Study of ^{99m}Tc Pertechnetate Radiopharmaceuticals in Relation to Thyroid Hormone for Toxic and non-Toxic Diffuse Goiter

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ABSTRACT

Abnormalities of the thyroid gland in the form of enlargement of the thyroid gland are called a goiter. Goiter is divided into two types, namely toxic and non-toxic diffuse goiter. Diagnosis could be done with thyroid scan (in vivo) and test for thyroid hormone value (in vitro). Thyroid scan is applied by giving injection of ^{99m}Tc Pertechnetate as much as 2 - 5 mCi intravenally in the arm and then thyroid gland and salivary glands imaging were conducted in the fifth minute, tenth minute and fifteenth minute using gamma camera. Thyroid hormones test in blood is done with radioimmunoassay method. The same pattern showed the accumulation polad of the radioactive number from quotation of salivary glands. The accumulation percentage activity of ^{99m}Tc Pertechnetate in thyroid gland for the case of toxic diffuse goiter is larger than the case of non-toxic diffuse goiter. The results of this study indicate that the predictors for the case of toxic diffuse goiter could be characterized by high thyroid uptake which the the value of T_3 hormone $\geq$ 3.3 ng/dl, the value of T_4 hormone $\geq$ 165 nmol/l, and the value of TSH hormone $\leq$ 0.2 µIU/ml. While the case of non-toxic diffuse goiter could be characterized by low thyroid uptake which the value of T_3 hormone $\geq$ 1.2 ng/dl, the value of T_4 hormone $\geq$ 90 nmol/l, and the value of TSH hormone $\leq$ 1.8 µIU/ml.

INTRODUCTION

Nuclear medicine studies are more likely to be used to evaluate a wide range of congenital conditions but also can be helpful for evaluating acquired conditions such as infection, cancer, and trauma [1]. One of the organs that can be studied with nuclear medicine studies is the thyroid gland. Assessment of thyroid gland function in nuclear medicine can be used to establish the diagnosis of dysfunction, such as hyperthyroidism, hypothyroidism, thyroiditis, thyroid nodules and thyroid cancer abnormality [2].

Kandeel *et al* [3] studied post-operative patients who showed indications of hyperthyroidism, the uptake in the thyroid tissue remaining catch fewer radiopharmaceutical compared with salivary glands. Stephen's *et al* [4] reported the value of the average radiopharmaceutical uptake in the parotid gland and the submandibular gland were 0.30 % and 0.17 % respectively. The study was carried out for 15 minutes, and the result showed that the radiopharmaceutical activity in the parotid gland was still increasing, while in the submandibular gland has reached the highest peak or already declining.

Abnormalities of the thyroid gland may enlarge gland and changes the work function of the normal state. Normal thyroid gland function is characterized by the percentage uptake (catch) radiopharmaceutical approximately 1.6 to 7.6 % [5]. This study was conducted in patients with thyroid gland disorders, both toxic and non toxic diffuse goiter.

EXPERIMENTAL METHODS

The number of patients studied were 70 people with diffuse goiter cases (35 toxic and 35 non toxic) who underwent examination in vivo (thyroid scan) and in vitro (test hormone, T_3, T_4 and TSH in the blood).

Radiopharmaceutical used for in vivo is ^{99m}Tc Pertechnetate. 2-5 mCi of ^{99m}Tc Pertechnetate is injected through an intravenous, and then imaging was performed using a gamma

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camera. Imaging time variation of the thyroid gland and salivary glands were conducted at 5, 10 and 15 minutes after the injection.

Radiopharmaceutical accumulation in the thyroid gland are called the thyroid uptake. Thyroid uptake calculations can be done by manual calculation [6].

Count values of thyroid gland obtained from the ROI (Region of Interest) in the thyroid gland with a size corresponding to the shape of the gland. Background count is obtained from the ROI outside the thyroid gland with a size of 1 x 1 cm. Salivary glands were examined by ROI footage, on the left and right parotid gland with a size of 1.5 x 1.5 cm, on the left and right submandibular gland and the sublingual gland with the size 1 x 1 cm.

Figure 1 shows the image before and after it is created ROI.

