

Oncology, Original Article**Successful Complete Ablation Rate Post a Second Ablation Dose of 30 mCi Radioactive Iodine (I131) in Patients with Papillary Thyroid Cancer**

Wagieh Sh.*, Al Salman Kh.*, Munshy T.*, El Refaei Sh.***, Abd- El Kareem M.***, and Abd-El Razeq Sh****.

*Nuclear Medicine departments, King Abdulla Medical City (KAMC), Saudi Arabia, Cairo** and Assuit*** Universities, Egypt*

ABSTRACT: Ablation outcome in patients with papillary thyroid cancer after a single dose of I131 depends on several factors. No single group has achieved a successful complete ablation rate of 100% and a second ablation dose is needed for patients with residual functioning thyroid tissue. The aim of the current study is to assess successful complete ablation rate post second ablation dose of 30 mCi I131.

Patients and methods: 100 patients with papillary thyroid cancer (T1 or T2-N0&M0) candidates for post total thyroidectomy ablation received first ablation dose of 100 mCi. Six months later follow up I131 whole body scan (I131 WBS) was performed. Patients with residual functioning thyroid tissue in the neck received another ablation dose of 30 mCi I131 on out patient basis in the same day of scanning. Follow up I131WBS was performed 6 months later to assess ablation outcome whether complete or incomplete. **Results:** 91% of patients are females with an overall age range of 17-68

years (mean 43 ± 23 years). Successful complete ablation after first 100 mCi I131 ablation dose is 64%, as compared to 72% post second ablation dose of 30 mCi I131. No significant difference as regards age, gender and histopathological details between patients who achieved complete ablation and those with non complete ablation after reablation dose of 30 mCi can be detected. The overall successful complete ablation rate after overall dose of 130 mCi is 90%.

Conclusion:

The successful complete ablation rate after a second ablation dose of is higher than first ablation dose of 100 mCi I131. No significant difference between completely and non-completely ablated patients after the second ablation dose (30 mCi) as regards age, gender and histopathological details. The overall complete ablation rate after 130 mCi is 90%, this figure is significantly higher than the same figure post either first or second ablation dose separately.

INTRODUCTION:

Papillary thyroid cancer (PTC) is the commonest thyroid malignancy. Total or near total thyroidectomy followed by radioiodine (I131) ablation of residual thyroid tissue (remnant ablation) is considered the ideal treatment for PTC [1]. Radioiodine ablation of thyroid remnant has been defined as "the destruction of residual, macroscopically normal thyroid tissue following surgical thyroidectomy" [2]. There are several compelling reasons for remnant ablation in patients with PTC. These factors include proper detection and treatment of nodal or distant metastases. Also, to achieve high TSH levels needed to enhance tumor I131 uptake and to make the results of unsuppressed serum thyroglobulin (Tg) level more reliable [3]. Remnant ablation was reported to be an independent variable that reduces locoregional recurrence, distant metastases, and cancer death [4]. Although I131 has been used for many years to ablate thyroid remnant following surgery, a single optimal ablation strategy is still not established. Variable reports on the amount of I131 required to achieve successful ablation, criteria for successful ablation, long term disease survival and recurrence rates show considerable variation [5,6]. No single group has achieved an ablation rate of 100% after first ablation dose, with variable complete ablation rate according to many factors. In addition to different factors that can influence ablation outcome, the

variability in ablation outcome results could possibly be also explained by varying radiosensitivity of thyroid tissue to I131. This may be attributed to the fact that thyroid remnant owes different degrees of defective iodine organification in variable individuals, which may be due to different levels of decreased expression of sodium iodide symporter (NIS) [7,8]. In well-differentiated thyroid cancer, the aim is to achieve a reasonably good ablation rate (~80%) after a single dose with an effective activity of I131 that can be administered [8,9]. Patients, who fail to achieve successful complete ablation after first dose of I131, require a second ablation dose to achieve complete ablation. Multiple studies have established the adequacy of low dose I131 in successfully ablating remnant thyroid in selected patients with a first ablation dose as low as 30-50 mCi [10]. To our knowledge no single study assessed the successful complete ablation rate post a second low ablation dose in patients who failed to achieve complete ablation after the first ablation dose. The aim of the current study is to assess the successful complete ablation rate post a second ablation dose of 30 mCi of I131 in patients who failed to achieve complete ablation after a first ablation dose of 100 mCi and to assess the overall complete ablation rate post both ablation doses of I131.

