การคำนวณปริมาณสารรังสีไอโอดีน-131 ที่ใช้รักษาผู้ป่วยต่อมธัยรอยด์เป็นพิษ โดยใช้ค่าการทำงานของต่อมธัยรอยด์ที่ 3 ชั่วโมง

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บทคัดย่อ

วัตถุประสงค์: สามารถใช้ค่าการทำงานของต่อมธัยรอยด์ที่ 3 ชั่วโมง (3RAIU) เพื่อมาคำนวณปริมาณสารรังสีไอโอดีน-131 ที่ใช้รักษาผู้ป่วยต่อมธัยรอยด์เป็นพิษ

วิธีดำเนินการวิจัย: ศึกษาผู้ป่วยต่อมธัยรอยด์เป็นพิษจำนวน 361 รายโดยแบ่งเป็น 2 กลุ่ม ผู้ป่วยกลุ่มที่หนึ่งมีจำนวน 180 ราย นำมาหาความสัมพันธ์ระหว่างค่าการทำงานของต่อมธัยรอยด์ที่ 3 ชั่วโมงและ 24 ชั่วโมง (24RAIU) และหาความสัมพันธ์ระหว่าง 24 ชั่วโมงและ 48 ชั่วโมงโดยใช้วิธีทางสถิติคือ linear regression analysis แล้วนำสมการความสัมพันธ์ระหว่าง 3 ชั่วโมงและ 24 ชั่วโมงที่ได้จากผู้ป่วยกลุ่มที่หนึ่งมาพยากรณ์ค่า 24 ชั่วโมง (P24RAIU) โดยใช้ค่า 3 ชั่วโมงที่วัดได้ของผู้ป่วยกลุ่มที่สองจำนวน 181 ราย หลังจากนั้นนำค่า 24 ชั่วโมงที่พยากรณ์ได้และค่า 24 ชั่วโมงที่วัดได้จริงของผู้ป่วยกลุ่มที่สองนี้ มาคำนวณปริมาณสารรังสีไอโอดีน-131 ที่จะให้แก่ผู้ป่วยเหล่านี้

ผลการวิจัย: สมการความสัมพันธ์ระหว่างค่าการทำงานของต่อมธัยรอยด์ที่ 3 ชั่วโมง และ 24 ชั่วโมงของผู้ป่วยกลุ่มที่หนึ่ง คือ 24RAIU = 32.5 + 0.702 (3RAIU) มีค่า r = 0.85 ($p<0.05$) สมการความสัมพันธ์ระหว่าง 24 ชั่วโมงและ 48 ชั่วโมงคือ 48RAIU = 4.77+ 0.888 (24RAIU) มีค่า r = 0.94 ($p<0.05$) สมการความสัมพันธ์ระหว่าง 24 ชั่วโมงที่พยากรณ์ได้และ 24 ชั่วโมงที่วัดได้จริง (24RAIU) ของผู้ป่วยกลุ่มที่สองคือ P24RAIU = 20.6 + 0.685 (24RAIU) มีค่า r = 0.82 ($p<0.05$) และได้นำค่า 24 ชั่วโมงที่พยากรณ์ได้มาคำนวณปริมาณสารรังสีไอโอดีน-131 ในผู้ป่วยกลุ่มที่สองนี้ สมการความสัมพันธ์ระหว่างปริมาณสารรังสีไอโอดีน-131 ที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่พยากรณ์ได้ (predicted dose) และที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่วัดได้จริง (actual dose) คือ predicted dose = 19.23+0.551 (actual dose) ค่า r = 0.86 ($p<0.05$) และพบว่าประมาณ 90% ของผู้ป่วยกลุ่มที่สองนั้นปริมาณสารรังสีไอโอดีน-131 ที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่พยากรณ์ได้และที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่วัดได้จริงนั้นต่างกันไม่เกิน 1 มิลลิคูรี่