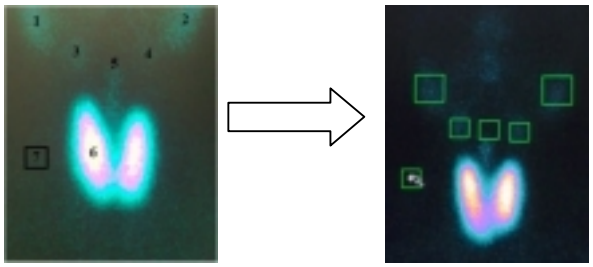

Fig. 1. Manufacture of ROI to get the value of the count. (1) Right parotid gland, (2) Left parotid gland, (3) Right submandibular gland, (4) Left submandibular gland, (5) Sublingual gland, (6) The thyroid gland, (7) Background.

In vitro techniques used to determine levels of thyroid hormones in the blood. Radioisotopes ^{125}I is mixed with the kit farmaka and blood serum of patients and then enumerated using a gamma counter [7]. The results of in vitro examination is the thyroid hormone (T_3, T_4 and TSH) in blood. From both of the technical tests, further correlation was searched using diagnostic tests.

Diagnostic test consists of the gold standard of thyroid scan from in vivo technique, and examination test of the thyroid hormone from in vitro.

The both of these techniques were compared with the Cut of Point value (COP). COP is an index that is used as the boundary between normal and abnormal from the case, or the limit value of positive test results and negative test results. COP value is determined based on reference values from the results of examination [8]. Then, the next step is determine diagnostic value with 2 x 2 diagnostic studies table. The table consists of the gold standard and test results, which produce some value, such as true positive, false positive, false negative and true negative [9]. All of the value can be used to determine the sensitivity and specificity values by manual calculation.

A function of sensitivity and specificity value can be used to found the correlation of these examination techniques using Receiver Operating Characteristic curve (ROC). The point of intersection between sensitivity and spesificity value are called a cutoff. Cutoff with high sensitivity values can be used as a decision making process for the purpose of treatment and care of patients, whereas the cutoff with a high specificity value can be used as the final stage of diagnosis [8].

RESULTS AND DISCUSSION

The thyroid uptake

The mean changes in the thyroid uptake percentage for the toxic and non-toxic diffuse goiter which occurred at 5, 10 and 15 minutes after radiopharmaceutical injection was shown in Fig. 2.

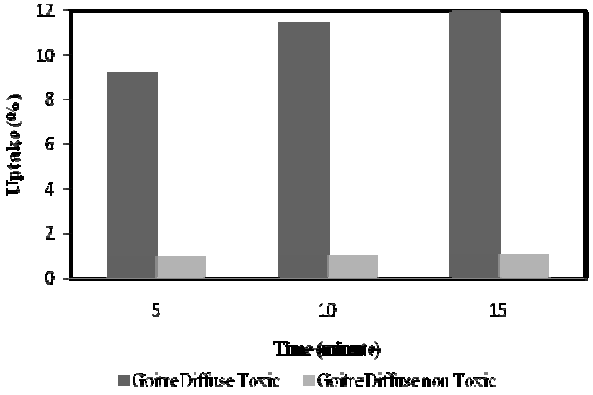

Fig. 2. The mean change of uptake percentage for toxic and non-toxic diffuse goiter.

Figure 2 showed that the both cases had a mean percentage of ^{99m}Tc-pertechnetate uptake in the thyroid gland were increasing for a longer time interval. Since the ^{99m}Tc pertechnetate is not absorbed by the thyroid gland, so it can follow the body's metabolic processes. Percentage uptake for toxic diffuse goiter is greater than non-toxic diffuse goiter case. This is due to the hiperfunction performance of the thyroid gland for the toxic diffuse goiter case.

The accumulation count of ^{99m}Tc pertechnetate on salivary glands

Average value of the radioactivity accumulation in the salivary glands for toxic diffuse goiter were shown in Fig. 3 and Fig. 4.

