

Impact of ablation dose in the treatment of thyroid cancer with I-131

Cholid Badri, Dharma Gayo, Suryo Seto

Abstrak

Tujuan : Untuk menilai keberhasilan terapi ablasi dengan lodium-131 menggunakan dosis yang berbeda pada penderita karsinoma tiroid berdiferensiasi baik yang telah menjalani operasi tiroidektomi total atau hampir total.

Cara : Penelitian retrospektif terhadap 42 pasien yang dirawat di Rumah Sakit Dr Cipto Mangunkusumo antara tahun 1993 - 1996. Diberikan ablasi dengan dosis 80 mCi dan 100 mCi pada kelompok pasien yang masing-masing terdiri dari 21 penderita. Sebelum ablasi, dilakukan pemeriksaan dengan sidik tiroid dan seminggu sesudah ablasi dilakukan sidik seluruh tubuh. Penilaian keberhasilan ablasi dilakukan 3 bulan setelah ablasi dengan pemeriksaan sidik seluruh tubuh dengan 5 mCi I-131.

Hasil : Keberhasilan terapi ablasi dengan dosis 100 mCi berbeda bermakna dengan dosis 80 mCi, yaitu sebesar 85,7 % dibandingkan dengan 57 % ($p = 0,04$). Efek samping akut dijumpai sebanyak 19 % pada pemberian dosis 100 mCi dan 4,8 % pada dosis 80 mCi. Sidik tiroid yang dilakukan 1 minggu setelah ablasi menunjukkan metastasis sebanyak 19 % dengan pemberian dosis 100 mCi dan 4,8 % dengan dosis 80 mCi.

Kesimpulan : Ablasi dengan dosis 100 mCi I-131 memperlihatkan hasil yang lebih baik dibandingkan dosis 80 mCi dan tidak meningkatkan efek samping pengobatan secara bermakna. Di samping itu ablasi dengan dosis 100 mCi kemungkinan dapat lebih baik dalam menemukan adanya metastasis jauh dibandingkan dengan dosis 80 mCi.

Abstract

Purpose : To evaluate the efficacy of ablation therapy using Iodine-131 with two different doses on patients with well-differentiated thyroid cancer who had been operated upon with total or near-total thyroidectomy.

Methods: A retrospective study was conducted on 42 patients admitted at the Dr. Cipto Mangunkusumo Hospital, Jakarta between 1993-1996. Thyroid ablation was performed with 80 mCi and 100 mCi on each group consisting of 21 patients respectively. Thyroid scan was performed before ablative procedure, and followed by whole body scanning one week after the ablation. Efficacy of the treatment was evaluated three months after ablation therapy using whole body scanning with 5 mCi of I-131.

Results : The efficacy of ablation therapy with a dose of 100 mCi was 85.7 %, significantly better than 57. % with a dose of 80 mCi dose ($p=0,04$). Acute side effects were seen in 4,8 % with a dose of 100 mCi and 19 % of patients with a dose 80 mCi. Whole body scanning performed one week after ablation therapy revealed 19% distant metastases with the dose of 100 mCi as compared to 4,8 % with the dose of 80 mCi.

Conclusions : Thyroid ablation with a dose of 100 mCi I-131 showed a better result as compared to 80 mCi dose, as side effects of the treatment were not significantly different. Moreover, ablation therapy with a dose of 100 mCi probably could detect more distant metastases as compared to 80 mCi dose.

Keywords : Thyroid cancer, radioiodine treatment, ablation dose

INTRODUCTION

Ablation with radioiodine (I-131) is to eliminate thyroid tissue remnants in thyroid cancer patients after surgical treatment. Some retrospective studies showed that treatment with radioiodine was the only best prognostic indicator on free of disease interval and improvement of survival rate of well differentiated thyroid cancer patients.^{1,2}

Surgery is the primary treatment of thyroid cancer, and all follicular and papillary carcinomas with a diameter of more than 1 cm - 1,5 cm are suggested to undergo total or near-total thyroidectomy due to multicentricity of the tumour.^{2,4}

Such aggressive surgical approach could enhance the ability of I-131 to ablate the remaining gland and to treat distant metastases. Residual thyroid tissue will prevent detection of local and distant metastases on follow-up with I-131 scanning.⁵

Incidence of thyroid cancer is low and the presentation too variable, thus until now no treatment protocols

Department of Radiology, Faculty of Medicine University of Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

have been evaluated in randomized control manner for efficacy of therapy.^{6,7} Nevertheless, there are two different opinions on the dosage that should be given for thyroid cancer ablation. It is known that the low dose ranges from 30 - 50 mCi and the high dose from 80 - 150 mCi of I-131.

