A RECORD REVIEW STUDY ON THE SUCCESSFULNESS OF RADIOIODINE ABLATION IN POSTOPERATIVE WELL DIFFERENTIATED THYROID CARCINOMA PATIENTS USING 100 mCi OF ^{131}I IN HUSM

by

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Dedicated to,

My beloved husband Dr Razman Mohd Rus

&

My enchanting little angels: Luqman Hakim, Amalia Izzati, Amir Hakim and Ammar Hakim

&

My parents; Hj Muhammed Nordin Muhamed and Hjh Natrah Omar

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABREVIATIONS

AGES	Age of patient and tumor grade, extent, and size
AMES	Age of patient, presence of distant metastatic lesions, extent and size of primary tumor
DTC	Differentiated Thyroid Carcinoma
FNAB	Fine Needle Aspiration Biopsy
λ	Gamma
HUSM	Hospital Universiti Sains Malaysia
^{131}I	Iodine- 131
RAI	Radioiodine ablation
Tg	Thyroglobulin
TSH	Thyroid Stimulating Hormone
TNM	T-primary tumor, N-regional lymph node and M-distant metastases
mCi	miliCurie
Bq	Becquereles
mR/hr	mili-Roentgen per hour

ABSTRAK

Tajuk:

Kajian ke atas rekod kes pesakit untuk mengetahui kejayaan pesakit kelenjar tirod yang telah menjalani pembedahan dan mendapat rawatan 'radioablation' menggunakan radioaktif iodine sebanyak 100 mCi di HUSM.

Pengenalan:

Penyakit kanser kalenjar tirod merupakan penyakit yang senang diubati dan mampu memanjangkan jangka hayat pesakit sekiranya dikesan di peringkat awal. Rawatan 'radioablation' selepas pembedahan kelenjar tirod sangat bermanfaat kepada pesakit. Namun, dos optima bagi memastikan kejayaan rawatan ini masih lagi kontroversi disebabkan kurangnya kajian secara prospektif diadakan. Walaubagaimanapun banyak terbitan-terbitan terdahulu mengatakan rawatan 'radioablation' dengan menggunakan dos sebanyak 100 mCi adalah terbukti secara statistik boleh menghapuskan kesemua saki-baki kelenjar tirod yang telah dibuang semasa pembedahan.

Objektif:

Tujuan kajian ini ialah untuk mengetahui prevalen pesakit yang dirawat dengan regim dos radioaktif iodin ('radioablation') iaitu sebanyak 100 mCi adalah berkesan untuk menghapuskan saki-baki sel tiroid bagi pesakit kanser tirod jenis papilari dan folikular. Objektif yang selanjutnya untuk mengetahui hubungkait faktor-faktor yang boleh mempengaruhi keberkesanan kaedah rawatan melalui 'radioablation' ini.

Metodologi:

Kajian ini merupakan kajian secara retrospektif untuk selama 10 tahun (dari 1 Januari 1997 hingga 31 Disember 2007). Sebanyak 214 sampel yang telah memenuhi kriteria dikaji. Keputusan skan seluruh badan ('whole body scan') semasa pemeriksaan ulangan dan faktor-faktor yang berhubungkait dengan kajian ini direkodkan oleh pengkaji.

Keputusan:

Prevalen kejayaan rawatan ('radioablation') dalam populasi negara kita ialah 54.2% iaitu lebih rendah berbanding dengan data terbitan terdahulu daripada negara lain. Jenis pembedahan tirod yang dilakukan merupakan satu-satunya faktor yang mempengaruhi kejayaan rawatan di dalam kajian ini. Manakala, prevalen pesakit yang mengalami masalah sel kanser merebak ke organ lain ialah sebanyak 23.8%. Sel kanser di dapati paling banyak merebak ke kelenjar limfa.

Kesimpulan:

Kesimpulannya, regim yang digunakan sekarang iaitu sebanyak 100 mCi adalah efektif untuk merawat saki-baki penyakit kanser tirod jenis papilari dan folikular ini. Di samping itu, di dapati kaedah pembedahan tirod juga satu-satunya faktor yang mempengaruhi kejayaan rawatan 'radioablation'.

