DETERMINATION OF NORMAL THYROID TECHNETIUM-99M UPTAKE VALUE IN A SINGLE CENTRE PAKISTANI POPULATION

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ABSTRACT

Objective: To determine the normal value of thyroid Technetium-99m uptake value in a single centre Pakistani population.
Study Design: Cross-sectional study.
Place and Duration of Study: Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi, from Feb 2019 to Apr 2020.
Methodology: A total of 90 patients who presented to Nuclear Medical Centre for parathyroid dual radiopharmaceutical scintigraphy were included in study and selected by non-probability consecutive sampling technique. Thyroid uptake studies were calculated via gamma camera acquisition. Pre injection counts were taken from the Technetium-99m pertechnetate filled syringe, thyroid counts were taken from the anterior thyroid image 20 minutes post injection and to look for any residual radiopharmaceutical counts of the empty syringe were also taken.
Results: Out of total of 90 patients, 32 (35.6%) were male while 58 (64.4%) were female with male to female ratio of 1:2. The mean age was 38.4 ± 12.7. Mean Thyroid Stimulating Hormone values were 1.6 ± 0.8 and mean T4 values were 11.9 ± 3.5. The 5^{th}-95^{th} percentile range was 0.4-2.2% and median was 1.2%. The interquartile range was calculated to be 0.9-1.5%.
Conclusion: Normal value of thyroid Technetium-99m uptake value in a single centre Pakistani population values varies significantly as compared to global figures i.e. 0.3-4.5% and is different than the one used in our own department i.e. 0.5-2.0%.

Keywords: Radio-iodine uptake, Technitium-99m, Thyroid uptake.

INTRODUCTION

The thyroid gland is a vital organ of the endocrine system. The main role of thyroid gland is regulating metabolism, growth and development of the human body by the production of thyroid hormones. Two forms of thyroid hormones are secreted by the thyroid gland i.e. Thyroxine (T4) and Triiodothyronine (T3). T4 is the main form of thyroid hormone released to the blood and has a longer half-life than T3. Thyroid hormones help regulate the basal metabolic rate as well as influence many functions, such as physical growth, development, adolescence, organ function, fertility and body temperature. Out of 80-90% of thyroid hormones secreted from the gland is T4 and about 10-20% is T3. Iodine from food is absorbed in the gut, transported to the thyroid gland and is used for production of thyroid hormone[1]. This led to the use of radioactive iodine for scintigraphy and thyroid uptake studies to assess thyroid function and morphology.

Thyroid disorder are not uncommon in Pakistan however there is lack of statistical evidence. Thyroid gland function and anatomy can be evaluated using scintigraphy and uptake studies. The main purpose of thyroid uptake is to differentiate between different types of thyrotoxicosis and to calculate dose of Iodine-131 for Radioiodine Ablation in benign diseases. Thyroid uptake can be performed with radiopharmaceuticals such as I-131, Technetium-99m (99mTc) and iodine -123 (I-123). I-131 was the first radioisotope used for radioiodine ablation. It is the main radiopharmaceutical used for thyroid uptake in our setup, however it is least used in developed countries nowadays. As an isotope of the stable iodine used by the thyroid for organification it has high accuracy in determination of thyroid uptake. But I-131 has few disadvantages. These include administration of high radiation doses which has its own significant adverse effects. Secondly as the readings have to be taken 24 hours post administration, which is inconvenient to some patients visiting from far flung areas. Its main gamma photon has high energy (364 keV) that is ineffectively collimated by most conventional gamma cameras, its images are of poor quality and needs prior iodine restriction in diet. In addition to this it also emits β- radiation which increases the radiation dose of patients (1300 rads per milli curie of I-131 to thyroid at 25% uptake value)[2].

