RADIOIODINE THERAPY IN THYROID CARCINOMA AT RANGPUR,BANGLADESH

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ABSTRACT

OBJECTIVE : To show the usefulness and success of small doses of radioiodine I^{131} in the treatment of well-differentiated thyroid carcinoma.

MATERIALS & METHODS : Since 1990,in the small town Rangpur in North-west Bangladesh we are using radioactive iodine uptake (RAIU),isotope scanning (I^{131} and Tc-99m) and ultrasonography of thyroid nodules.In 1998,we started radioassay of thyroid hormones (T3 & T4) and thyrotropin (TSH). About 6500 patients were tested for suspected thyroid problems. We have given post - thyroidectmy radioiodine therapy using small doses (Table 1) to six patients (M3,F3) with clinical improvements in the follow - ups.

RESULTS: Initial results are encouraging as shown in Table 1.

CONCLUSION : We feel broad-based long-term study should be done to optimize the dose schedule of radioiodine therapy.

Key words : Radioiodine therapy,thyroid carcinoma.

INTRODUCTION

In the general population one expects to encounter one case of thyroid cancer for each 27000 individuals examined.[1] The commonest presenting feature of papillary and follicular thyroid carcinomas is an asymptomatic neck mass.Rarely skeletal or pulmonary metastases are presenting signs.Thyroid nodules are extremely common,found at palpation in 4% to 7% of an asymptomatic population,[2] in 17% to 27% of cases at sonography,[3-5] and in 50% of cases at autopsy.[6] Although most thyroid nodules are benign ,approximately 4% to 14% are malignant.[2,7-9] As an aid in determining which thyroid nodules are more likely to be cancerous,physicians have been using the functional information provided by I^{131} uptake of thyroid for more than six decades. Initially these thyroid nodules were evaluated using point-by-point counting of radioiodine distribution using collimated Geiger-Mueller(G-M) detectors. In the early 1950's the motor-driven scintillation probe with focused collimater that traversed the neck in a rectilinear fashion (scanner) was introduced. More recently,the I^{131} has been replaced by I^{123} in many countries which provides similar clinical information but delivers a much lower radiation dose to the patient.In addition the scintillation camera fitted with a pinhole collimator has largely replaced the rectilinear scan for thyroid imaging.Tc-99m pertechnetate is quite suitable for thyroid imaging but cannot provide functional information on thyroid nodules as can I^{123},but it is not yet available in Bangladesh.Several gray scale

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sonographic characteristics have been found to be highly suggestive of thyroid cancer,including microcalcifications and irregular margins,[10] but the role of color Doppler sonography in the evaluation of a thyroid nodule for malignancy has not been defined.Several reports have described no correlation between the presence of flow on color Doppler sonography and malignancy,particularly when color flow is considered as an isolated criterion.[10,11]Others have suggested that a pattern of either spotty intranodular flow[11] or hypervascular central flow [8, 12-14] on color Doppler sonography may be associated with malignancy.Frates and colleagues suggest to use color Doppler sonography in multi- nodular goitre to guide fine needle aspiration (FNA)from type 4 vascularity in a solid nodule (extensive internal flow with or without a peripheral-ring). However,the color Doppler characteristics of a thyroid nodule cannot be used to predict or exclude malignancy confidently.[15] The uses of radionuclide study (NaI^{123} or Tc^{99m} pertechnetate) in thyroid nodules suggestive of follicular neoplasms. At cytologic examination, the nodules showing uptake of radioisotope are considered to represent functioning follicular adenomas and are categorized as benign.When a thyroid malignancy is detected,the initial treatment is thyroidectomy (total or near-total). In well-differentiated thyroid cancer (DTC), radioiodine I^{131} is given to post-thyroidectomy patients for ablation of the thyroid remnants, so that occult metastasis is detected in the whole body gamma scan.Thyroid metastasis can also be ablated by radioiodine if it is iodophile in nature i.e.concentrates radioiodine.[16] In the Institute of Nuclear Medicine (Dhaka),725 patients were treated with radioiodine for DTC,amongst them one patient developed poorly differentiated mucoepidermoid carcinoma of the right parotid gland after 15 years of mixed papillary -folicular carcinoma of thyroid treated with total thyroidectomy,block dissection of lymph nodes and radioiodine therapy (80 mCi in 1987,92 mCi in 1992,200 mCi in 1996).[17] Another patient died 24 hours after a second doses of radioiodine (200 mCi) due to laryngeal stridor.[18] The optimum doses of radioiodine is controversial,and we like to focus our initial experiences of small doses.