MATERIAL & METHODS:

The current prospective study includes 100 patients referred to three nuclear medicine centers post total thyroidectomy for papillary thyroid cancer (T1&T2, N0, M0) candidates for I131 ablation therapy. I131 whole body scan (I131 WBS) revealed presence of residual functioning thyroid tissue in the neck with no lymph nodal or distant metastases in all patients. All patients received an ablative dose of 100 mCi. Six months later follow up I131 WBS and unsuppressed serum Tg levels were performed. According to results, patients were divided into 2 groups, those who achieved complete ablation with serum Tg level of < 2 ng/ml with normal I131 whole body scan showing no residual functioning thyroid tissue in the neck and no functioning metastases. The second group includes patients with serum Tg level equals to or > 2 ng/ml and partial ablation of residual functioning thyroid tissue in the neck, with persistent smaller remaining functioning thyroid tissue in the neck in follow up I131 WBS and no metastases. Patients in the latter group received 30 mCi of I131 as a second ablation dose on out patient basis in the same day as I131 WBS imaging (72 hours post oral intake of 2 mCi of I131). Again, 6 months later unsuppressed serum Tg level and I131 WBS were performed and the successful complete ablation rate was

calculated based on the same criteria.

Statistical methods: Categorical data are represented as percentage while numeric data are presented as mean \pm standard deviation. For comparison of percentages, the chi squared test is used. The Mann Whitney U test is used to compare numeric data. A P value of 0.05 is set as the threshold for statistical significance. SPSS v.16 is employed for statistical analysis.

RESULTS:

Out of the 100 patients, females represent 91 % (91 patients), with only 9 male patients (9%). The age of the whole group ranges from 17 – 68 years with a mean value of 43 ± 23 . Successful complete ablation was achieved after a single dose of 100 mCi I131 therapy in 64 patients (64%). During follow up after 6 months they have normal I131 WBS (Fig1), with unsuppressed serum Tg level in all patients < 2 ng/ml (mean value 0.64 ± 0.43 ng/ml). On the other hand the remaining 36 patients (36%) had achieved partial ablation outcome post 100 mCi radioactive iodine (I131) with smaller residual functioning thyroid tissue in the neck in I131 WBS and unsuppressed serum Tg level of all patients > 2 ng/ml, (mean value 9.3 ± 5.3 ng/ml) (table 1). This group of patients received a second ablation dose of 30 mCi on outpatient-basis. On follow up 6 months post second dose ablation therapy

I131 WBS was completely free from any functioning thyroid tissue in 26 patients (72%), representing successful complete ablation with unsuppressed serum Tg level < 2 ng/ml (mean value 0.49 ± 0.31 ng/ml). The

remaining 10 patients (28%) have still residual functioning thyroid tissue in the neck in I131 WBS (Fig2) with serum Tg with serum Tg level > 2 ng/ml (mean value 4.7 ± 2.1 ng/ml) (table1).

Table 1: Mean value of unsuppressed serum Tg level post ablation doses in those who achieved complete and incomplete ablation after first and second ablation I131 doses.

| | Number of patients | Mean value of serum Tg |
|------------------------------------------------------|--------------------------------------|------------------------|
| Post first ablation dose 100 mCi (100 patients) | Complete ablation (64 patients) | 0.64 ± 0.43 ng/ml |
| | Incomplete ablation (36 patients) | 9.3 ± 5.3 ng/ml |
| Post second ablation dose 30 mCi (36 patients) | Complete ablation (26 patients) | 0.49 ± 0.31 ng/ml |
| | Incomplete ablation (10 patients) | 4.7 ± 2.1 ng/ml |

The overall ablation outcome post 100-mCi first ablative I131 dose is 64%, while after second reablation dose of 30 mCi I131 is 72% (Table2). The overall successful complete ablation outcome post the two doses of I131 (130 mCi) is 90%. The remaining 10% do not achieve complete

ablation (table2). No significant difference as regards age, gender and histopathological details (size of primary lesion, capsular or vascular invasion) between patients who achieved complete ablation and those with non-complete ablation after reablation dose of 30 mCi can be detected (table 3).

Table 2: Successful complete ablation outcome post first and second I131 ablation doses.