Since 1990, at the Dr. Cipto Mangunkusumo Hospital, a dose of 80 mCi has been used for ablation and the success rate achieved was 58% for the group of papillary type, and 70% for the follicular type. But, with a re-irradiation, a higher success rate could be achieved as high as 67% and 80% respectively. Therefore, it was estimated that a dose higher than 80 mCi would be needed to achieve better ablation result. According to Beierwaltes, the effective ablation dose is between 100 - 150 mCi despite reports from other authors showing that a lower dose was also effective as well.¹¹ Based on these references, since 1993 some of the patients were irradiated with a dose of 100 mCi for ablation instead of 80 mCi.

The aim of this study is to compare the efficacy of the treatment using both different doses and its toxicity as well.

METHODS

Data were collected - from medical records of all patients who underwent ablation during 1991 to 1996 at the Radiotherapy Unit, Dr. Cipto Mangunkusumo Hospital. The diagnosis of thyroid cancer was routinely confirmed and classified according to the WHO classification at the Department of Anatomic Pathology, Faculty of Medicine University of Indonesia. The follicular variant of papillary thyroid cancer was categorized into the papillary type, while the Hirthle type was put into the follicular one.

Patients who came to the Radiotherapy Unit generally had been operated upon previously at the Department of Surgery of the same institution or from other hospitals. The determination of clinical staging was based on physical examination, surgical report, histopathologic examination and on the possibility of metastatic spread to regional lymph nodes or distant metastases. The TNM system was used and based on the UICC classification of 1987.⁹

The subjects were all patients who fulfilled the inclusion criteria, consisting of a well differentiated thyroid cancer (follicular or papillary), residual thyroid tissue detected on postoperative thyroid scanning, had been on a low iodine diet for more than 1 week and had undergone total or near-total thyroidectomy. The ex-

clusion criteria were thyroid cancer of other type than follicular or papillary type, poor general condition and blood hemoglobin less than 10 g%.

Post-operative thyroid scanning was performed with 1 mCi I-131, mostly within 4 to 6 weeks after thyroidectomy. The administration of substitute hormone after surgery, if any, should be withheld 2 weeks before the scanning. If residual thyroid tissue was still found on the scanning, the preparation for the ablative procedure was started. Patients were subsequently put on a low iodine diet and withheld from the substitute hormone for about 2 weeks. At the end of the preparation, laboratory tests were performed including among others: T3, T4, TSH, serum thyroglobulin, hemoglobin, leucocytes, and thrombocytes.

The ablation should be performed soon after the preparation was completed. During the administration of I-131, the patients were put into an isolation room. The patients were asked to drink much water and urinate frequently as a method to lower radiation dose to whole body and particularly to the bladder. Urine and faeces were collected and treated as a special waste. Acute side effects, if occurred, were treated symptomatically as needed.

Body uptake was measured using a survey meter, at 1 hour after administration of I-131, and repeated 48-72 hours afterwards. Patients were allowed to leave the hospital when measurement from 3 meter distance gave a finding of less than 0,37 mR/hour.

Post-ablative whole body scanning was performed 1-2 weeks after the ablation to find out the possibility of existing distant metastases. After whole body scanning, thyroid hormone was continuously given to the patients as a suppressive therapy.

Clinical follow-up was done regularly after 1 week, 1 month, 3 months, 6 months, 1 year, and every 2 years after the ablation. Follow-up with whole body scanning was performed using a dose of 5 mCi I-131, at 3 months after ablation.

Ablation was taken as successful if the whole body scanning did not reveal any residual thyroid tissue. If no residual thyroid tissue nor metastases was found on scanning, administration of suppressive therapy was continued. If residual thyroid tissue was noted, ablation was immediately repeated with the same procedure as before. Whole body scanning was repeated after 6 months, 1 year, and subsequently every 2 years (F_{131}).

