Some Physiological and Blood Parameters result From Low and High Dose of Radioactive Iodine-131 .

بعض التغييرات في المعايير الوظيفية والدمية الناتجة من الجرع الواطئة والعالية لليود المشع -131 لمرضى الغدة الدرقية.

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Abstract

This study was conducted at Al-Yarmouk teaching hospital / Nuclear Medicine Unit by selection of 10 patients which they have been administered with low doses of radioactive iodine-^{131}I / RAI (6-18 mCi) and at Radiotherapy Nuclear Medicine institute by selection of 10 patients that they have been administered with high doses (100-150 mCi) . Both groups of patients were suffered from different thyroid diseases (different thyrotoxicoss and various thyroid carcinoma) .Blood samples were collected to perform two steps of tests (thyroid hormones, liver enzymes, kidney function and blood picture) before and after radioactive iodine administration . The values of serum creatinine and urea were shown a significant decreasing level ($p\leq o.o5$) after high and low doses of administration with significant increasing level of serum potassium and sodium at low dose($p\leq o.o5$) when compared with the same values before RIA administration.

The results obtained shown a significant increasing level($p\leq o.o5$)of total bilirubin, indirect bilirubin, GOT and ALP for high dose and total bilirubin in low dose in a comparison to the control group.

The values of blood components shown a significant increase ($p\leq o.o5$) Total Protein,Globulin and Bas% in high dose and Total Protein, Mon% and Eos% in low dose, also the results obtained shown a significant ($p\leq o.o5$) decreasing levels of Lym% and MCHC in high dose and WBC, Neu#,Lym#,Neu%, MCV, RDW-SD and PLT in low dose when compared with the same value before RIA administration.

The values of thyroid hormones shown a significant increase values ($p\leq o.o5$) of T4 hormone in high and low dose and T3 hormone in low dose with a significant decreasing values ($p\leq o.o5$) of TSH hormone in high and low doses when compared with the same values before RAI administration.

الخلاصة

شملت الدراسة عشرون مريضا(14 إناث و6 ذكور) بأعمار تتراوح بين 40-55 سنة من المصابين بأمراض الغدة الدرقية الذين يراجعون مستشفى اليرموك التعليمي / وحدة الطب النووي و مستشفى الإشعاع والطب النووي, جمعت نماذج الدم على مرحلتين لغرض إجراء الفحوصات التالية (هرمونات الغدة الدرقية, أنزيمات الكبد , ووظيفة الكلى والدم) قبل وبعد إعطائهم جرعات مختلفة من اليود المشع. قسم المرضى إلى مجموعتين , المجموعة الأولى أُعطيت جرعات اليود الواطئة(6.8-16.68 ملي كيوري) اما المجموعة الثانية فقد أُعطيت جرعات اليود العالية (100- 150ملي كيوري). وجمعت نماذج الدم من المجموعتين لإجراء نفس الفحوصات أعلاه بعد فترة زمنية تراوحت بين (10- 30 يوم) . بينت النتائج انخفاض معنوي($p\leq o.o5$) في قيم يوريا وكرياتنين المصل وارتفاع معنوي ($p\leq o.o5$) في قيم ايونات الصوديوم والبوتاسيوم بعد إعطاء الجرعة العالية والواطئة عما هي عليه قبل إعطاء الجرعة ، كما لوحظ ارتفاع معنوي($p\leq o.o5$) في قيم البليروبين الكلي ، البليروبين الغير مباشر و أنزيمات ALP, GOT للجرع العالية و البليروبين الكلي للجرع الواطئة عن قيمها قبل إعطاء الجرعة.أما قيم صورة الدم قد بينت تغيرات مختلفة حيث ارتفعت معنويا ($p\leq o.o5$) قيم مكونات الدم (Total Protein،Globulin ، Bas% عند الجرع