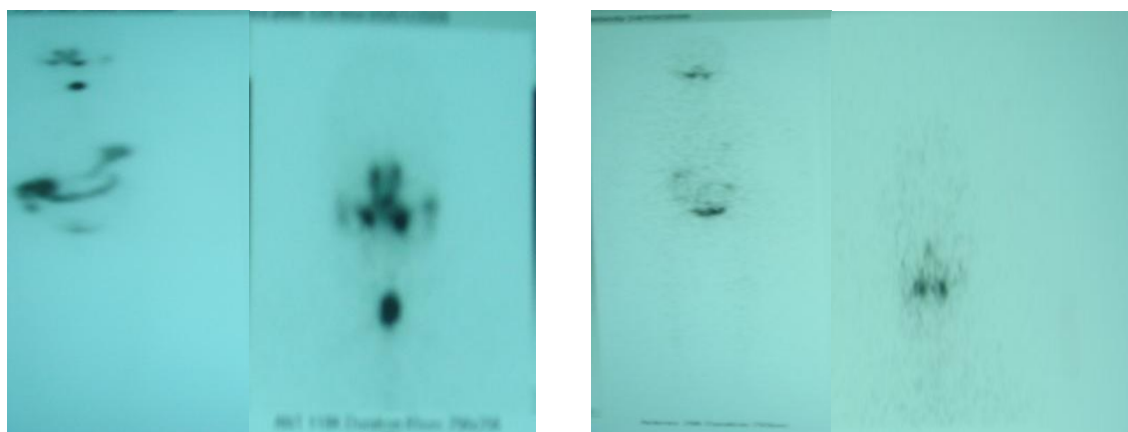
| | First ablation dose 100 mCi I131 | Second ablation dose 30 mCi I131 | Post 2 ablation Doses |
|-----------------------------|-------------------------------------|-------------------------------------|--------------------------|
| Total number of patients | 100 patients | 36 patients | 100 patients |
| complete ablation | 64 patients (64%) | 26 patients (72%) | 90 patients (90%) |
| Incomplete ablation | 36 patients (36%) | 10 patients (28%) | 10 patients (10%) |

Table3: difference between those who achieved complete ablation and those who failed to achieve complete ablation post a second ablation dose of 30 mCi. (P value > 0.05).

| | Complete ablation post 30mCi (26 patients) | Incomplete ablation post 30 mCi (10 patients) | P value |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|--------------------------------------------------|----------------------------------|
| <ul style="list-style-type: none"> • Gender : -Females - Males | 23 (88.5%) 3 (11.5%) | 9(90%) 1(10%) | >0.05 >0.05 |
| Age | 43±19years | 42±16years | >0.05 |
| <ul style="list-style-type: none"> • Histopathological data: - Tumor size - Capsular invasion - Vascular invasion | 2.1±.9cm. 13(50%) 9 (35%) | 2.3±1.1cm. 5(50%) 3(30%) | >0.05 >0.05 >0.05 |
| <ul style="list-style-type: none"> • Non neoplastic tissue histopathology: -Normal -Hashimoto's thyroiditis -Multinodular goiter - others | 9 (35%) 8 (31%) 6 (23%) 3 (11%) | 4 (40%) 3(30%) 2 (20%) 1 (10%) | >0.05 >0.05 >0.05 >0.05 |

No statistically significant difference between the successful complete ablation rate post first and post second ablation doses, which is 64% and 72% respectively (P value >0.5). On the other hand, the

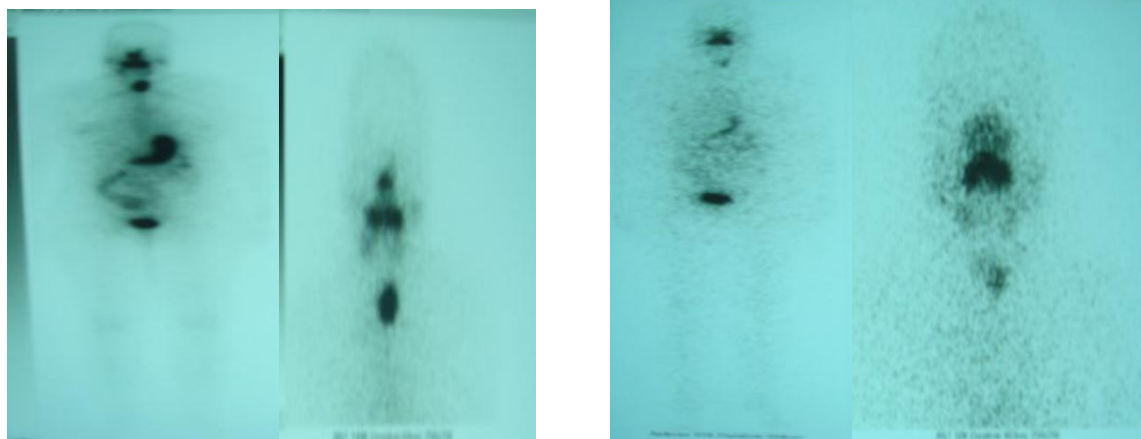
overall successful complete ablation rate after both doses (90%) is significantly higher in comparison to successful complete ablation figure of either first (64%) and second (72%) ablation doses separately (P value < 0.05).



