakenly low. RIT was not considered as successful in patients with detectable Tg levels and/or positive DWBS. We treated again with ^{131}I most of this cases. In this study we evaluated the indications of retreatments and also we evaluated the demographic and pathological features of patients who were retreated.

Results

Seventy-seven of the 945 patients (8.1 %) were treated more than one in our clinic. Twenty-one patients were male and 56 were female. Mean age was 48.6±15 years. Histological examination revealed papillary thyroid carcinomas in 69 patients and follicular thyroid carcinomas in 8 patients.

Sixteen patients (20.8 %) were received a second dose of RIT for complementary ablation because of the residual uptake in the thyroid bed on DWBS which was performed 6 months after the first RIT. All patients had a stimulated Tg level under 2 ng/ml measured just before DWBS. In fourteen patients, anti-Tg antibody level was negative, but in 2 patients it was positive for 238 and 462.

Twenty-eight patients (36.4%) without known distant metastasis who had high stimulated Tg levels 6 months after RIT were retreated empirically. To control the first RIT efficacy, DWBS was planned 6 months later. Before DWBS, stimulated Tg levels were measured. These patients had Tg levels higher than expected and retreated with 125-175 mCi ^{131}I empirically without DWBS. The Tg cutoff level for empiric ^{131}I therapy (EIT) was accepted 10 ng/ml. PWBS was performed to all patients7-10 days after EIT. PWBS was positive in 14 patients and negative in 14 patients. In PWBS positive patients, pathological ^{131}I uptake was in only thyroid bed in 10 patients and in only mediastinum in 4 patients. ^{18}F-FDG PET CT was performed to PWBS negative 14 patients. It was positive in 11 patients and negative in 3 patients. ^{18}F-FDG PET CT showed hypermetabolic lymph nodes in 10 patients and hypermetabolic recurrent thyroid tissue with hypermetabolic lymph node in one patient. These 11 patients were referred to surgery.

Twenty-nine patients (37.6 %) were retreated for distant metastasis. Sixteen patients had only lung metastasis, 7 patients had only bone metastasis, 4 patients had lung and bone metastasis, and 2 patients had lung, bone and soft tissue metastasis.

Four patients (5.2 %) were treated again for recurrence identified on the follow-up. These patients had stimulated Tg levels under 2 ng/ml and negative DWBS 6 months after first RIT. On the follow-up, rising of Tg levels were detected and this situation was considered as recurrence. Lymph node metastases were detected in all patients. The distribution of retreatment indications was given in figure 1.

Discussion

Radioiodine was firstly used for the treatment of thyroid cancer in 1946 by Seidlin et al (7). Radioiodine is taken up and concentrated in thyroid follicular cells with a membrane sodium-iodide transporter. The sodium-iodide symporter (NIS) is also found in several other

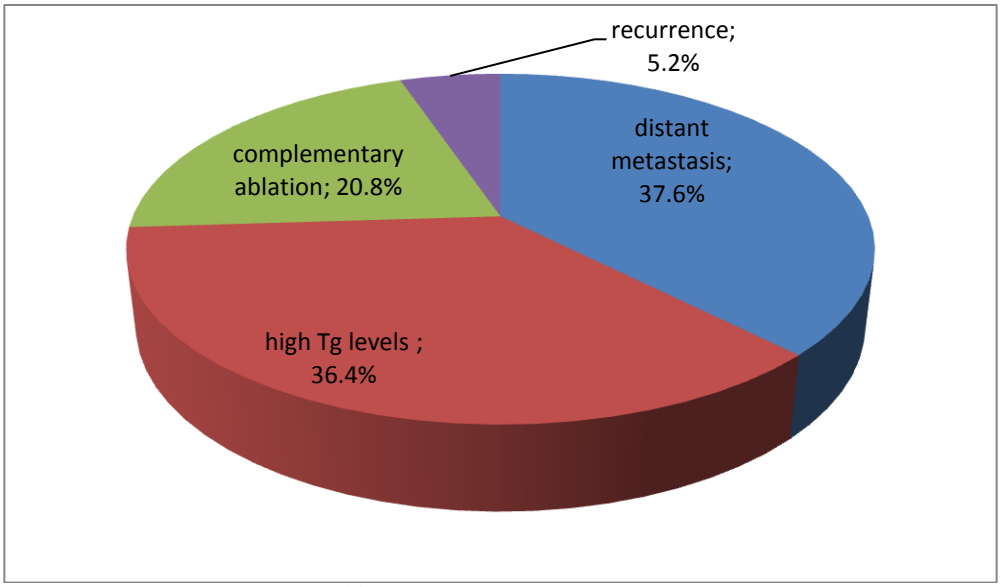

Figure 1. The distribution of retreatment indications.

tissues that capture iodine such as the stomach, salivary glands, lactating breasts, nasal mucosa, lacrimal glands, and placenta (8).

