Radioiodine Therapy in Patient with Differentiated Thyroid Cancer and End-Stage Renal Disease on Maintenance Hemodialysis: Case Report with Review of Literature

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Surgical resection followed by radioactive iodine (^{131}I) therapy constitutes a standard treatment for differentiated thyroid cancer. ^{131}I is normally excreted through the kidneys, and treatment of patients with end-stage renal disease on hemodialysis requires special attention to the dose of ^{131}I, the timing of dialysis, and radiation safety. We present a case of end-stage renal disease in a postthyroidectomy patient on hemodialysis who required radioactive iodine ablation, and we review the literature.

Key Words: radioiodine therapy; ESRD; thyroid cancer

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Thyroid carcinoma is the most common endocrine malignancy, and surgical resection followed by radioactive iodine (^{131}I) administration for ablation or therapy is a standard treatment for differentiated thyroid cancer (DTC) (*1*). ^{131}I is administered to a patient and absorbed by the thyroidal tissue, and most of the remaining circulating ^{131}I is cleared by the kidneys. The clearance of circulating ^{131}I is significantly reduced in patients with chronic kidney disease (CKD), resulting in a prolonged effective half-life and potentially resulting in an increased patient radiation exposure, particularly to the bone marrow (*2*). Clearance of ^{131}I in patients with CKD is achieved via dialysis, which can be either peritoneal dialysis or hemodialysis. But the use of dialysis in a patient administered ^{131}I poses various questions, such as those concerning the dose of ^{131}I, the timing of dialysis, and radiation safety precautions. The literature on the treatment of DTC with ^{131}I in patients with CKD consists of only a few case reports, with no formal guidelines. We present a review of the literature followed by a description of our case.

REVIEW OF LITERATURE

The incidence of cancers, including DTC, is relatively higher in patients with end-stage renal disease than in patients with normal renal function. A few of the postulated reasons are the increasing use of neck ultrasonography for parathyroid imaging, the higher prevalence of DTC in patients with high parathyroid hormone levels, and the higher survival rate of end-stage renal disease patients undergoing hemodialysis (*3–5*).

CKD causes prolonged excretion of ^{131}I, resulting in comparatively higher side effects such as sialadenitis, xerostomia, and marrow depression (*6*). Therefore, the hemodialysis session needs to be adjusted to ensure maximal thyroidal uptake and a minimal extrathyroidal concentration, thereby maximizing the therapeutic effect and minimizing the short- and long-term radiation effects.

DOSE OF ^{131}I

Two general approaches to determining the dose of ^{131}I in patients with thyroid cancer are either to give the empiric dose or to perform dosimetry. Individual dosimetry for calculation of the maximum tolerable dose of ^{131}I takes into consideration a patient's variables such as the volume of the thyroid remnant, metastases, renal dysfunction, TSH levels, and the dialysis schedule. But the process is cumbersome, and one needs to ensure that no changes in variables occur between dosimetry and therapy.

The American Thyroid Association guidelines recommend use of ^{131}I in patients with intermediate- and high-risk DTC with the intent of ablative treatment, adjuvant treatment, and treatment of metastatic disease (*7*). Howard et al. calculated that the effective half-life of ^{131}I was 4.5 times higher in patients on hemodialysis than in patients with normal renal function, and the investigators reduced the dose of ^{131}I (*8*). This finding was supported by other

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investigators too (*9–11*). However, some other investigators recommended increasing the ^{131}I dose, as they found faster clearance of ^{131}I in CKD patients during dialysis sessions and reduced effectiveness of a lower dose (*12,13*).

Another factor important for effective treatment with ^{131}I is the prior stimulation of thyroid cancer cells with raised levels of thyrotropin (thyroid-stimulating hormone [TSH]), which can be achieved either via withdrawal of thyroxine supplementation for 3–4 wk or via intramuscular injection of recombinant human TSH. Vermandel et al., in their study of 6 DTC patients with end-stage renal disease, gave a single 0.9-mg dose of recombinant human TSH 48 h before ^{131}I administration to avoid prolonged and excessive TSH levels instead of giving the standard 2 doses (*10*). Both thyroxine withdrawal and recombinant human TSH are efficient in increasing TSH levels in patients with end-stage renal disease and have no major side effects. Unfortunately, the data are insufficient to comment on whether one method is to be preferred over another.