ABSTRACT

Title:

A record review study on the success of radioiodine ablation in postoperative well differentiated thyroid carcinoma patients using 100 mCi of ^{131}I in HUSM.

Introduction:

Well differentiated thyroid carcinoma is curable when discovered at an early stage. Post-operative radioiodine ablation is very useful. Its management, however, is often a challenge because there have been no prospective randomized trials and the optimal dose for successful single ablation is still a controversy. However, many published data showed a single high dose ablation is statistically significant in the treatment of post-operative well differentiated thyroid carcinoma.

Objectives:

The objectives of this study are 1) to determine the prevalence of success of single dose of radioiodine ablation using 100 mCi of ^{131}I, 2) to correlate successful ablation with other factors and 3) to determine the prevalence of patients that developed distant metastases after ablation therapy.

Methods:

This is a record review study over a period 10 years (1st January 1997 till 31st December 2007). A total of 214 samples that fulfilled the inclusion criteria were studied. The attached formal reported result of first whole body scan and related associated factors were reviewed and the required data were retrieved and studied by the main researcher.

Result:

The prevalence of successful ablation in our population was 54.2% which is slightly lower than that of reviewed published data from other countries. Total thyroidectomy was found to be the only significant associated factor in this study. The prevalence of patients developed metastases after initial ablation was 23.8% with lymph node being the commonest site of metastases.

Conclusion:

In this study, we conclude that the present ablative dose of 100 mCi is effective in the treatment of well differentiated thyroid carcinoma remnants. We also found that only the type of thyroid surgery had a significant association with the outcome of radioiodine ablation.

CHAPTER 1

INTRODUCTION

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1 INTRODUCTION

1.1 Background of study

Kelantan is situated in the East Coast of Peninsular Malaysia. Based on the population census (year 2000), the estimated population in Kelantan was 1.4 million, comprising of almost equal ratio of male (50.01%) and female (49.99%). The Malay ethnic group formed the largest group (95.1%), followed by the minorities such as Chinese (3.7%), Indian (0.3%), other Bumiputra (0.8%) and Others (1.0%) .

Hospital Universiti Sains Malaysia is situated in Kubang Kerian, Kelantan. It is a tertiary-care centre in East Coast Malaysia and a referral centre for radioiodine ablation of post-operative thyroid carcinoma for East Coast Malaysia. In 10 years time from 1997 till 2007, there were 478 cases of post operative well differentiated thyroid carcinoma patients with average of 47.8 cases per year underwent RAI in our centre.

1.2 Justification of the study

Papillary and follicular thyroid cancer are differentiated thyroid cancer and usually curable when discovered at an early stage. Its management, however, is often a challenge because there has been no prospective randomized trials of treatment given its typically prolonged course and relative infrequency.

Differentiated thyroid carcinoma (DTC) is more likely to be completely resected and ablated with iodine-131 (^{131}I), an approach that has become more popular in the past several decades, when discovered at an early stage. However a single optimal dose has not been established.

There are three approaches to ^{131}I therapy: empiric fixed doses, upper bound limits that are set by blood and whole-body dosimetry, and quantitative tumor dosimetry (Brant and Helms, 2007). A fixed ^{131}I dose is the most widely used and simplest method. Its main advantages are simplicity and safety; its main disadvantage is that insufficient ^{131}I may be administered to adequately treat tumor.

The philosophy of large dose ^{131}I ablation for remnant thyroid tissue is based on a contentious issue of "large dose not only ablates remnant thyroid but also ablates possible micrometastatic deposits". The proponents of initial high dose ^{131}I ablation argue that low doses are less effective for ablation of the micrometastases that are not visualized in post-therapy whole body scan, which at later date may result in higher local as well as distant recurrence rate (Beierwaltes *et al.*, 1984).

Recently many centers use 30 mCi to ablate a remnants of thyroid tissue after surgery. This has been a popular way to avoid hospitalization, which no longer necessary in most states because of the 1997 change in federal regulations that permits the use of much larger ^{131}I doses in ambulatory patients (Hackshaw *et al.*, 2007).