Remnant ablation has an important role in the treatment protocol of DTC. It is related with lower recurrence rates, lower rates of distant metastasis, and reduced cancer mortality rates (9, 10). Chow et al. (10) reported that recurrence rate was 20.9 % in patients without RIT after surgery and 9.2% in patients treated with radioiodine after 15 years follow-up. There are several reasons for routine postsurgical remnant ablation (11). Radioiodine can destroy remaining normal thyroid tissue and microscopic deposits of carcinoma, thus Tg can be use as an important tumor marker on the follow-up of DTC patients. Also possible tumor foci outside the thyroid bed may be detected and treated with remnant ablation (12) Success rate of radioiodine treatment for the remnant ablation is high. Many researchers reported the succes of ablation rate as approximately 80% (13, 14). Verburg et al (15) reported that patients with successful ablation had a better prognosis than patients with unsuccessful ablation. They found that 87% of the patients with a successful ablation were still free of the disease after 10 years, whereas only 50% of the patients with an unsuccessful ablation were free of disease. Some factors can influence the success of ablation. These factors include Tg levels at time of ablation, presence of pathological lymph nodes and distant metastasis (15). Several studies including us, have reported that high Tg levels at the time of ablation can be related to initial metastasis (16-18). According to our experience the size of the postsurgical remnant and the preparation of patient before radioiodine treatment are the other factors that effecting the success of RIT. Ablation success is evaluated 6–12 months after AIT. Negative DWBS, absence of detectable stimulated Tg with negative anti-Tg antibodies and negative findings on neck ultrasonography are associated with successful ablation (19). Detectable or elevated Tg levels are associated with persistent disease (20, 21). Tg level after treatment of DTC above 10 ng/ml is considered pathologic by many investigators because such levels are highly predictive of residual or recurrent disease (22). Empiric ^{131}I treatment (EIT) is an important choice in these patients.

Radioiodine is also used for treatment of DTC patients with distant metastasis. Treatment of metastatic lesions is difficult. The patients with inoperable iodine-avid distant metastasis are typically treated with multiple administrations of ^{131}I (23, 24). The results of RIT are superior for microscopic or small macroscopic tumors than for larger lesions (25). Also lung metastasis responds to RIT better than bone metastasis.

Lifelong follow-up is needed in all DTC patients. Because the lifetime recurrence rate is high, reaching to 10–30% (26). Subsequent therapies are needed for appreciable number of patients. In our clinic, we treated 77 of the 945 patients (8.1 %) more than one.

In conclusion, radioiodine is the main method for the treatment of DTC patients after surgery and its success rate is high. DTCs are not aggressive tumors and this situation plays an important role for this high success rates. However, in some cases, especially in metastatic patients, repeated treatments are needed. Also, resistance to treatment can be seen and carcinoma can be dedifferentiated. Besides all, radioiodine maintains the fundamental position for the treatment of DTC today.