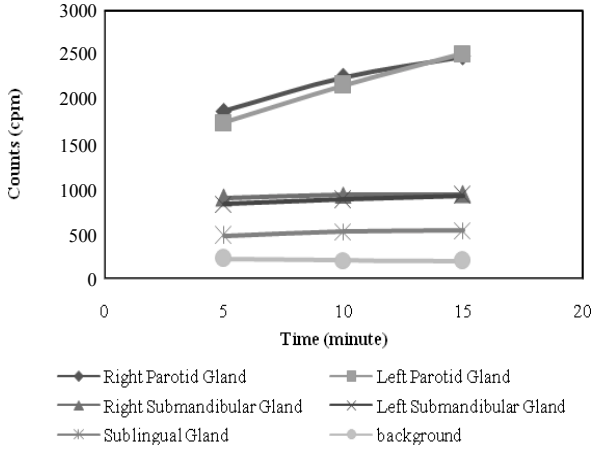

Fig. 3. The mean change in the accumulation count of radiopharmaceutical in the salivary glands for toxic diffuse goiter.

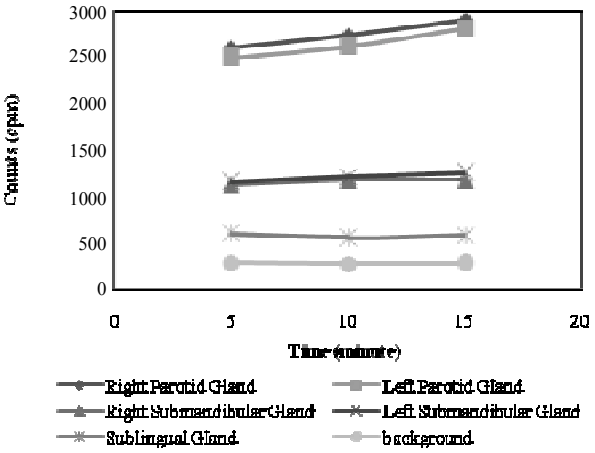

Fig. 4. The mean change in the accumulation count of radiopharmaceutical in the salivary glands for non-toxic diffuse goiter.

Between the toxic and non toxic diffuse goiter have some difference. The difference lies in the accumulation count of radiopharmaceutical between submandibular and parotid gland. In toxic diffuse goiter, many radiopharmaceutical activity accumulates in the thyroid gland so that the radiopharmaceutical is only slightly towards the salivary glands. It's different for non-toxic diffuse goiter, radiopharmaceutical activity uniformly distributed in each gland. The differences of ^{99m}Tc Pertechnetate accumulation count obtained from the manufacture of ROI in the salivary glands depends on the size and performance (function) gland.

The accumulation activity of ^{99m}Tc pertechnetate in thyroid gland

In this research, the value count of 1 mCi ^{99m}Tc Pertechnetate by a gamma camera was equivalent to 261,111 cpm. Figure 5 shows the number of radiopharmaceutical activity in the thyroid gland at 5, 10 and 15 minutes.

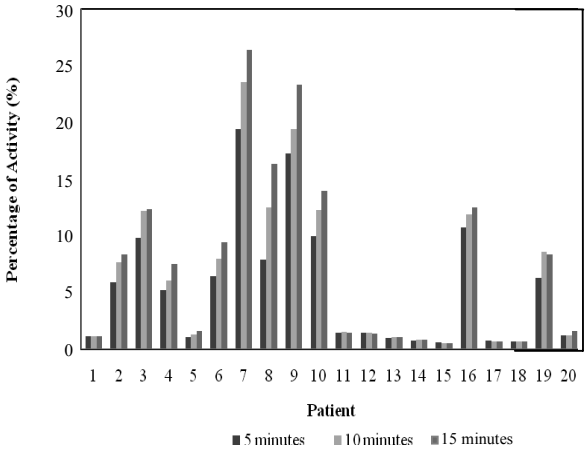

Fig. 5. Percentage of radiopharmaceutical activity in the thyroid gland of patients for toxic and non-toxic diffuse goiter.

The calculation of this activity aims to determine the activity of ^{99m}Tc -pertechnetate in the thyroid gland from a total injection. From Fig. 5, it can be seen that toxic diffuse goiter is demonstrated in patients 2, 3, 4, 6, 7, 8, 9, 10, 16 and 19, while the other is non-toxic diffuse goiter. The results obtained by calculating the mean value of the accumulated percentage of ^{99m}Tc pertechnetate showed that the activity in toxic diffuse goiter larger than non-toxic diffuse goiter. In toxic diffuse goiter at 5,10 and 15 minutes were 9.89, 12.22, and 13.85 % respectively, while for non-toxic diffuse goiter at 5, 10 and 15 minutes were at 1.02, 1.05 and 1.11 % respectively.