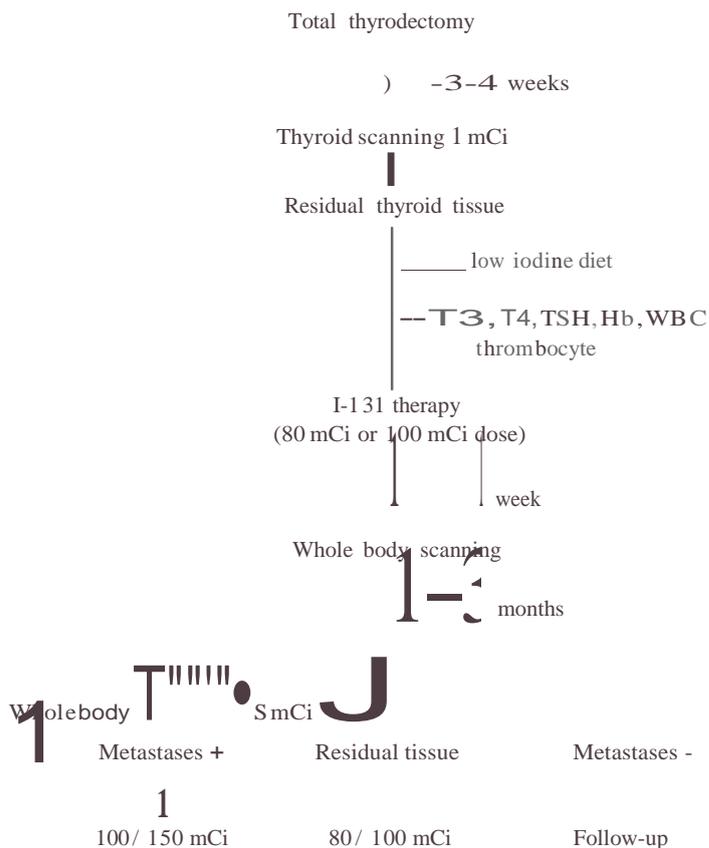


Figure 1. Management of therapy for thyroid cancer with I-131 at Radiotherapy Unit Dr. Cipto Mangulikusumo Hospital

RESULTS

Patient Characteristics

Among 42 patients, the most frequent histopathologic finding was the papillary type, found in 27 patients (64,3%). Most patients (15 out of 42 patients, 36 %) were in the age group of 21-30 year. Out of all patients studied, the most frequent were female, i.e. 27 patients (64,3%) and in this female group, the histopathologic findings were nearly equal, 14 of papillary and 13 of follicular type. There were 15 male patients and 13 (86,6 %) of them had a histology of papillary type (p = 0,002). Thus in this study the papillary type was significantly more frequent than the follicular type in the male patients.

The distribution of age, sex and histopathologic types are presented in Tables 1 & 2.

Table 1. Distribution of age and histopathologic types

| Age | Histopathologic types | | Total |
|---------|-----------------------|------------|-------|
| | Papillary | Follicular | |
| Year | | | |
| 21 - 30 | 8 | 7 | 15 |
| 31 - 40 | 3 | 1 | 4 |
| 41 - 50 | 9 | 3 | 12 |
| 51 - 60 | 3 | 3 | 6 |
| > 60 | 4 | 1 | 5 |
| Total | 27 | 15 | 42 |

Table 2. Distribution of sex and histopathologic types

| Sex | Histopathologic types | | Total |
|--------|-----------------------|------------|-------|
| | Papillary | Follicular | |
| Male | 13 | 2 | 15 |
| Female | 14 | 13 | 27 |
| Total | 27 | 15 | 42 |

The Extent of Tumor

Among 42 patients with a well differentiated thyroid cancer included in this study, the highest number of cases were in Stage I, 24 patients (57%). The others were included in stage II, 5 patients (12 %) and stage III, 7 patients (17%). Six patients (14 %) were classified into stage IV according to metastatic lesions detected on whole body scanning after ablation. The relationship between stages and histologic finding as well as relationship between age groups and stages are presented in Table 2 and Table 3.

Table 3. Relationship between stage and histopathologic types

| Stage of Tumor | Histopathologic types | | Total |
|----------------|-----------------------|------------|-------|
| | Papillary | Follicular | |
| I | 14 | 10 | 24 |
| II | 3 | 2 | 5 |
| III | 5 | 2 | 7 |
| IV | 5 | | 6* |
| Total | 27 | 15 | |

* Stage IV was confirmed after ablation

Surgery

The highest number of surgery performed was total thyroidectomy, with or without dissection of neck lymph nodes (95%). In this study, 1 patient underwent right isthmolobectomy. Since this patient refused to undergo a second surgery, an external radiation was added to the neck with a dose of 50 Gy. However, even after the external radiation the thyroid scanning still showed uptake of I-131. Relationship between types of surgery with doses of ablation is presented in Table 5.