DIALYSIS

Inorganic iodine is cleared via the kidneys, and in CKD, the ^{131}I excretion is further hampered by increased levels of stable iodine in the body. Clearance of ^{131}I is 4–5 times higher through hemodialysis than renally (*14*), making planning of the dialysis sessions crucial so as to allow ^{131}I to be present in a dose sufficient for it to have a therapeutic effect before it is removed by hemodialysis.

To avoid any emergency need for immediate hemodialysis between the planned timings and to achieve an optimum therapeutic effect for ^{131}I, patients should undergo dialysis immediately before the administration of ^{131}I.

The timing of dialysis after administration of ^{131}I differs in various case reports (Table 1). Ideally, after radioiodine administration, the first dialysis should be done after ^{131}I uptake maximizes in the remnant thyroid tissue or malignant cells. Patients on hemodialysis have shown 6% and 10% uptake of ^{131}I in the thyroid remnant at 24 and 48 h, respectively (*8*). Thus, waiting for 48 h before the first dialysis session seems appropriate, and dialysis before 48 h may lead to undertreatment. However, if the dose is kept the same or increased, the first dialysis session may begin early, which in most case reports is within 24 h after dose administration.

TOXICITY

Vermandel et al. retrospectively calculated the radiation dose to bone marrow in 6 postthyroidectomy patients with renal dysfunction, treated with ^{131}I. The mean estimated dose to the bone marrow was 0.992 Gy for all patients, with no significant hematologic toxicity seen in any of them (*10*). Mello et al. reported a fall in hemoglobin levels after a second treatment of 3,700 MBq (100 mCi) of radioiodine requiring a blood transfusion, though the duration for which the fall in hemoglobin level was seen after ^{131}I was not specified (*12*). Mild sialadenitis and bilateral neck pain below the ears has also been reported after ^{131}I treatment (*9,15*).

RADIATION SAFETY

Hemodialysis can be performed safely after radioiodine administration and should be done with appropriate shielding. In addition to the standard safety precautions that are followed after radioiodine therapy, additional measures were described by other authors, such as providing lead aprons to all personnel attending the patient, maintaining a distance of 2 m between technicians and patients, or having the dialysis technician sit outside the lead-shielded room with the door left ajar (*16,17*). Mello et al. used a lead shield between the patient and the dialysis technician; each member of the technical staff was changed after spending 2 h with the patient (*12*). None of the authors reported any significant exposure to the personnel or contamination of the dialysis machine or room.

Therefore, special precautions should include keeping an adequate distance and shielding between the patient and the technician, providing protective wear to the attending personnel, covering the room with absorbent sheets, and disposing of the dialysate directly into the sewer system. More than one technician and nurse may be used, to reduce the radiation exposure. After 3–4 such dialysis sessions after radioiodine administration, the patient can undergo dialysis in the usual manner.

CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD)

Experience with using CAPD in such a setting is even more limited. In CAPD, excretion of iodine is a slow, continuous process, at approximately one third the rate of normal renal excretion. Similar to hemodialysis, CAPD requires reduction of the dose of ^{131}I (*18*). Toubert et al. administered 814 MBq (22 mCi) of ^{131}I instead of the usual 3,700-MBq (100 mCi) dose in a patient with follicular thyroid carcinoma (*19*). Wang et al. recommended oral administration of ^{131}I after 1 session of CAPD followed by 3 more courses of CAPD, each performed at an interval of 6 h. The investigators even preferred CAPD to hemodialysis because of the ease with which radiation contamination of the environment could be prevented, as the collected dialysate could be allowed to decay (*20*).