(A)

(B)

Fig1 (A): I131 WBS (anterior& posterior WBS and spot views) 5 days post 100mCi I131 ablation dose, with proper tracer localization in residual thyroid tissue in the neck with no remote metastases.(B): Follow up I131 WBS (anterior &posterior WBS and neck spot views), 6 months post ablation therapy, showing successful complete ablation with no functioning metastases.(Serum Tg level:0.12 ng/ml)



(A)

(B)

Fig2 (A): I131 WBS 5 days post 100mCi I131 therapy dose, with proper tracer localization in residual thyroid tissue in the neck and no functioning metastases. Fig2(B): Follow up I131 WBS (anterior& posterior WBS and anterior neck spot view), 6 months post second ablation dose of 30 mCi, showing incomplete ablation with small neck remnant (serum Tg level: 5.7ng/ml).

DISCUSSION:

All patients included in the current study have PTC, they presented post total thyroidectomy for I131 ablation therapy. The outcome of I131 ablation therapy is unpredictable for individual patients. Ablation outcome depends upon many

factors including given I131 dose, I131 uptake, size of residual thyroid tissue and tumor stage. Other reports stated that histopathology of non neoplastic thyroid tissue as well as stunning effect have an impact on ablation outcome. However, all these factors are somehow interlinked with

each other ^[10]. Maxon et al, 1992 ^[11] reported complete ablation in 86% of patients using initial dose of 100 mCi, Where (2006) Zaman et al. reported an ablation rate of 54% was achieving the same dose ^[9].

On the other hand Ackshaw et al, 2007 ^[12] stated that approximately half of the studies reported 80% complete ablation rate post 100 mCi I131 ablation dose and the rate was 90% in 5 out of the 26 estimates, indicating that only one in five studies (20%) achieved a very high ablation rate. Zidan et al, 2004^[13] gave I131 ablation doses based on the 24-hours percentage of neck uptake in the postoperative I131 WBS scans. They concluded that patients with differentiated thyroid cancer can be treated with doses of I131 according to the percentage of neck uptake of postoperative total body scan, with in the present study the overall ablation rate for patients included in the current study after a fixed first ablation dose of 100 mCi is 64%, The lower rate of ablation as compared to other studies. This may be related to relatively bigger residual functioning thyroid tissue post total thyroidectomy which differs from one surgeon to another as patients included in the current study are pooled from different hospitals in three main nuclear medicine centers.. Finally individual variations likely attributed to variable degrees of expression of NIS may be responsible for this relatively

lower complete ablation rate, yet, it is within the reported range ^[12].

Patients who failed to achieve complete ablation after the first dose usually are given a second ablation dose to achieve complete ablation. Also, high TSH levels necessary to enhance tumor I131 uptake cannot be ordinarily achieved with a large thyroid remnant. Third, serum thyroglobulin (Tg) measurement under TSH stimulation, which is the most sensitive test for the detection of recurrence. To our knowledge no single study reported the successful complete ablation rate post a second ablation dose of I131. For those who did not achieve successful complete ablation after a first ablation dose, usually they have small remnant that can be ablated by low dose of I131 on outpatient basis, so a small reablation dose of 30 mCi is given in the current study as a second ablation dose. The rationale behind the use of 30 mCi low dose I131 reablation therapy came from the data published about the use of low dose I131 as a first ablation dose. The first report of low dose therapy that emphasized its effectiveness relative to higher doses was reported in 1976 by McCowen et al ^[15]. The argument about using low doses of I131 was that low doses can not ablate micrometastases if present that are not visualized in whole body scan. Also, Mazzarferri and Kloos, 2001 ^[4] addressed these arguments and stated that there is no