The most outstanding feature of most thyroid malignancy is that complete cure and / or long term remission is possible even in stage IV, provided appropriate and adequate treatment is made available. The reason being that the differentiated thyroid carcinoma including metastases retains its property of concentrating iodine and therefore enabling radioiodine therapy to delivery a very high radiation dose capable of completely eliminating the malignant tissues.

Despite reports of successful of ablation rates as a result of low dose (30 mCi) ^{131}I therapy, there has been controversy; although low dose ^{131}I therapy has advantages of outpatient administration, lower total expense and lower radiation exposure (Siddiqui *et al.*, 1981). The use of lower dose for ablation therapy is discussed in a number of recent publications advocating lower radioiodine dose for initial ablation therapy. It appears that a dose beyond 50 to 80 mCi does not increase the rate of initial ablation (Das *et al.*, 2006)

A meta-analysis on 967 patients was performed from 19 studies and revealed a statistically significant advantage for a single high dose (75-100 mCi) over a single low dose (30 mCi) of ^{131}I (Doi *et al.*, 2007).

The total ^{131}I dose needed for successful ablation was significantly higher in males, patients with higher post-operative thyroglobulin (Tg) levels and patients with a higher stage of disease (Arslan *et al.*, 2001). However, M. Karam *et al* (2003) found that there was no association with age, gender, tumor histology, TSH level, diagnostic, neck uptake and successful ablation dose.

Controversies exist regarding thyroid remnant ablation following thyroidectomy. The optimal dose of ^{131}I for remnant ablation has not been agreed. The dose of ^{131}I in the treatment of well differentiated thyroid carcinoma with distant metastases is also controversial.

1.3 Rationale of study

Well differentiated thyroid carcinomas are among the most curable cancers and associated with a high survival rate (>90%). Even if the disease is not totally cured, through repeated high dose radioiodine therapy the progress of the disease can be controlled with significant improvement in quality of life for many years (Das *et al.*, 2006).

However the optimal dose of ^{131}I for remnant ablation is still controversial; some advocate that a large activity of 100–150 mCi of ^{131}I is required for successful ablation, whereas others believe that an activity as small as 30–50 mCi is sufficient to achieve the same goal (Bal *et al.*, 2004).

It is imperative to try to achieve ablation with one dose of ^{131}I because there is increasing evidence that a suboptimal radiation dose decreases the biologic half-life of subsequent radiation doses, thus decreasing the chance of curing the patient (Beierwaltes *et al.*, 1984).

However, all the data available and the studies were done abroad where the quality of care and technology available are different from our local set up. Hence there is a need to

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However, all the data available and the studies were done abroad where the quality of care and technology available are different from our local set up. Hence there is a need to

explore and establish new data that is applicable and representative to our local population and environment.

CHAPTER 2

LITERATURE REVIEW

CHAPTER TWO

2 LITERATURE REVIEW

2.1 General Overview

Radioactive iodine is used both for post-operative thyroid remnant ablation and also for treatment of distant metastases in well differentiated thyroid carcinoma patients (Beierwaltes *et al.*, 1984). Many studies have shown that postoperative radioiodine treatment was associated with improved cancer-specific mortality rates and disease progression in both papillary and follicular cancer. However, major unresolved controversial issue is the optimal dose of radioactive iodine(^{131}I) used for ablation therapy (Bal *et al.*, 2004).

2.2 Anatomy of thyroid gland

The thyroid is a brownish-red and highly vascular gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The gland varies from an H to a U shape and is formed by 2 elongated lateral lobes with superior and inferior poles connected by a median isthmus (with an average height of 12-15 mm) overlying the second to fourth tracheal rings. Occasionally, the isthmus is absent, and the gland exists as 2 distinct lobes. Each lobe is 50-60 mm long, with the superior poles diverging laterally at the level of the oblique lines on the laminae of the thyroid

cartilage. The lower poles diverge laterally at the level of the fifth tracheal cartilage. Thyroid weight varies but averages 25-30g in adults (slightly heavier in women).

