Comparison of 1073 MBq and 3700 MBq Iodine-131 in Postoperative Ablation of Residual Thyroid Tissue in Patients with Differentiated Thyroid Cancer

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In a randomized prospective study, we compared the efficacy of low dose (1073 MBq) and high dose (3700 MBq) iodine-131 administration in postoperative ablation of residual functioning thyroid tissue in 63 patients with differentiated thyroid cancer. We were unable to demonstrate any difference between the low- and the high-dose of radioactive iodine in scintigraphic ablation of remnant tissue. In 81% (21/26) of the patients, 1073 MBq ablated after the first dose, 77% (21/26 + 3/5 = 24/31) after the first plus second dose, and 69% (24/31 + 0/4 = 24/35) after the first, second, and third dose. Radioiodine (3700 MBq) ablated in 84%, 73%, and 69% of the patients after respectively 1., 1. plus 2., and 1. plus 2. plus 3. dose. Forty percent of the patients ablated with the low dose and 44% ablated with the high dose had elevated thyroglobulin levels at the time of complete scintigraphic ablation. In conclusion, we did not find any difference between 3700 MBq and 1073 MBq iodine-131 as regard to number of doses needed for complete scintigraphic ablation of residual functioning thyroid tissue.

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Well-differentiated thyroid tumors generally run a very indolent course. Until 1986, only 56 (6.5%) of the 859 patients followed at the Mayo Clinic from 1946 through 1970 have died as a result of papillary thyroid cancer. In this study in which 84% of the patients had less than total thyroidectomy and only 3% had radioiodine ablation, the overall excess mortality was only 3% (*1*). There is no consensus of opinion on whether iodine-131 (^{131}I) given postoperatively is of any benefit. No evidence can be found in the literature that conclusively states that prophylactic radioiodine therapy improves survival, especially in patients less than 40 yr of age (*1-5*). Despite the controversies, many centers advocate ablation of residual functioning thyroid tissue with radioiodine after thyroid surgery followed by thyroid-stimulating hormone (TSH) suppression with thyroxine (*6-10*). There is a wide variation in the radioiodine dose different centers employ varying from 1110 MBq (3,11,12) to 7400 MBq (*13*).

It always seems desirable to give the smallest effective dose of radioiodine as possible to human beings. Low-dose (1110 MBq) radioiodine therapy was originally advocated by McCowen et al. (*14*). They compared this dose with higher doses (2960-5550 MBq) and concluded that the lower dose was nearly equivalent in achieving ablation. They successfully ablated 58% with differentiated thyroid carcinoma with the low dose and 64% with the higher doses. Several other groups (*3,11, 12,14-16*) repeated McCowen et al.'s study in small groups of patients in either retrospective, uncontrolled or non-randomized studies and with different results.

In a randomized prospective recent study of a small group of 20 patients with differentiated thyroid cancer, Creutzig (*17*) did not find any significant difference in the effectiveness between a 1073- and 3700-MBq radioiodine dose.

In the present randomized study, we prospectively compared the efficacy of 1073 MBq and 3700 MBq in scintigraphic ablation of residual functioning thyroid tissue after total or subtotal thyroidectomy in 63 patients with differentiated thyroid cancer and no palpable neck swelling or distant metastases.

PATIENTS AND METHODS

Seventy-five patients with well-differentiated thyroid cancer were randomly selected to receive either 1073 MBq or 3700 MBq ^{131}I for scintigraphic ablation of residual functioning thyroid tissue 1.5 mo (median) after total or subtotal thyroidectomy. Twelve patients were excluded from the study because they developed palpable disease or metastases or became pregnant. We were thus left with 63 patients for the study. If the first postablation thyroid scan of patients who had had a total thyroidectomy showed a substantial uptake in the thyroid bed, they were classified as having had a subtotal thyroidec-

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tomy. It was recorded, based on histology, if the patients had local neck lymph nodes, capsular, and vascular invasion at the time of surgery.

Table 1 gives the clinical characteristics of the patients in the two groups. A family history refers to the presence of neck swelling or thyroid surgery in a close relative.

Patients who had not stopped thyroxine treatment or who were not hypothyroid following surgery were stimulated with TSH 10 units daily for 3 days intramuscularly before radioactive iodine was given. 46% of the patients in the 1073 MBq group and 39% in the 3700 MBq group who were ablated with three doses or less received TSH injections. The patients were not placed on a low-iodine diet before ablation therapy. Patients were given a therapeutic ablation dose of radioactive iodine (1073 or 3700 MBq) every 3–4 mo until there was no pathologic radioiodine uptake seen after 24 hr (1073 MBq) or 72 h (3700 MBq) on the neck and whole-body scan. Thyroid scanning was performed using a pinhole collimator gamma camera. Whole-body scan was performed with a flat-field collimator gamma camera (General Electric, camera system, Milwaukee, WI).