difference in 30 years recurrence rate between patients ablated using low dose (29-50 mCi) and those using high dose of I131 (51-200 mCi). This may be due to the reported facts that the cytotoxic doses of I131 for normal and neoplastic thyroid tissue show significant variations. In patients receiving only 120 Gy of radiation-absorbed dose, whereas a radiation-absorbed dose of 600 Gy could not achieve ablation in another patient. This observation could possibly be explained by varying radiosensitivity of thyroid tissue, measurement of which remains an elusive factor. This biological variable is unknown, undefined, and unpredictable and varies from one individual to another. This may be explained by the fact that iodine organification is defective in thyroid remnant which may be due to decreased expression of NIS^[7,8].

The rate of complete ablation post low dose of I131 (30 mCi) as a first ablation dose was clearly variable ranging from 10-80% and no study reported success rate greater than 80%. The success rate in the 2 largest studies was 70%^[12]. This figure is comparable to the 72% reported as a complete ablation rate using 30 mCi as a second ablation dose in the current study. The low dose of 30 mCi was employed as a second ablation dose in the current study as multiple studies have established the adequacy of low dose I131 in addition to its advantages. There are several advantages of

30 mCi of I131 for both the patient and health care provider. The proposed advantages of this low dose are lower financial cost, less post treatment precautions that patient would need to take to prevent accidentally exposing other people to potentially harmful radioactivity, and minimizing whole body radiation exposure, hence lowering the potential risk of leukoemogenesis. In addition to the practical advantages of economy and convenience of out patient treatment in many countries^[14], other advantages include less time in isolation and reduced exposure of the environment to radioactive I131. Besides, it was reported that the lower the administered activity the lower the risk of second malignancy^[12]. Rubino et al, 2003^[17] estimated that 53 solid tumors are expected to occur among 10,000 patients after 10 years if they were treated with 100 mCi I131 compared with only 16 if they had been treated with 30 mCi I131. On the other hand, the disadvantages of 30 mCi as a first ablation dose are in the fact that around half of the patients require more treatment, resulting in more periods of replacement therapy withdrawal and associated hypothyroidism in addition to a longer time to achieve complete ablation^[16]. Second, unrecognized metastases may be inadequately irradiated, thus reducing the function of the neoplastic cells but not their growth. These disadvantages encourage us

to save the use of a small ablation dose of 30 mCi for second ablation dose, getting the formerly mentioned advantages of this low dose therapy on a second dose basis post fixed ablation dose 100 mCi of I131.

The reported complete ablation rate of second ablation dose in the current study of 72% , is not significantly different from the successful complete ablation rate after the first dose of I131 in the same group of patients (64%). This may raise the impression that same individuals have no difference as regards complete ablation rates, whether after first or second ablation doses, more affected by individual variable factors including variability in individual NIS expression. Also, no statistically significant difference between the 26 patients (72%) who achieved complete ablation and the remaining 10 patients (28%) who failed to achieve complete ablation as regards age, gender and histopathological details. In this small sample, these findings denote that these factors do not have significant impact on ablation outcome. This may be somewhat different from some previous reports (10). This difference can be explained by the smaller number of patients who received 30 mCi in the current study; however, further studies on higher number of patients may be needed for proper evaluation of these factors. The overall complete ablation rate after both ablation doses of 100 mCi

followed 6 months later by 30 mCi is 90%. This figure is significantly higher than the figure of either first and second ablation dose alone in the current study. This figure was comparable to some reports of successful ablation post single dose of 100 mCi of I131. This high rate was reported in only five out of 26 estimates, indicating that only one in five studies (20%) achieved a very high complete ablation rate ^[12] which may be related to small residual and absent stunning effects as well as other unknown factors related to individual differences. Also, it is comparable to the figure (94%) reported by Zidan et al, 2004 ^[13] who gave I131 ablation doses based on the 24-hours percentage of neck uptake in the postoperative I131 WBS scan.

CONCLUSION:

The use of 30 mCi as a second ablation dose post 100 mCi fixed ablation first dose achieves a successful complete ablation rate of 72%. No statistically significant difference between this figure and the complete ablation figure post first ablation dose of 100 mCi (64%). The overall successful complete ablation outcome rate for the whole group of patients after a total dose of 130 mCi in a 6-month period is 90%. This figure is significantly higher than either complete ablation figure post first or second ablation dose separately.

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