Table 4. Relationship between Age group and Stage

| Age (in years) | Stage | | | Total | |
|----------------|-------|-----|----|-------|----|
| | II | III | IV | | |
| 21 - 30 | 13 | 2 | | 15 | |
| 31 - 40 | 4 | | | 4 | |
| 41 - 50 | 7 | 3 | 1 | 12 | |
| 51 - 60 | | 3 | 2 | 6 | |
| > 60 | | | 3 | 5 | |
| Total | 24 | 5 | 7 | 6 | 42 |

Table 5. Relationship between types of surgery and dose of ablation

| Types of Surgery | Dose of ablation | | |
|-----------------------------------|------------------|---------|-------|
| | 80 mCi | 100 mCi | Total |
| Total thyroidectomy | | | |
| - With lymph glands dissection | 7 | 6 | 13 |
| - Without lymph glands dissection | 13 | 14 | 27 |
| Near-total thyroidectomy | | 1 | 1 |
| Isthmolobectomy | | | 1 |
| Total | 21 | 21 | 42 |

Result of Ablation

The correlation among sex, age, stage, type of surgery, histopathologic finding, dose of medication, and failure of ablation was analyzed statistically with chi-square test and Fischer test.

Evaluation of results achieved in the first three months were as follows :

success rate based on dose administered for 100 mCi and 80 mCi groups were 86% and 57% respectively (p < 0.04).

success of ablation achieved was 80% in males and 67% in females (p > 0,05);

for age less than 45 years, success achieved was 79%, and for the age group of 45 years and older was 57% (p > 0,05).

based on histopathologic findings, success achieved for papillary type was 77%, and 63% for follicular type (p > 0,05);

success rate for Stage I was 75 % as for Stage II-IV was 67% (p > 0,05).

Side Effects

Ablation with the dose of 80 mCi produced acute side effects in 4 out of 21 patients (19%) in the form of nausea in 1 patient, dysphagia in 1 patient and hoarseness in 2 patients. Ablation with the dose of 100 mCi produced acute side effects only in 1 out of 21 patients (4,8%) in the form of neck edema. These complaints were taken care off with symptomatic therapy. Corticosteroid therapy was given for neck edema, and the patient recovered within a few days.

DISCUSSION

In this study, the factor of the dose amount resulted in significant difference of ablation results. A dose of 100 mCi gave a success rate of 86%, while a dose of 80 mCi gave only 57%. Several results of previous studies showed that a high initial dose of I-131 will improve the success rate of ablation and lessened the need for a repeat ablation. -

Beierwaltes¹³ suggested that residual tissue which still took I-131 in the thyroid bed should be given a dose of ablation no less than 100 mCi. As an adjuvant therapy, a dose of 100-150 mCi should be given to ablate micrometastases unseen in I-131 scanning with 1-5 mCi, particularly if prior to ablation tumor uptake was known to be quite low (<4%).^{10, 14}

At our institution, the ablation procedure has been applied since 1987 in several patients with a dose of 30 mCi. This low dose was chosen to make it possible for the patient to get ambulatory treatment since the waste treatment facility was poor. One year later, with a better waste treatment facility, the dose was increased to 50 mCi. In 1990, a general consensus with other departments and considering many references produced a protocol for ablation with a dose of 80 mCi.

On evaluation of patients treated from 1990-1992,⁸ using the dose of 80 mCi, the average success rate of ablation performed on 44 patients was 64%, with a higher success rate on follicular type (70%) compared with papillary type (58%). Patients who were not ablated at the first treatment, most of them will be ablated on subsequent treatment, therefore the success rate for ablation could be improved from 64% to 79,5%. This fact lead to an assumption that the dose given on the first ablation was relatively less than optimal, and this was also in accordance with Beierwaltes' opinion who suggested 100-150 mCi as the dose for ablation.¹⁰

The present study showed that administration of 100 mCi ablation dose resulted in a significant better success rate than 80 mCi, that was 85,7% as compared to 57% ($p=0,04$). These findings were found to have no significant correlation between success rate of ablation with those variables such as age, sex, type, stage and histopathologic type.

Therefore, radiation with a dose of 100 mCi was better than 80 mCi because the success rate was higher, and there was no need for the patient to undergo a second ablation. It can reduce days of hospitalization, shorten the hypothyroid period in ablation preparation, and may also lessen the occurrence of metastases before a second ablation was performed.

Ablation with 80 mCi dose caused side effects in 4 out of 21 patients (19%), those were nausea in 1 patient, dysphagia in 1 patient, and hoarseness in 2 patients. With 100 mCi dose, side effects occurred in the form of neck edema in 1 patient (4,8%). Nausea was an early side effect of I-131 therapy and lasted from 1 hour to 2 days, and responded well to anti-emetic administration. Pain, unease feeling and disturbance of salivary gland production were early complications which could be handled well.