CASE REPORT

The patient was a 35-y-old hypertensive man with CKD secondary to chronic tubulointerstitial nephritis. He had been on alternate-day hemodialysis for the past year and had presented with left-sided neck swelling 6 mo previously. Neck ultrasonography revealed a small, 9 × 7 mm, hypoechoic nodule with microcalcifications in the left lobe of the thyroid gland and multiple enlarged level III and IV cervical lymph nodes on the left side. After inconclusive cytology results for the thyroid nodule, a biopsy sample

TABLE 1
Summary of Literature on Hemodialysis in Patients with CKD After Radioiodine Therapy (n = 23)

Study	Age (y)	Cancer	Dose (mCi)*	Time of dialysis	Conclusion of studies
Vermandel (*10*)	67	PTC	60	42, 90 h	Use 30% reduction in dose for ablative and adjuvant treatments; for metastatic disease, dosimetry should be done; first dialysis 42 h after dose
	47	PTC	77, 82		
	63	PTC	61		
	63	PTC	50		
	29	PTC	60		
	71	VC	101		
Daumerie (*11*)	42	PTC	25 in 2 sessions 6 mo apart	2, 5, 7 d	Administer 25% of prescribed activity; first dialysis 24 h after dose
	62	PTC			
	27	PTC			
Jiménez (*16*)	42	PTC	75	Daily for 5 d	Use dosimetry to determine dose; dialysis every day for 5 d
	51	PTC	87		
	34	PTC	120		
Holst (*9*)	40	PTC	98	2, 3, 4 d	Use 21%–28% of dose; dialysis at days 2 and 4
Mello (*12*)	42	PTC	100	41, 98 h	Use dosimetry to determine dose
Sinsakul (*17*)	43	PTC	100	20 or 24 h	Perform dialysis 2–24 h after dose
	56	PTC	157		
Culpepper (*14*)	56	FTC	129	24, 43, 66 h	None
Howard (*8*)	34	PTC	80	—	Administer 22% of empiric dose; dialysis 48 h after dose
Morrish (*13*)	36	PTC	50, 120, 150, 250 over 4 y	24–48 h	Use significantly larger ^{131}I dose; first dialysis 48 h after dose
Magne (*21*)	43	PTC	50	1, 3, 6 d	Increase dose up to 25%
Gallegos-Villalobos (*22*)	51	PTC	100	1, 2 d; administer same dose with normal renal function	Administer same dose with normal renal function; use 2 subsequent dialysis sessions daily
	52	PTC	100		
Bhat (*23*)	49	PTC	50	15, 27, 43 h	None

*1 mCi = 37 MBq.
PTC = papillary thyroid carcinoma; VC = vesicular carcinoma; FTC = follicular thyroid carcinoma.

from the left cervical lymph node revealed metastatic papillary carcinoma of the thyroid. Within 1 mo, he underwent total thyroidectomy with central and lateral neck dissection. Histopathologic examination revealed a multifocal papillary carcinoma of the thyroid (maximum tumor dimension, ~2.3 cm), with lymphovascular invasion and without extrathyroidal extension. Twenty-six of the 42 lymph nodes dissected were positive for metastatic disease (T2 N2b Mx), putting him in an intermediate risk category according to the American Thyroid Association (*7*).

For preparation, the patient was asked to withhold the thyroxine supplementation for 4 wk. His TSH level rose to 50 μIU/mL, and his stimulated thyroglobulin level was 132 ng/mL, with normal antithyroglobulin levels. A low-dose whole-body ^{131}I scan done with 44.4 MBq (1.2 mCi) showed that the thyroid bed tracer uptake was likely a thyroid remnant (Supplemental Fig. 1; supplemental materials are available at http://jnmt.snmjournals.org).

A patient with normal renal function in an intermediate risk category would have received a dose of 3,700 MBq (100 mCi) of ^{131}I for ablation of the thyroid remnant and as adjuvant treatment. For our patient, after a literature review and a discussion by the tumor board, the dose of ^{131}I was reduced to 50% (1,850 MBq [50 mCi]) to maximize the effect and reduce the radiation exposure to normal tissues.