สรุป: ปริมาณสารรังสีไอโอดีน-131 ที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่พยากรณ์ได้และที่ได้จากการคำนวณโดยใช้ค่า 24 ชั่วโมงที่วัดได้จริงนั้นมีความสัมพันธ์กันอย่างดีมาก ดังนั้นสามารถใช้ค่าการทำงานของต่อมธัยรอยด์ที่ 3 ชั่วโมง เพื่อมาคำนวณปริมาณสารรังสีไอโอดีน-131 ที่ใช้รักษาผู้ป่วยต่อมธัยรอยด์เป็นพิษ ซึ่งทำให้ผู้ป่วยสามารถได้รับการวัดค่าการทำงานของต่อมธัยรอยด์และรักษาด้วยสารรังสีไอโอดีน-131 ในวันเดียวกัน ทำให้สะดวก ประหยัดเวลาและค่าใช้จ่ายของผู้ป่วย

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Abstract

Therapy Dose Calculation in Hyperthyroidism Using the 3-Hour Early I-131 Uptake Measurements

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Objective: The purpose of this retrospective study was to assess the feasibility of using the radioactive iodine uptake (RAIU) at 3 hours (3RAIU) value in the calculation of ^{131}I treatment dose in hyperthyroidism patients.

Methods: A group of 361 hyperthyroidism patients were randomly divided into two groups (180 and 181 patients). Data from the first group were analyzed to find a mathematical equation describing relationship between the 3RAIU and 24RAIU by linear regression analysis. Similar manner was also performed between 24RAIU and 48RAIU. The predicted 24RAIU and the predicted ^{131}I treatment doses were calculated for the second group of patients based on the relationship equation. Linear regression analysis was also employed to determine statistically significant relationship.

Results: The regression relationship equations were 24RAIU = 32.5 + 0.702 (3RAIU), r = 0.85 ($p<0.05$) and 48RAIU = 4.77+ 0.888 (24RAIU), r = 0.94 ($p<0.05$). The regression relationship equation between P24RAIU and actual measured 24RAIU of the second group patients was P24RAIU = 20.6 + 0.685 (actual 24RAIU), r = 0.82 ($p<0.05$). The P24RAIU was then used to calculate to ^{131}I treatment doses to be given the second group patients. The regression relationship equation between calculated ^{131}I treatment doses from P24RAIU and ^{131}I treatment doses from the actual measured 24RAIU was dose (predict) = 19.23+0.551 dose (actual), r = 0.86 ($p<0.05$). In approximately 90% of the second group patients (N=163), the dose calculated using the P24RAIU was found within a margin of 1 mCi of the dose calculated using the actual measured 24RAIU.

Conclusion: Based on the predicted 24RAIU form 3RAIU, significant correlation between the predicted and the actual prescribed ^{131}I treatment doses was shown. We conclude from our study that the hyperthyroidism patients can possibly treated by ^{131}I in the same day of 3RAIU measurement with reduction in the cost of patient care and without compromising in its quality.

Key words: 3-hour radioactive iodine uptake, hyperthyroidism

Introduction

The measurement of radioactive iodine uptake (RAIU) by the thyroid gland, first introduced in human beings in late 1930s[1], has been widely used in the assessment of thyroid function since 1940[2-6]. Evolution of precise indices of thyroid function, including sensitive measurements of thyroid

stimulating hormone (sTSH), total and free thyroxine (T_4) and triiodothyronine (T_3) and detection of thyroid stimulating immunoglobulin (TSI) in the blood have refined the process of thyroid diagnostic testing replaced the RAIU measurements[7]. At present, RAIU measurement is less commonly relied upon to make a fine distinction between patients who are subtly hyperthyroid versus those who are euthyroid because the normal values for thyroid RAIU changed as dietary iodine[8]. Small day-to-day variations in dietary iodine, provided the total intake of iodine is less than 1 mg per day, have little or no effect on the RAIU[9].