The differences of accumulation from ^{99m}Tc Pertechnetate activity is depending on the size of the gland as well as the ability (function) gland. The size of the thyroid gland for toxic diffuse goiter is larger and more responsive than the thyroid gland for non-toxic diffuse goiter.

Correlation of thyroid hormone levels and thyroid uptake

This study present thyroid uptake value and hormone value (T_3, T_4 and TSH hormones in the blood). Normal T_3 hormone ranged

from 1.00 to 3.00 ng/dl, normal T_4 hormone ranged from 55 to 170 nmol/l and normal TSH hormone ranged from 0.27 to 3.75 μIU/ml [5].

The case of toxic diffuse goiter

Correlation of thyroid uptake with T_3 hormone

Correlation of thyroid uptake with T_3 hormone can be determined using the table COP analysis, the ROC curve and the curve of sensitivity and specificity. COP values used in this correlation range from 1.9 to 4.2 with interval 0.1. Figure 6 shows an uneven distribution of patient data at each COP indexes that have been determined.

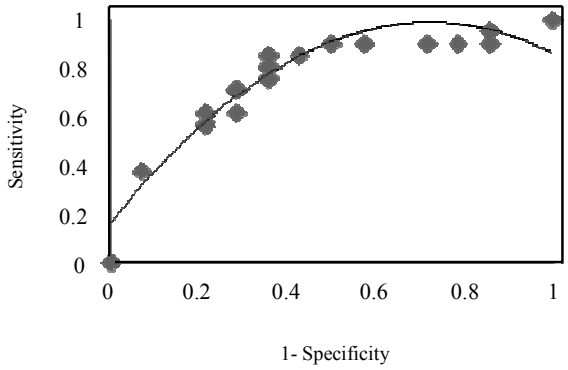

Fig. 6. Sensitivity and (1-specificity) of diagnostic tests between the thyroid uptake and T_3 hormone.

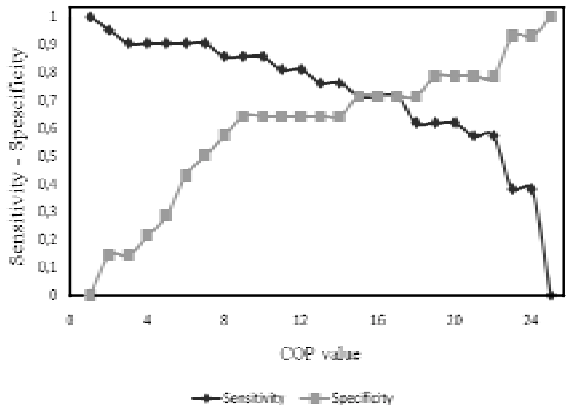

Fig. 7. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and T_3 hormone.

From Fig. 7, it can be seen on the cut off values at the point 15 on the COP ≥ 3.3 that the sensitivity, specificity, positive and negative expected value were 71, 71, 79 and 63 % respectively. Optimal cutoff point was used as a benchmark determination of patients diagnosed as having case of toxic diffuse goiter with high thyroid uptake and T_3 hormone ≥ 3.3 ng / dl.

Correlation of thyroid uptake with T_4 hormone

COP values are used to determine correlation of thyroid uptake with T_4 hormone was 85 to 220 with interval 5. The correlation between sensitivity and specificity values of COP calculation is described in the form of curves such as Fig. 8. It can be seen that some sensitivity and specificity values were in the same range, therefore not all points were formed in the surrounding withdrawal line.

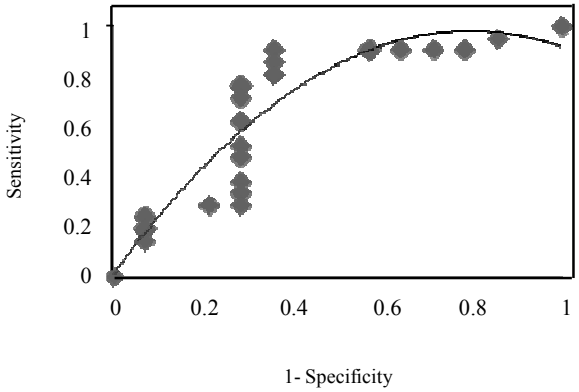

Fig. 8. Sensitivity and (1-specificity) of diagnostic test between the thyroid uptake and T_4 hormone.