TABLE 1 : Radioiodine therapy in thyroid carcinoma

Sex	Age (Years)	Type of carcinoma	I-131 (mCi)	Date	T3 (nmol/L)	T4 (nmol/L)	TSH (mIU/L)	Dose of thyroxin (mcg/day)
F	60	Papillary	24	19 Nov.96	2.3	87	1.45	100
M	68	Follicular	21	Nov.99-Dec.2000	2.15	77	7.75	100-150
			75	8 Jan.2001	Follow-ups in 2002 & 2003 (March/03)			
M	40	Follicular	13	4 Dec.2000	2.2	86	5.25	100
			75	8 Jan.2001	Follow-ups in 2002 & 2003 (March/03)			
M	25	Papillary	18	29 May 2001	2.7	59	0.1	100
			11	9 Aug 2001	Follow-ups on 19 Sep. & 10 Dec.2001			
F	55	Follicular variant of papillary	16	6 Aug 2001	2.2	124	3.5	50-100
			75	23 Aug 2001				
F	40	Struma ovarii (10cm pelvic mass operated)	34	31 Mar.-11 April/2002	0.1	121	0.75	
			Whole-body scans upto 9 May 2002 show tumor is shrinking and the patient is improving gradually.					

TABLE 2 : Potential complications of Radioiodine Therapy

A. Short-Term

Transient sialoadenitis and xerostomia (patients may chew gum or suck citrus sweets)[34]
Radiation gastritis
Acute radiation sickness (nausea in the first 48h,treated with anti-emetics)
Vocal cord paralysis
Transient bone marrow depression (patients of West African and West Indian background)[34]
Pain,edema and hemorrhage in metastases
Thyroid storm (thyrotoxic crisis)
Nasal pain and epistaxis
Transient impairment of testicular function[35]

B.Long-Term

Leukemia/(Total does over 1 Ci with intervals of less than 6m between treatments)[30,36]
(?)Anaplastic transformation (4 of 46 patients)[37]
Radiation pneumonitis or pulmonary fibrosis (cumulative doses over 1.5 Ci)[38]
Hyperparathyroidism
Bladder cancer (cumulative dose over 1 Ci)[30]
Permanent sterility[39]

CASE REPORTS

Case 1:

A lady aged 60 years received 24 mCi of I^{131} on 19-11-96 after near-total thyroidectomy for papillary carcinoma of thyroid.She was isolated in a cabin for one week,but no untoward side-effect was found and then she was released with a prescription of thyroxine tablets 100 micrograms/day and advised to come after 1 month for follow-up.She attended our centre on 31-12-96,17-02-97 and 23-07-97 when no thyroid-related problem was found.On 26-10-98 she was seen last when she was taking 150 microgram of thyroxine daily.She is on longterm follow up now.

Case 2:

A man of age 66 years with long-standing nontoxic multinodular goitre presented with a bony swelling on right shoulder and mild thyrotoxicosis in November/1999.Biopsy revealed follicular carcinoma of thyroid metastasized to skeletal system.Bone scan (99m Tc MDP) on 25-11-99 at Institute of Nuclear Medicine (Dhaka) revealed multiple bony metastases to left 9th and 10th ribs and right scapula.He had a near-total thyroidectomy on 18-12-99. Due to scarcity of radioisotope in the country,we gave him only 8 mCi of I^{131} on 11-1-2000 which was taken up avidly in the thyroid remnant and each of the bony metastases mentioned above.He experienced mild degree of sialadenitis after radioiodine therapy,however,it was self-limited.He is clinically euthyroid on 20-03-2000,and 23-04-2000,when he received 6 mCi of I^{131}.He is euthyroid on 3-7-2000 and on 24-03-2003.

Case 3:

A man of age 40 years came to our centre on 4 December/2000 (end of Ramzan fasting) with a post-thyroidectomy scar and a biopsy report of follicular carcinoma.His operation site was healing slowly and he went to Dhaka,but he came back to Rangpur with an advice to attend our centre. His general condition was poor-he could not sit even.We gave him 13 mCi of I^{131} and advised to follow after

the Eid holiday.He came with surprising improvements and took 75 mCi capsule on 8 January/2001.He is on thyroxine 100 micrograms/day and is now free from thyroid carcinoma as confirmed by whole body scans on March/2002 and March/2003.