Thyroglobulin was measured in the hypothyroid state using a thyroglobulin-Tg kit (Behringwerke, Marburg, West Germany). Lower detection level is 5 μg/l). Undetectable thyroglobulin concentrations were recorded as 5 μg/l. Interassay coefficient of variation was 15% at thyroglobulin levels of 10 μg/l, 10% at 50 μg/l, and 15% at 100 μg/l.

Medians and 95% confidence limits were calculated by standard procedures and Fisher's exact test was used to compare frequences.

RESULTS

Table 1 reveals that the clinical characteristics of the patients in the group receiving a low (1073 MBq) and a high (3700 MBq) ^{131}I dose were very similar.

In this randomized prospective study of the efficacy of 1073 and 3700 MBq ^{131}I in scintigraphic ablation of residual thyroid tissue in patients with residual thyroid tissue were unable to demonstrate any difference between the two doses.

Table 2 shows that the number of patients who were scintigraphically ablated after 1 dose with 1073 MBq was 81%, after 1. plus 2. dose 77%, and after 1. plus 2. plus 3. dose 69%. The frequency of ablation after 3700 MBq after 1. dose was 84%, after 1. plus 2. dose 73%, and after 1. plus 2. plus 3. dose 69%. One patient in the 1073 MBq group required five doses for complete ablation and one patient in the 3700 MBq group received four doses but was not ablated by this dose.

Fifteen of the 26 (60%) who were ablated with 1073 MBq had undetectable thyroglobulin concentrations (i.e., <5 μg/l) and 10 of the 18 (56%) ablated with complete ablation had undetectable thyroglobulin. In the ablated subjects with elevated thyroglobulin, the elevated thyroglobulin concentrations in the two groups were not statistically significant.

The number of total thyroidectomies was not different in the high and the low iodine-dose groups ($p = 0.26$). The percentage of patients who were ablated with 1 or 2 doses of ^{131}I for total ablation was 81% in the total thyroidectomy group and 69% in the subtotal thyroidectomy group ($p = 0.47$).

DISCUSSION

In this prospective randomized study, we compared the effectiveness of a low-dose (1073 MBq) versus a high-dose (3700 MBq) of radioiodine in scintigraphic ablation of remnant thyroid tissue in patients with differentiated thyroid cancer. We found no significant difference in the number of doses required to achieve ablation in the two groups. Similar results from a prospective study have recently been reported by Creutzig (*17*) in a much smaller group of patients with less "severe" disease. our patients have larger tumours, more nodal metastases, and more local invasion than is usually reported in Western series (*1,17,18*). The efficacy of a dose of radioiodine will obviously depend on the severity of initial disease and amount of residual thyroid tissue left after the surgery.

TABLE 1
Clinical Data

RAI dose (MBq)	N	Age (yr)	Sex (F/M)	Family* history	Duration of symptoms (yr)	Tumor size (CM2)	Lymph nodes (Y/N)	Total thyroid-ectomy (Y/N)	Capsular/ angio invasion (Y/N)
1073	36	42† (35–49)	29/7	4/32	1.5 (0.5–3)	12.2 (6–16)	14/22	15/21	10/26
3700	27	40 (29–49)	23/4	4/23	2.0 (1–5)	12.1 (9–24)	11/16	13/14	6/21
Total	63	41 (35–46)	52/11	8/55	2.0 (1–3)	(11–16)	25/38	28/25	16/47

* Neck swelling or thyroid surgery.
† Median and 95% confidence limits.

TABLE 2
Ablation Data

RAI dose (MBq)	Ablated after Doses		
	1. dose	1. + 2. dose	1. + 2. + 3. dose
1073	21/26 (81%; 61–93)*	21/26 + 3/5 = 24/31 (77%; 59–90)	24/31 + 0/4 = 24/35 (69%; 51–83)
3700	14/17 (84%; 57–96)	14/17 + 2/5 = 16/22 (73%; 50–89)	16/22 + 2/4 = 18/26 (69%; 48–86)

* Median and 95% confidence limits.

Despite the experience of the Mayo Clinic (*1*) and despite the lack of evidence in the literature that convincingly shows that radioiodine adds any further advantage in the treatment of non-metastasing differentiated thyroid cancer, several groups have consistently advocated high dose radioiodine treatment post-thyroidectomy (*6,8,9*).