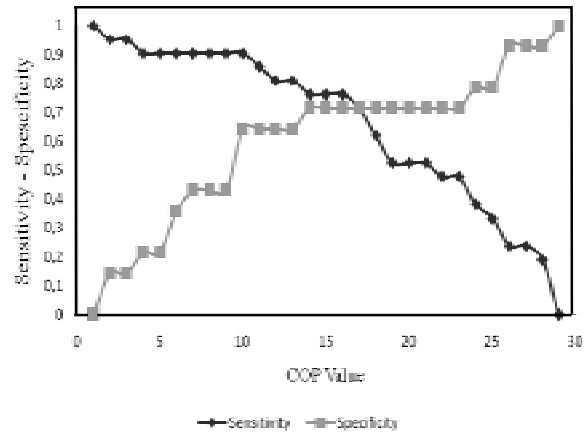

Fig. 9. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and T_4 hormone.

Cutoff values obtained from Fig. 9 at the point 17 on the COP ≥ 165 showed that the sensitivity, specificity, positive and negative

expected value were 71, 71, 79 and 63 % respectively. Optimal cutoff point was used as a benchmark determination of patients diagnosed with toxic diffuse goiter with high thyroid uptake and T_4 hormone $\geq$ 165 nmol/l, then the patient has high possibility had toxic diffuse goiter.

Correlation of thyroid uptake with TSH hormone

COP value are used in this correlation value from 0.09 to 0.33 with interval 0.01. The correlation between sensitivity and specificity values of COP calculation is described in the form of curves such as Fig. 10.

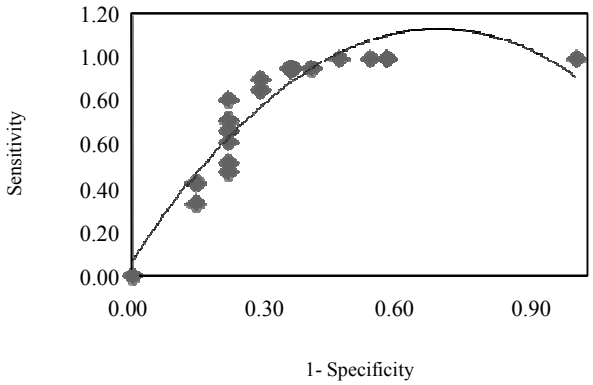

Fig. 10. Sensitivity and (1-specificity) of diagnostic test between the thyroid uptake and TSH hormone.

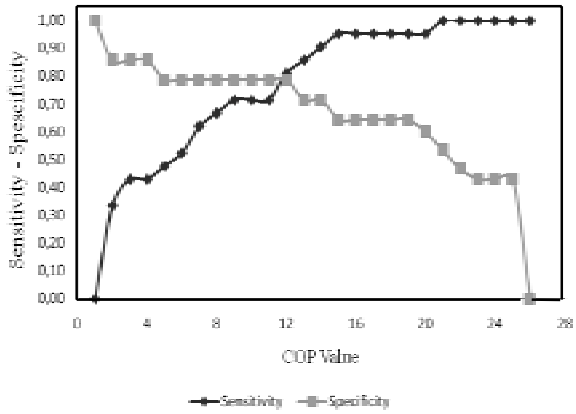

Fig. 11. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and TSH hormone.

Cutoff value obtained from Fig. 11 at the point 12 on the COP $\leq$ 0.2 showed that the sensitivity, specificity, positive and negative expected value were 81, 79, 85 and 73 % respectively. Optimal cutoff point can be used as a benchmark determination of patients diagnosed with toxic diffuse goiter with high thyroid uptake and TSH hormone $\leq$ 0.2 µIU/ml, then the patient should take the treatment for this case.