On the day of therapy, the patient underwent dialysis in the morning and received a ^{131}I dose of 1,850 MBq (50 mCi) after 2 h (day 0). This was followed by dialysis at 48, 72, and 96 h. The whole-body radioactivity was measured at the stomach level with the patient standing, using an ionization chamber-based gun monitor (Ram Ion; Rotem Industries) at a distance of 1 m. The whole-body radioactivity was measured at various time intervals and after each session of dialysis (Supplemental Fig. 2). A reduction in whole-body radioactivity by 69% was achieved after the first dialysis session. The findings were consistent with the literature, which showed clearance in the range of 50%–80% (*9,16*).

A posttherapy whole-body iodine scan after 5 d showed tracer uptake in the thyroid bed region—the same region as seen on the low-dose diagnostic scan. The patient was discharged 4 d after radioiodine administration, with an exposure rate of about 3 μSv/h measured at the stomach level at a distance of 1 m. The patient remained asymptomatic on follow-up; at 6 wk after ^{131}I therapy, there was no change from baseline in his white blood cell count (5,300 vs. 5,240 cells/mm^3) or hemoglobin level (8.2 vs. 8.4 g/dL).

Under the supervision of a radiation safety officer, the patient underwent dialysis in the nephrology department at the end of the day when there were no other patients in the room, because our hospital did not have a portable dialysis facility or a separate dialysis room with shielding. (Under normal conditions, more than 4 patients at a time undergo dialysis in the same room.) Care was taken to avoid any blood or fluid spills and contamination. The floor near the patient bed was covered with absorbent sheets. During the 4-h hemodialysis procedure, the technician wore all the necessary protective clothing (shoe covers, gloves, face mask, and lead apron). All personnel attending the patient, including the dialysis technician, were given a pocket dosimeter (Rad-60S; Rados; Mirion Technology) for real-time monitoring of the exposure rate. The dialyzer, blood lines, absorbent sheets, and linen used during the procedure were collected in polyethylene sheets and allowed to decay in the radioactive waste storage room of the isolated ^{131}I therapy ward. The dialysate drain line was connected to the sewer system. After the dialysis, the hemodialysis machine was put on rinsing mode to eliminate any ^{131}I contamination, though no contamination was observed in the hemodialysis machine when checked with a Geiger–Müller counter (Ram Gene-1; Rotem Industries). The total dose received by the patient's attendant and dialysis technician was 37 and 16 μSv, respectively—far below the permissible levels.

The patient showed a decline in stimulated serum thyroglobulin level to 5 ng/mL, with a TSH level of 60 μIU/mL, after 6 mo of follow-up. The low-dose ^{131}I scan showed resolution of the previous tracer uptake in the thyroid bed (Supplemental Fig. 3), and the patient was followed on suppressive thyroxine doses, with a target TSH level of 0.1–0.5 IU/mL.

CONCLUSION

Treatment of thyroid cancer with radioiodine therapy in patients with renal dysfunction on maintenance hemodialysis can be performed safely by following a standardized radiation safety protocol and with the combined efforts and coordination of the nuclear medicine physician, nephrologist, radiation safety officer, and dialysis team. The literature on the treatment of DTC with ^{131}I in patients with CKD consists of only a few case reports with variable experiences and recommendations. Therefore, more literature and systematic prospective studies are required to formulate standard procedure guidelines.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: What parameters can be suggested for dose requirements, timing of dialysis, and special radiation safety protocols in CKD patients requiring radioactive iodine?

PERTINENT FINDINGS: A multidisciplinary approach involving the endocrinologist, nuclear medicine physician, nephrologist, radiation safety team, and dialysis team is required for management of these cases.

IMPLICATIONS FOR PATIENT CARE: Fifty percent of an empiric ^{131}I dose followed by dialysis at 48, 72, and 96 h was used in our intermediate-risk DTC patient on maintenance hemodialysis.

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