The thyroid gland is ensheathed by the visceral fascia and received its blood supply from the superior and inferior thyroid arteries and, occasionally, the thyroidea ima artery. These arteries have abundant collateral which anastomoses with each other, both ipsilaterally and contralaterally. The inferior thyroid artery arises from the thyrocervical trunk, a branch of the subclavian artery. The inferior thyroid artery has a variable branching pattern and is closely associated with the recurrent laryngeal nerve. The latter also ascends in the tracheoesophageal groove and enters the larynx between the inferior cornu of the thyroid cartilage and the arch of the cricoid. The recurrent laryngeal nerve can be found after it emerges from the superior thoracic outlet, in a triangle bounded laterally by the common carotid artery, medially by the trachea, and superiorly by the thyroid lobe. The nerve can be found deep to the inferior thyroid artery (40%), superficially (20%), or between branches of the artery (35%) (Dorion and Lemaire, 2008).

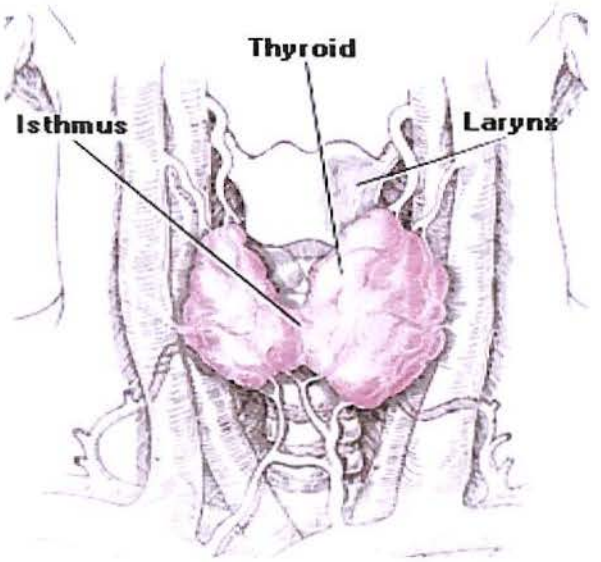

Figure 1: Anatomy of thyroid gland. Adapted from Snell Anatomy Text Book.

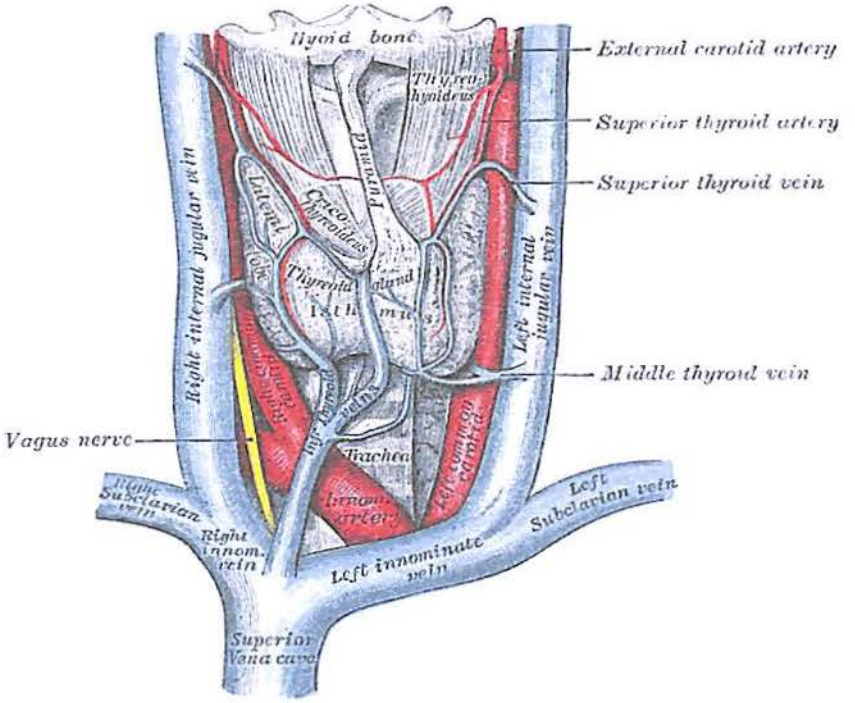

Figure 2: The thyroid gland and its relations. Adapted from Anatomy of the Human Body by Henry Gray (1825–1861), 1918.