The case of non-toxic diffuse goiter

Correlation of thyroid uptake with T_3 hormone

COP value are used to determine correlation of thyroid uptake with T_3 hormone is 0.55 to 1.6 with interval 0.05. From the value of COP, then it is made the ROC curve as in Fig. 12.

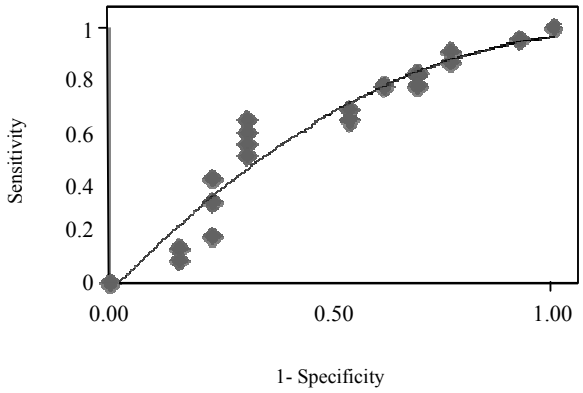

Fig. 12. Sensitivity and (1-specificity) of diagnostic tests between the thyroid uptake and T_3 hormone.

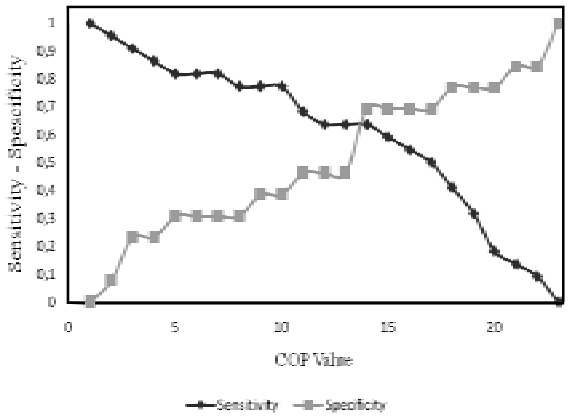

Fig. 13. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and T_3 hormone.

Curve intersection point of sensitivity and specificity of diagnostic tests between the thyroid uptake with T_3 hormone are shown in Fig. 13. Based on Fig. 13, it can be seen on cutoff value at the point 14 on COP $\geq$ 1.2 that the sensitivity, specificity, positive and negative expected value were 64, 69, 78 and 53 % respectively. Optimal cutoff point can be used as a benchmark determination of patients diagnosed. If a person acquired with a low

thyroid uptake and T_3 hormone ≥ 1.2 ng/dl, the patient can be diagnosed as non-toxic diffuse goiter.

Correlation of thyroid uptake with T_4 hormone

COP value are used to determine correlation of thyroid uptake with T_4 hormone is 45 to 130 with interval 5. The results of calculation of sensitivity and specificity values of COP values shown in Fig. 14.

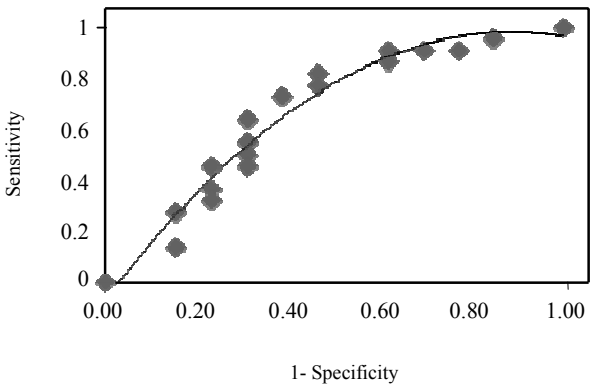

Fig. 14. Sensitivity and (1-specificity) of diagnostic test between the thyroid uptake and T_4 hormone.

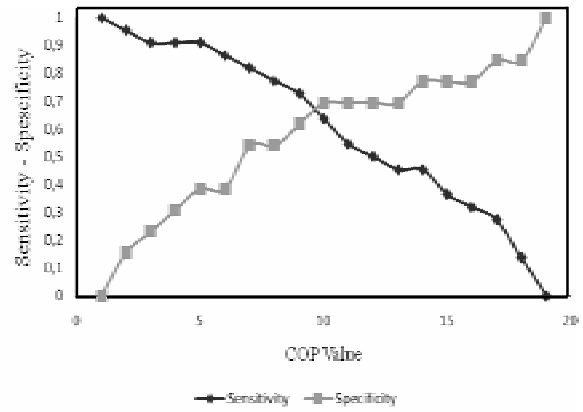

Fig. 15. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and T_4 hormone.