Iodine-123 (I-123) is a good substitute for I-131 because it has a shorter half-life (13 hours), a gamma photon suitable for imaging using conventional gamma cameras i.e. 159 keV and it does not emit any β-radiation. However, it is produced in a cyclotron which

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is not available in every setup and has a high cost. Secondarily due to short half-life transportation to different centers from the production area is limited. In addition, contaminants like I-124 and I-125 may be formed depending on the procedure of production and these may increase the dosimetry and cause image degradation.

99mTc pertechnetate is the most common radiopharmaceutical used all over the world. The pertechnetate ion is injected into the blood, from where the iodide concentrating mechanism transports it into the thyroid tissue, likely because it has the same charge and is the same size as iodide. However, it is not metabolized and therefore, rapidly diffuses out of thyroid cells[3]. 99mTc has several advantages over I-131 including its short half-life i.e. 6 hours resulting in acquiring early thyroid uptake, it stays in the gland for a short time so imaging is performed early, is easily available through a generator and emits no β-emission providing much less radiation dose to the patient[4]. 99mTc thyroid uptake can be performed without iodine intake restriction and can be done immediately after diagnosis of hyperthyroidism. However, it has been found that thyroid uptake differs with geographical location[5].

The rationale of study was to determine the range of 99 mTc thyroid uptake so that it can be used instead of I-131 which has many disadvantages i.e high radiation dose to the patient, beta emission and requirement of 24-hour uptake study for results. We are currently using I-131 for thyroid uptake in our setup.

METHODOLOGY

This cross-sectional study was conducted at Nuclear Medical Center, Armed Forces Institute of Pathology, Rawalpindi, from February 2019 to April 2020. A total of 90 patients, who visited the Nuclear Medical Center, Armed Forces Institute of Pathology for parathyroid scintigraphy during study period were included in this study. All patients were selected by non-probability consecutive sampling technique. Informed written consent was sought from all the participants and all possible due care was taken care off.

As per dual radiopharmaceutical agent protocol for thyroid, they underwent thyroid scintigraphy with 99mTc pertechnetate before 99mTc Sestamibi scan. The individuals were evaluated by taking a thorough medical history, history of iodinated contrast radiographic procedures in the last six months, history of previous medication, physical examination especially related to thyroid and laboratory investigation to exclude those with renal, cardiac or thyroid diseases that may interfere with normal thyroid uptake. Individuals with history of functional thyroid disorders, patients who has been taking Thionamides or Iodine containing drugs like Amiodarone, having history of radioiodine uptake or had undergone iodine contrast studies in last 6 months were excluded from the study. Thyroid function was evaluated by laboratory assessment via measurements of serum TSH and T4 to look for any thyroid functional disorders. Those with deranged thyroid function tests were ruled out of the study sample. Prior approval for conducting the study was acquired from Research, Ethics and Academic Department (READ) of Armed Forces Institute of Pathology vide READ-IRB Certificate no. FC-NMC 18-10/READ-IRB/19/179.

Each participant received 2 milli Curie (mCi) of 99mTc pertechnetate (74MBq) intravenously. Cor Cam Gamma Camera System (DDD-Diagnostic Denmark) was used for all the images. Full syringe counts were taken before injecting the radiopharmaceutical and empty syringe counts were taken after injecting the radiopharmaceutical to assess residual 99mTc pertechnetate in the syringe for measuring exact counts of 99mTc administered. After injecting the radiopharmaceutical an image of the site of the injection was obtained to look for any extravasation of 99mTc pertechnetate that may interfere with the thyroid percent uptake calculation. Anterior spot views of the neck were taken with a high resolution parallel whole collimator at 20 minutes post injection. A 128 × 128-pixel matrix and a zoom of 1.0 was selected from the computer for the images of anterior thyroid. Each image was acquired for 1 minute (fig-1). Processing was done with Segami OASIS V1. 9 software (Segami Corporation USA) by drawing a custom region of interest (ROI) on the thyroid and the background as shown in fig-1. The percent thyroid uptake was calculated by using thyroid counts, full syringe counts and counts taken from the syringe after