Hoarseness was caused by a temporary edema of the salivary glands which resulted in pressure to the recurrent nerve. The characteristic of neck edema was seen as a painful swollen neck, which occurred 48 hours after therapy, and was related to invasion of tumor to the soft tissues or due to too much thyroid remnant left.¹

Using a dose of 100 mCi in this study did not increase quantitatively side effects compared to a dose of 80 mCi. Qualitatively, the side effects found in the group given a 100 mCi dose was a little more grave, such as

edema of the neck, but this side effect could be managed with administration of corticosteroids.

As the ablation dose of 80 mCi used in this study showed 4,8% metastases (1/21) in the bones, the 100 mCi dose revealed 19% of metastases (4/21) including 3 metastases in the bones and 1 in the lymph node. The number of patient with metastases was higher in the ablation dose of 100 mCi as compared to the dose of 80 mCi (19% vs 4,8%). The probable cause could be the fact that metastatic deposits of carcinoma took less activity on whole body scanning. Nevertheless, the possibility remained that those patients who were given a dose of 100 mCi had in fact distant metastases in a greater number compared to the group which was given a 80 mCi dose.

There are several limitations found in this study, such as no records were available about the size of the tumor, multicentricity, estimation of residual thyroid gland, TSH blood level before ablation, and results of follow-up on ablation for the first three months after ablation. Those variables should be considered in further studies of the ablation dose.

REFERENCES

1. Varma VM, Beierwaltes WH, Nofal MM, Nishiyama RH, Copp JE. Treatment of thyroid cancer: Death rate after surgery and after surgery followed by sodium iodine 1-131. *JAMA*, 1970; 214: 1437-42.
2. Mazzaferri EL, Jhiang SM. Long term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994; 97: 418-23.
3. Ramli HM, Kamajaya. Penatalaksanaan karsinoma tiroid di Bagian Bedah Sub Bagian Bedah Onkologi FK U I/RSCM. Dalam: Keganasan kulit leher dan kepala. Semarang: Badan Penerbit Univ. Diponegoro, 1991; 185-200.
4. Wanebo HJ, Andrews W, Kaiser DL. Thyroid cancer: some basic considerations. *Am J Surg* 1981; 142: 474-9.
5. Sweeney DC, Johnston GS. Radioiodine therapy for thyroid cancer. *Endocrinol Metab Clin North Am* 1995; 72: 828-32.
6. Maxon III HR, Smith HS. Radioiodine-131 in the diagnosis and treatment of metastatic well differentiated thyroid cancer. *Endocrinol Metab Clin North Am* 1990; 19: 685-718.
7. Robbins J. Thyroid cancer: A lethal endocrine neoplasm. *Ann Intern Med* 1991; 115: 133-9.
8. Badri C, Kuswanto O, Gondhowirdjo S, Astarto B, Kusumawidjaya H. Papillary and follicular thyroid cancer: Impact of treatment in 44 patients at the Cipto Mangunkusumo Hospital. *Med J Univ Indon* 1994; 4: 42-7.
9. Hermanek P, Sobin LH. TNM classification of malignant tumors. International Union Against Cancer. 4th ed. New York: 1987.

- IO. Beierwaltes WH, Rabbani R, Dmuchowski C, Lloyd RV, Eyre P, Mallette S. An analysis of ablation of thyroid remnants with I-131 in 511 patients from 1947-1984: Experience at the University of Michigan. *J Nucl Med* 1984; 25: 1287-93.
11. DeGroot LJ, Reilly M. Comparison of 30 and 50 mCi dose of Iodine-131 for thyroid ablation. *Ann Intern Med* 1982; 96:51-53.
12. Mazzaferri EL, Young RL. Papillary thyroid cancer: A 10 year follow-up report of the impact of therapy in 576 patients. *Am J Med* 1981; 70:511-8.
13. Beierwaltes WH. The treatment of thyroid cancer with radioactive iodine. *Semin Nucl Med* 1978; 8: 79-93.
14. N, Triaspolitica. "Mengenai Penyakit Kanker, Jenis, Gejala, Penyebab Berikut Pengobatan Kanker." *Mau Nanya Dong Dok*. N.p, 20 June 2017. Web. 28 June 2017. <<https://nanyadongdok.blogspot.com/2017/06/mengenai-penyakit-kanker-jenis-gejala.html>>.