Curve intersection point of sensitivity and specificity of diagnostic tests between the thyroid uptake with T_4 hormone are shown in Fig. 15. It shows the cutoff value obtained at the point 10 on COP ≥ 90 that the sensitivity, specificity, positive and negatif expected value were 64, 69, 78 and 53 % respectively. If someone is detected with low thyroid uptake and T_4 hormone ≥ 90 nmol/l, it can be diagnosed as non-toxic diffuse goiter.

Correlation of thyroid uptake with TSH hormone

COP value are used to determine correlation of thyroid uptake with TSH hormone were in the range 0.6 to 3.8 with interval 0.2. The results of calculation of sensitivity and specificity values of COP values shown in Fig. 16.

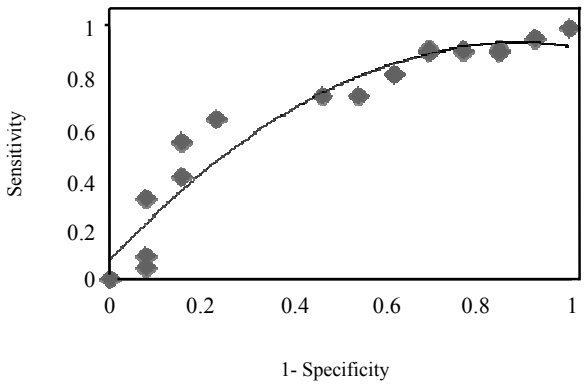

Fig. 16. Sensitivity and (1-specificity) of diagnostic test between the thyroid uptake and TSH hormone.

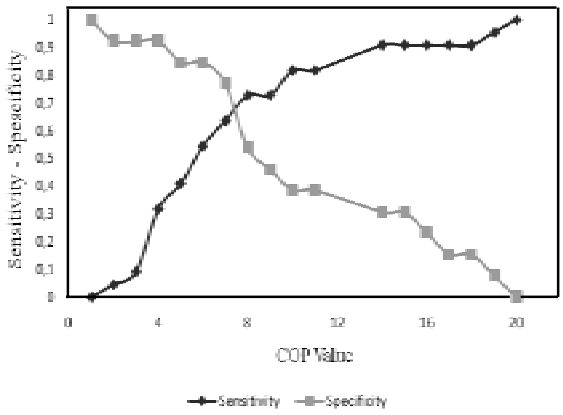

Fig. 17. The curve of sensitivity and specificity of diagnostic tests between the thyroid uptake and TSH hormone.

Cutoff value obtained from Fig. 17 at the point 7 on COP ≤ 1.8 showed that the sensitivity, specificity, positive and negative expected value were 64, 77, 82 and 56 % respectively.

Optimal cutoff point can be used as a benchmark so when someone is detected with low thyroid uptake and TSH hormone ≤ 1.8 µIU/ml, it can be diagnosed as non-toxic diffuse goiter.

CONCLUSION

From this research it can be concluded as follows:

The average value of radiopharmaceutical uptake increased along with increasing scan time of 5, 10 and 15 minutes.

The radiopharmaceutical accumulation on parotid and submandibular glands for toxic diffuse goiter is lower than non-toxic diffuse goiter.

The accumulation of radiopharmaceutical ^{99m}Tc - Pertechnetate in toxic diffuse goiter is larger than non-toxic case.

The case of toxic diffuse goiter could be characterized by high thyroid uptake, which the value of T_3 hormone $\geq$ 3.3 ng/dl, the value of T_4 hormone $\geq$ 165 nmol/l, and the value of TSH hormone $\leq$ 0.2 µIU/ml. While the case of non-toxic diffuse goiter could be characterized by low thyroid uptake, which the value of T_3 hormone $\geq$ 1.2 ng/dl, the value of T_4 hormone $\geq$ 90 nmol/l and the value of TSH hormone $\leq$ 1.8 µIU/ml

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