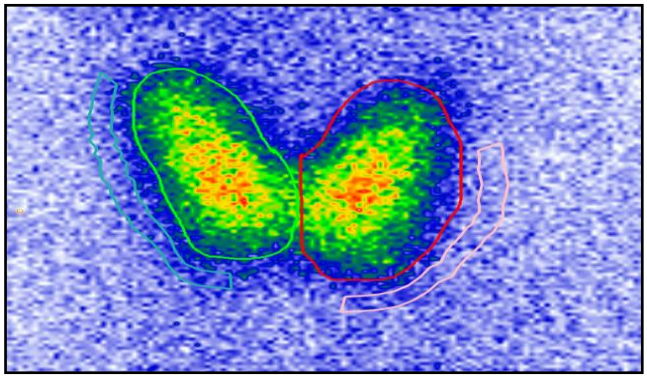

Figure-1: Region of interest drawn on an anterior thyroid image.

injecting the radiopharmaceutical. The parathyroid imaging with sestamibi performed afterwards was not contributory to the results.

Data were entered and analyzed with SPPS-25. The percent thyroid uptake frequencies were analyzed and the 5th - 95th percentile was taken as range.

RESULTS

Out of total 90 patients, 32 were male while 58 were female with male to female ratio of 0.55. The mean age was 38.4 ± 12.7 with a range of 18-75 years while mean TSH values were 1.6 ± 0.8 and mean T4 values were 11.9 ± 3.5. Mean age for the males (32) was 37.7 ± 15.5 and females (58) was 38.8 ± 10.9. The 5th - 95th percentile range was calculated to be 0.4-2.2% for all the patients (n=90). Median normal 99mTc uptake was found to be 1.2 % and the interquartile range was 0.9-1.5 %. For male patients the median normal 99mTc uptake was 1.1%, the 5th-95th percentile range was 0.36-2.0% and the interquartile range was 0.72-1.3%. Similarly, in female population the median normal 99mTc thyroid uptake was 1.2%. The 5th-95th percentile range was 0.4-2.5% and the interquartile range was 0.8-1.5%. The relationship between age and uptake in both male and female sample are demonstrated in figure-1 & 3.

Figure-2: Relationship between age of patients and uptake in females.

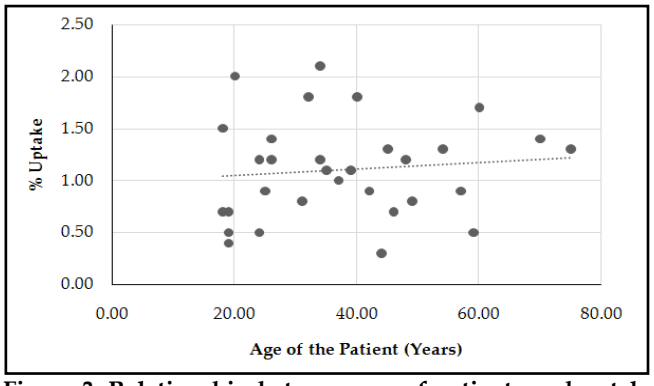

Figure-3: Relationship between age of patients and uptake in males.

The Pearson correlation analysis for female population (fig-2) show a non-significant correlation between age of the patients and uptake values, r=-0.17, n=58, *p*=0.18 (two-tailed) and that for male population (fig-3) also show non-significant correlation between age and uptake values, r=+0.10, n=32, *p*=0.57 (two-tailed).

DISCUSSION

Geographical location-based reference range for thyroid uptake of 99mTc pertechnetate are rarely found in literature and the normal reference values for thyroid uptake of 99mTc pertechnetate changes significantly from time to time[6,7]. 99mTc for thyroid uptake is now commonly used in several countries but fluctuations in the normal reference values of 99mTc thyroid uptake has been documented at different centers[8]. The normal value for 99mTc uptake recommended globally is 0.3-4.5%[9]. The normal reference range of 99mTc followed in our setup is 0.5-2.%. It has been generally recognized that each nuclear medicine department must found its own criteria to describe the normal for better assessment of thyroid uptake studies[10].