Measurements of RAIU are used to distinguish among different causes of thyrotoxicosis, occasionally for the diagnosis of hyperthyroidism, and to calculate ^{131}I treatment doses for the hyperthyroidism patients[10]. The commonly used benefit of the RAIU measurement is for the calculation ^{131}I treatment doses. The RAIU during the initial 3 to 6 hours after the oral administration of ^{131}I dose reflects mainly the rates of trapping and organification. At 24 hours and later times, the RAIU reflects these functions and the rate of release of radioactive iodine from the gland. Currently, 24RAIU has become the standard indicator for calculation of the ^{131}I treatment doses. The inconvenience and expense often associated with 2 days measurements or 3 days in some institutes.

Measurements of RAIU in the Division of Nuclear Medicine, BMA Medical College and Vajira Hospital were performed at 3 hours, 24 hours and 48 hours after the oral administration of ^{131}I dose. The use of the 48RAIU was only for hyperthyroidism patients who had 48RAIU rapidly decreased from the 24RAIU. Those hyperthyroidism patients will be treated with more doses than 24RAIU calculated doses.

We hypothesized that calculation of ^{131}I treatment doses using 3RAIU measurements, after adjusted with the predictive equation, could be feasibly employed with results comparable to those obtained using the measured 24RAIU results.

Methods

The medical records of 426 patients who were diagnosed by ^{131}I RAIU measurements in the Division of Nuclear Medicine, BMA Medical College and Vajira Hospital between January 1999 and September 2004 were reviewed. The clinical diagnosis of the hyperthyroidism patients was supported by elevation of serum T_4 or T_3 with or without ancillary measurements of TSH. The surgical patients were excluded, but those patients who had received antithyroid drugs and those with previous ^{131}I treatment doses were included in this study. All medications that could interfere with RAIU were stopped 1 to 2 week before RAIU measurements. Among this selected group of patients, 65 of them whom diagnosed rapid turn over (3RAIU to 24RAIU ratio > 1.0) were excluded before being randomly divided into 2 separate groups.

The first group consisted of 180 hyperthyroidism patients (137 female and 43 male, age 45.8±12.58 yrs., range 21-79 yrs.). The second group consisted of 181 hyperthyroidism patients (137 female and 44 male, age 44.98±13.55 yrs., range 21-79 yrs.). The hyperthyroidism patients in these two groups had 3RAIU to 24RAIU ratio < 1.0

All patients were administered a capsule containing approximately 60 μCi of ^{131}I. The RAIU measurements were performed at 3 hours, 24 hours and 48 hours using a scintillation probe with a 2"x2" NaI (Tl) crystal at distance of 22 cm. A standard ^{131}I source was also counted in a tissue-equivalent lucite neck phantom at the same distance. The ^{131}I standard counts and patient counts were calculated according to the following equation:

$$\% \ ^{131}I \text{ RAIU} = \frac{(\text{patient neck counts-thigh counts}) \times 100}{(^{131}I \text{ standard counts-background counts})}$$

Each the hyperthyroidism patient was evaluated by an experienced nuclear medicine physician who

estimated the gland weight by thyroid palpation. The estimated thyroid gland weight was recorded in the chart. The ^{131}I treatment dose calculations in the Division of Nuclear Medicine, BMA Medical College and Vajira Hospital are based on the following formula:

$$\text{Dose to patient (mCi)} = \frac{100\ \mu\text{Ci/g}) \times \text{gland weight (g)}}{\%\ 24\text{RAIU of } ^{131}\text{I} \times 10}$$

Note that the micro curies per gram of thyroid tissue dose may be 150-200 μCi/g for the large gland patients.

Data from the first group of randomly selected patients was analyzed to find a mathematical equation describing relationship between 3RAIU and 24RAIU was determined by linear regression analysis. Similar manner was also performed between 24RAIU and 48RAIU. The predicted 24RAIU and the predicted ^{131}I treatment doses were calculated for the second group of patients based on the relationship equation. Linear regression analysis was also employed to determine statistically significant relationship.

Statistical analysis

A Linear regression was employed for the prediction of correlation between RAIU at different times after ^{131}I administration. A p-value of less than 0.05 was deemed significant.