Case 4:

A man of age 25 years with papillary carcinoma of thyroid had total thyroidectomy and was given 18 mCi of I^{131} on 29 May/2001. He was improved and received 11 mCi as the second dose of I^{131} on 9 August/2001. He was taking thyroxine 100 micrograms/day and was well clinically.Whole body scans were normal on 19 September and 10 December/2001

Case 5:

A woman of 55 years had total thyroidectomy for follicular variant of papillary carcinoma.She was given 16 mCi of I^{131} on 6 August/2001.She got 75 mCi on 23 August/2001.She is taking thyroxine 50-100 microgram/day and is well on March/2003.

Case 6:

A woman of age 40 years came with abdomino-pelvic lump (10 cm dia.) which was operated.Biopsy revealed a case of struma ovarii.She was given 34 mCi of I^{131} in divided doses from 31 March to 11 April/2002.She was improving gradually as shown by whole body scans upto 9 May/2002.

Long-term follow-ups are being done in all the six cases.

DISCUSSION

No serious complication was seen following radioiodine I^{131} therapy of thyroid carcinoma except mild sialadenitis in one patient which was self-limited (Table 2).Acute inflammation of the salivary glands (sialadenitis) develops in 10% of the patients treated with I^{131} for thyroid cancer.[19] Rarely,hyperthyroidism and thyroid cancer co-exist as in one of our follicular cancer patient-one study reported 9 thyroid cancer in 720 patients with hyperthyroidism.[20]

In post-surgical follow-up of well -differentiated thyroid cancer,the patient is given high dose radioiodine ablation therapy and thyroxine tablets to suppress thyrotropin (TSH) stimulation.Thyroid cancer patients should have whole body scan annually to check recurrence and/or distant metastasis, (which may also be ablated by I^{131} therapy), until there is no detectable tumor or metastatic uptake for two consecutive years.

Thyroid cancer patients are isolated for I^{131} therapy to avoid undue gamma radiation to the neighbours.However,the detailed regulations vary from country to country, e.g. the maximum dose allowed as outdoor patient is 5 mCi in some of the European countries,19 mCi in U.K.,but 29.9 mCi in U.S.A..Johansen at al[21] showed that 29 mCi was as effective as 100 mCi in ablating residual thyroid tissue since 81% were ablated by the first dose.Whole-body scan following high-dose I^{131} therapy provides improved detection of local and distant metastases as compared to low-dose diagnostic studies,[22,23] but a false-positive result may be found rarely.[24] Grigsby[25] showed that only 10% (6 of 63) of patients had additional information in post-treatment total body I^{131} scans.Arad et al.[26,27] and Rudavsky et al.[28] used 2 or 3 outpatient doses of 20 to 55 mCi each 48 hours or 1week apart which can reduce cost and patient inconvenience.Massino et al.[29] gave low dose of I^{131} (10-50mCi) often repeated and increased later in children and adolescent patients of thyroid cancer.Edmonds and Smith reported that risk of bladder cancer and possibly leukemia (3 cases each in a group of 258)are increased,particularly when many treatments are given with initial ablation dose of 80 mCi followed by 150 mCi at intervals of a few months,[30] but the Swedish Cancer Registry of large cohort of patients with

thyroid cancer treated with I^{131} did not show any long-term increase in incidence of solid tumors (including bladder tumors).[31] Large dose of I^{131} may produce side-effects e.g.tracheal compression or cerebral edema 12 hours after 200 mCi of I^{131}.[32]Rarely, if ever,are bone marrow metastases cured,even when total doses reach as high as 2.5 Ci.[33] Permanent sterility occurs in less than 10% of men cumulatively given 300mCi and over 90% treated with 800 mCi. In women,permanent sterility may occur in upto 60% of those receiving I^{131} in the range of 800mCi.[39]

Jixiao found that in general there were good correlation between[18] FDG findings and I^{131} scans, though discrepancy was also significant-FDG PET (flourodeoxyglucose positron emission tomography) scans revealed other 12 lesions that were not identified on I^{131} scans in 51 cases.[40]

CONCLUSION :

We fell broad-based long-term study should be done to optimize the dose schedule of radioiodine therapy.

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