This is the first study conducted in our setup for the evaluation of reference range for 99mTc thyroid uptake. The study revealed that the lower value of the reference range of 99mTc thyroid uptake is similar as compared to the values worldwide however the upper value of the reference range is much lower compared to recommended normal values worldwide 0.3-4.5.9 We also found that the reference range of 99mTc thyroid uptake value is slightly different than that used in our department i.e. 0.4-2%. The reasons for these lower values of 99mTc thyroid uptake are not clear from the study. Possible reasons may be the popularity of using iodinated salts in recent years and geographical variation of 99mTc thyroid uptake. The results in our study were comparable to studies done in recent years for 99mTc thyroid uptake. Macuely *et al* performed a study in United Kingdom (UK) in which the reference range was calculated to be 0.2-2%[11], which was lower than the range already used in UK. The study also suggested requirement of periodic studies to determine the normal uptake range. In Namibia a study was performed by Hamunyela *et al* that included 76 healthy euthyroid individuals of Namibian population who volunteered for the project and the reference range of thyroid 99mTc uptake was found to be 0.15-1.69% which was significantly lower than already used[12]. The thyroid uptake of 99mTc pertechnetate ranged from 0.4-1.7% in a study in Brazil performed by Ramos CD *et al* in the state of So Paulo[13]. The study revealed that

the upper limit is lower than the one previously used. It was also observed that studies done in recent times for calculating normal 99mTc thyroid uptake show significantly less range than older studies i.e. a study done by Atkins *et al*[14], (USA) calculated a range of 0.5–4.0 and study done in 1972 by Hurley *et al*[15], (USA) described a range of 0.24–3.4. Similarly, a study in UK by De-Garreta *et al*, described a range of 0.4–3.0.16

The range in females was found to be slightly higher than males as shown in Fig-1 & 2. Similar findings were observed by Damayanti *et al* suggesting a range of 2.1-2.55% in normal women and 1.49-1.74% in normal men[17]. Age of the patients does not significantly influence thyroid uptake of 99mTc pertechnetate.

The mechanism of 99mTc uptake by the thyroid gland is the same as for radioiodine uptake[18]. When there is Iodine deficiency, increased amount of thyroid stimulating hormones are released by the pituitary gland to maintain the circulating levels of T4 within normal limits which in turn stimulate the increased uptake of radio iodine/99mTc pertechnetate whenever administered[19]. When there is iodine deficiency the thyroid uptake of radioiodine is increased. With the increase in use of iodinated salts and dietary products rich in iodine the thyroid uptake of radioiodine has shown decrease in recent years. Ballas *et al* conducted a study to re-establish radioiodine uptake of thyroid in recent years and found considerable decrease in the radioiodine as compared to previously listed in literature[20]. The same mechanism may be responsible for low thyroid uptake of 99mTc pertechnetate in recent studies.

Due to obvious advantages, I-131 can be replaced with 99mTc as it uses the same mechanism of thyroid uptake[18]. It is useful in assessing patients known to have hyperthyroidism as well as acquiring uptake studies at the same time it's convenient for the patients and compliance rate is better.

LIMITATION OF STUDY

This study was conducted in a limited set up in Nuclear Medical Center, Armed Forces Institute Pathology Rawalpindi so its results may not be a true representation of national population. The study does not include hyperthyroid patients, so it cannot comment on the calculation of dose for radioiodine ablation using 99mTc uptake.

CONCLUSION

I-131 use for thyroid scintigraphy and uptake is practically declining all over the world[21]. Its best alternative I-123 being expensive and not easily available. 99mTc is favorable, affordable, safe, less time consuming and easily available. Our study determined the normal 99mTc thyroid uptake for our own department and surrounding population. Departmental based 99mTc uptake standardization can make 99mTc the best option for thyroid scintigraphy.

CONFLICT OF INTEREST

This study did not have any conflict of interest to be declared by any author.

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