Results

180 of 361 hyperthyroidism patients were randomly selected to develop a method for defining the relationship between 3RAIU and 24RAIU. A linear regression was plotted between 3RAIU and 24RAIU of the first group patients. The regression equation was 24RAIU = 32.5 + 0.702 (3RAIU). A significant correlation was found with r = 0.85, p < 0.05 (Fig 1).

Additionally, a linear regression was plotted between 24RAIU and 48RAIU. The regression relationship equation was 48RAIU = 4.77 + 0.888 (24RAIU). A strong correlation was also observed with r = 0.94, p < 0.05 (Fig 2).

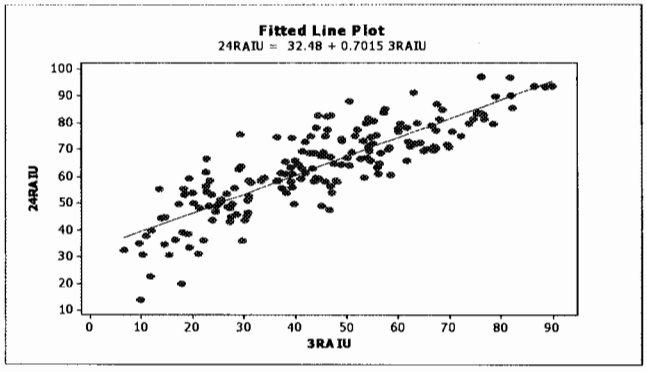

Fig 1: The relationship between 3RAIU and 24RAIU

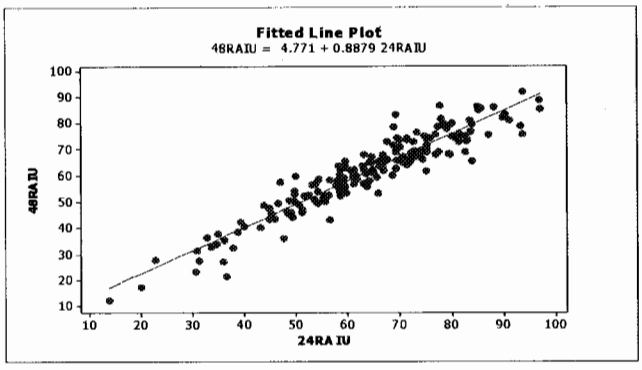

Fig 2: The relationship between 48RAIU and 24RAIU

By using the equation: 24RAIU = 32.5 + 0.702 (3RAIU), 24RAIU was predicted from 3RAIU in the second group of 181 hyperthyroidism patients. The regression relationship equation between P24RAIU and actual measured 24RAIU was P24RAIU = 20.6 + 0.685 (actual 24RAIU). A significant positive correlation was found with r = 0.81, p < 0.05 (Fig 3).

The P24RAIU was then used to calculate the therapy doses to be given in these patients. The regression relationship equation between calculated ^{131}I treatment doses from P24RAIU and ^{131}I treatment doses from the actual measured 24RAIU was dose (predicted) = 19.23+0.551 dose (actual). Our result also showed strong correlation between

the predicted ^{131}I treatment dose and the actual ^{131}I treatment dose ($r = 0.86$, $p < 0.05$) (Fig 4).