References

1. Bal CS, Kumar A, Pant GS. Radioiodine dose for remnant ablation in differentiated thyroid carcinoma: a randomized

clinical trial in 509 patients. J Clin Endocrinol Metab. 2004;89(4):1666-73
2. Mazzaferri EL, Robyn J. Postsurgical management of differentiated thyroid carcinoma. Otolaryngol Clin North Am. 1996;29(4):637–62.
3. Robbins RJ, Schlumberger MJ. The evolving role of (131)I for the treatment of differentiated thyroid carcinoma. J Nucl Med. 2005;46(1):28-37.
4. MazzafeRri EL. Treating differentiated thyroid carcinoma: where do we draw the line? Mayo Clin Proc 1991;66(1):105-11.
5. Arslan N, Ilgan S, Serdengecti M, et al. Post-surgical ablation of thyroid remnants with high-dose (131)I in patients with differentiated thyroid carcinoma. Nucl Med Commun 2001;22(9):1021-27.
6. Logue JP, Tsang RW, Brierley JD, et al Radioiodine ablation of residual tissue in thyroid cancer: relationship between administered activity, neck uptake and outcome. Br J Radiol 1994 ;67(803):1127-31.
7. Seidlin SM, Marinelli LD, Oshry E. Radioactive iodine theraph. Effect on functioning metastases of adenocarcinoma of thyroid. J Am Med Assoc 1946;132(14):838-47.
8. Shen DHY, Kloos RT, Mazzaferri EL, et al. Sodium iodide symporter in health and disease. Thyroid 2001;11(5):415–25.
9. Simpson WJ, Panzarella T, Carruthers JS, et al. Papillary and follicular thyroid cancer: impact of treatment in 1578 patients. Int J Radiat Oncol Biol Phys 1998;14(6):1063–75.
10. Chow SM, Law SC, Mendenhall WM, et al. Papillary thyroid carcinoma: prognostic factors and the role of radioiodine and external radiotherapy. Int J Radiat Oncol Biol Phys. 2002;52(3):784-95.
11. Schlumberger MJ. Papillary and follicular thyroid carcinoma. N Engl J Med. 1998 Jan 29;338(5):297-306.
12. Sugg SL, Ezzat S, Rosen IB, et al. Distinct multiple RET/PTC gene rearrangements in multifocal papillary thyroid neoplasia. J Clin Endocrinol Metab 1998;83(11):4116–22.
13. Samuel AM, Rajshekarrao B. Radioiodine therapy for well-differentiated thyroid cancer: a quantitative dosimetric evaluation for remnant thyroid ablation after surgery. J Nucl Med 1994;35(12):1944–50.
14. Lin JD, Kao PF, Chao TC. The effect of radioactive iodine in thyroid remnant ablation and treatment of well differentiated thyroid carcinoma. Br J Radiol 1998;71(843):307–13.
15. Verburg FA, de Keizer B, Lips CJM, et al. Prognostic significance of successful ablation with radioiodine of differentiated thyroid cancer patients. Eur J Endocrinol. 2005;152(1):33-7.
16. Grunwald F, Menzel C, Fimmers R, et al. Prognostic value of thyroglobulin after thyroidectomy before ablative radioiodine therapy in thyroid cancer. J Nucl Med 1996;37(12):1962–64.
17. Ronga G, Filesi M, Ventroni G, et al. Value of the first serum thyroglobulin level after total thyroidectomy for the diagnosis of metastases from differentiated thyroid carcinoma. Eur J Nucl Med 1999;26(11):1448–52.
18. Kalender E, Celen YZ, Elboga U, et al. The relationship between thyroglobulin (Tg) levels and distant metastases before radioiodine (RAI) treatment in differentiated thyroid carcinomas. Gaziantep Med J 2012;18(1):11-3.
19. Pacini F, Ladenson PW, Schlumberger M, et al. Radioiodine ablation of thyroid remnants after preparation with recombinant human thyrotropin in differentiated thyroid carcinoma: results of an international, randomized, controlled study. J Clin Endocrinol Metab. 2006;91(3):926–32.
20. Schlumberger M, Baudin E. Serum thyroglobulin determination in the follow-up of patients with differentiated thyroid carcinoma. Eur J Endocrinol. 1998;138(3):249–52.
21. Pacini F. Follow-up of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging. 2002;29(2):492–6.
22. Ozata M, Suzuki S, Miyamoto T, et al. Serum thyroglobulin in the follow-up of patients with treated differentiated thyroid cancer. J Clin Endocrinol Metab.1994;79(1):98 –105.
23. Beierwaltes WH, Nishiyama RH, Thompson NW, et al. Survival time and "cure" in papillary and follicular thyroid carcinoma with distant metastases: statistics following University of Michigan therapy. J Nucl Med. 1982;23 (7):561–68.
24. Pacini F, Cetani F, Miccoli P, et al. Outcome of 309 patients with metastatic differentiated thyroid carcinoma treated with radioiodine. World J Surg. 1994;18(4):600–4.
25. Durante C, Haddy N, Baudin E, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. J Clin Endocrinol Metab. 2006;91(8):2892–9.
26. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. Am J Med. 1994;97(5):418–28.