Like Beierwaltes et al. (*6*) we found that 3700 MBq ablated 84% in the first attempt. We also showed that 1073 MBq was as effective as 3700 MBq in ablating residual thyroid tissue since 81% were ablated by the first dose. The number of patients who had no residual disease using thyroglobulin as a marker was also the same in the two groups. Sixty percent of the patients had undetectable thyroglobulin levels after total ablation with the low and 56% after the high dose radioiodine. The therapeutic possibilities in patients with elevated thyroglobulin concentrations and negative scan are either surgical removal of residual tissue, external radiation, or suppression with thyroxine.

Proponents of the use of high doses of radioiodine argue that low doses are less effective and will reduce the uptake function but will not impair the growth of the neoplasm thereby reducing the effect of subsequent treatment with ^{131}I. This proposition is unproven.

The value of postsurgical ablative therapy in diminishing morbidity and mortality in patients with differentiated thyroid cancer has not yet been established. We can therefore advocate a conservative and economic approach to thyroid ablation (i.e., use of 1073 MBq for the first attempt of ablating residual functioning thyroid tissue). Higher doses should be reserved for cases where the low dose is not followed by total scintigraphic ablation in the first attempt, and for treatment of functioning distant metastases.

REFERENCES

1. McConahey WM, Hay ID, Woolner LB, van Heerden JA, Taylor WF. Papillary thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. *Mayo Clin Proc* 1986;61: 978–996.
2. Crile G Jr. Endocrine dependence of papillary carcinoma of the thyroid. *JAMA* 1966;195:721–724.
3. Snyder J, Gorman C, Scanlon P. Thyroid remnant ablation: questionable pursuit of an ill-defined goal. *J Nucl Med* 1983;24:659–665.
4. Goolden AWG. The indications for ablating normal thyroid tissue with ^{131}I in differentiated thyroid cancer. *Clin Endocrinol* 1985;23:81–86.
5. Bell RM. Thyroid carcinoma. *Surg Clin NA* 1986;66:13–33.
6. Beierwaltes WH, Rabbani R, Dmuchowski C, Lloyd RV, Eyre P, Malette S. An analyses of "ablation of thyroid remnants" with I-131 in 511 patients from 1947–1984: experience at University of Michigan. *J Nucl Med* 1984;25:1287–1293.
7. Sisson JC. Medical treatment of benign and malignant thyroid tumours. *Endocrinol Metab Clin North Am* 1989;18:359–387.
8. Mazzaferri EL, Young RL. Papillary thyroid carcinoma: a 10-year follow-up report of the impact of therapy in 576 patients. *Am J Med* 1981;70:511–518.
9. Simpson WJ, Panzarella T, Carruthers JS, Gospodarowicz, Sutcliffe SB. Papillary and follicular thyroid cancer: impact of treatment in 1578 patients. *Int J Radiat Oncol* 1988; 14:1063–1075.
10. Samaan NA, Maheshwari YK, Nader S, et al. Impact of therapy for differentiated carcinoma of the thyroid: an analysis of 706 cases. *J Clin Endocrinol Metab* 1983;56:1131–1138.
11. DeGroot LJ, Reilly M. Comparison of 30- and 50-mCi doses of iodine-131 for thyroid ablation. *Ann Intern Med* 1982; 96:51–53.
12. Ramacciotti C, Pretorius HT, Line BR, Goldman JM, Robbins J. Ablation of nonmalignant thyroid remnants with low doses of radioactive iodine: concise communication. *J Nucl Med* 1982;23:483–489.
13. Beierwaltes WH. Radioiodine therapy of thyroid disease. *Nucl Med Biol* 1987;14:177–181.
14. McCowen KD, Adler RA, Ghaed N, Verdon T, Hofeldt FD. Low dose radioiodine thyroid ablation in post surgical patients with thyroid cancer. *Am J Med* 1976;61:52–58.
15. Kuni CC, Klingensmith WC. Failure of low doses of ^{131}I to ablate residual thyroid tissue following surgery for thyroid cancer. *Radiology* 1980;137:773–774.
16. Siddiqui AR, Edmonson J, Wellman HN, et al. Feasability of low doses of I-131 for thyroid ablation in postsurgical patients with thyroid carcinoma. *Clin Nucl Med* 1981;6:158–161.
17. Creutzig H. High- or low-dose radioiodine ablation of thyroid remnants. *Eur J Nucl Med* 1987;12:500–502.
18. Simpson WJ, McLinney SE, Carruthers JS, Gospodarowicz, Sutcliffe SB, Panzarella T. Papillary and follicular thyroid cancer. *Am J Med* 1987;83:479–488.