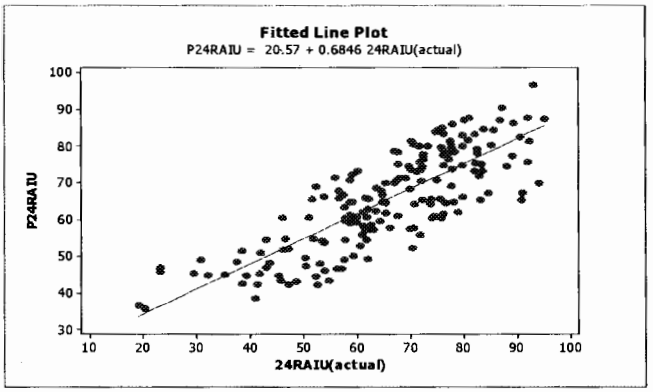

Fig 3: The relationship between P24RAIU and actual 24RAIU

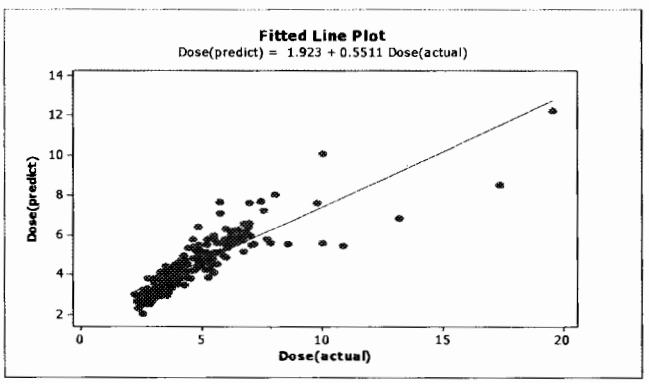

Fig4: The relationship between the predicted dose and the actual dose

Discussion

Approaches to selecting treatment doses for management of the hyperthyroidism patients vary widely. In some institutions, patients were treated by a fixed number of radioactivity (millicuries) while in other institution; an effort has been made to calculate the delivered dose in term of micro curies per gram of thyroid tissue[12]. The number of micro curies per gram of thyroid tissue was reported with range from 50 to 200 or more.

Presently, the Division of Nuclear Medicine, BMA Medical College and Vajira Hospital employed the method of calculating ^{131}I treatment dose based on the 24RAIU. This method requires that the patients need to come back for 24RAIU and 48RAIU measurements which take time and may be inconvenient for some patients. Our retrospective data analysis showed that 3RAIU can be used to predict both 24RAIU and 48RAIU with statistically confidence. In the 426 hyperthyroidism patients who diagnosed with ^{131}I RAIU measurements in our institute, we found that relationship between 48RAIU and 24RAIU were strongly correlated ($r = 0.94$, $p<0.05$). Among these patients in our study, those who had 48RAIU rapidly decreased 24RAIU (more 10%) was only 0.7% (N=3). Consequently, the 48RAIU measurements may be unnecessary.

Moreover, approximately 90% of the second group patients (N=163), the dose calculated using the P24RAIU was found within a margin of 1 mCi of the dose calculated using the actual measured 24RAIU. This clearly showed that we can use the 3RAIU to predict 24RAIU and calculate for the treatment dose without having the patients back for next day measurement. Our result was similar to both Vemulakonda[13] and Hayes[14] group whose correlation between the actual and the predicted treatment dose ranges from 0.82-0.97. The difference in our patients was that we did not exclude those with previous ^{131}I treatment and the treatment dose was calculated based on the prediction of 24RAIU from 3RAIU.

Theoretically, using only the 3RAIU to estimate the 24RAIU from which the ^{131}I treatment dose would be determined might result in ineffective treatment for the rapid radioiodine turn over patients. This possibility must be weighed against the cost saving and patient convenience using the 3RAIU calculated doses in the 85% of patients without rapid radioiodine turn over. However, our retrospective study showed that there was about 15% (N=65) of the patients had 3RAIU to 24RAIU ratio > 1.0 (rapid radioiodine turn

over). Similar result was reported by Aktay group who found 15% incidence rate in 433 patients and was associated with a near 50% ^{131}I treatment failure rate, whereas a 3RAIU to 24RAIU ratio <1.0 was associated with only an 11% failure rate[15]. Our results suggested that using the 3RAIU alone to predict the 24RAIU and the 48RAIU and calculate the ^{131}I treatment dose was practical since this will benefit larger portion of patients (85%) who expected to have a high treatment success rate.

Conclusion

The hyperthyroidism patients can be possibly treated by ^{131}I in the same day of the radioactive iodine uptake at 3 hours measurement with reduction in the cost of patient care and without compromising in its quality.

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