العالية وTotal Protein، Mon% ، Eos% عند الجرع الواطئة عن قيمها قبل اعطاء الجرعة. كما لوحظ انخفاض معنوي (p≤o.o5) لمكونات الدم (Lym% ، MCHC عند الجرع العالية و WBC ،Neu#، Lym%، Neu% ،MCV ،RDW- PLT،SD عند الجرع الواطئة) عند مقارنتها مع قيم الجرع قبل اعطاء الجرعة الأشعاعية.
و أظهرت النتائج أيضا تغيرات واضحة لمستويات هرمونات الغدة الدرقية تمثلت في ارتفاع معنوي(p≤o.o5) لهرموني T4, T3وانخفاض معنوي(p≤o.o5) في هورمون TSH عند إعطاء الجرعة العلية والواطئة مقارنة مع قيمها قبل إعطاء الجرعة.

Key words

Side effect of I-131 radiation, diagnostic &therapeutic doses of thyroid diseases, effect of blood radiation dose, effect of hepatic radiation dose**.**

Introduction

Radioactive iodine (RAI) is an isotope with emission of both beta and gamma energies during decay. Ninety percent of its energy is deposited with an effective range of 2 mm. The half-life of 'physical decay' is 8.02 days [1]. The median 'biological half-life' in the human body is around 14 hours, with substantial variations [2]. RAI is most commonly employed in thyrotoxicosis and thyroid cancer. It is administered by the oral route and excreted through the renal system. RAI will be accumulated in thyroid follicular cells or differentiated thyroid cancer cells. In patients with no gross postoperative disease, RAI ablation facilitates detection of early relapses by serum thyroglobulin (Tg) determination and RAI treatment of RAI-avid relapses. Early detection of relapses could be achieved by checking serum Tg or stimulated Tg (by endogenous thyroid-stimulating hormone (TSH) or recombinant human TSH (rhTSH). RAI has been shown to reduce the likelihood of relapse [3,4,5,6,7,8,9,10,11,12], and to improve survival [3,4,5, 8, 9, 12]. It is also effective for distant metastases. [9, 13,14,15,16,17]. The British Thyroid Association/Royal College of Physicians (2002) recommended RAI for tumors with ≥1 cm [18].

Short- term side effects:-

Preparation for RAI ablation includes thyroxin withdrawal for 4 to 6 weeks. Although not considered a side effect of RAI treatment, patients often attribute symptoms of 'hypothyroidism' to RAI. 'Hospitalization' and isolation for a few days according to radiation protection rules is also very inconvenient to some patients. Mild clinical effects are nausea, acute sialadenitis, transient neck pain related to thyroiditis (especially in patients with large thyroid remnant after surgery; e.g., lobectomy), and hematological expression [19,20,21]. Immediately after RAI administration, a study showed that 65.2% of patients had gastrointestinal complaints, 50% had salivary gland swelling with pain, 9.8% had change in taste and 4.4% of patients had headache [22].

Long-term and organ-specific side effects:-

The most common chronic side effect after RAI treatment is decreased saliva production. Severe long-term side effects are rare. Organ-specific side effects are found in salivary glands, lacrimal glands, bone marrow, lungs and reproductive organs (ovary and testis). Incidence of secondary malignancies and leukaemiaight increase with higher RAI doses. The effects on salivary glands, bone marrow and lungs are dose- dependent.

Bone Marrow and Secondary Leukemia:-

Transient leucopenia and thrombocytopenia were observed after RAI administration,[21,23,24,25] the marrow toxicity being dose-dependent[23,24].Severe leucopenia and thrombocytopenia is only seen after high-dose therapy (>22.2 GBq). The frequency of micronuclei in peri-pheral lymphocytes increased, indicating that RAI therapy induces chromosome damage in these lymphocytes [25]. The sensitivity of lymphocytes to the effects of RAI depends on lymphocyte phenotype and RAI activity.

NK cells are most sensitive, followed by B lymphocytes and then T-helper lymphocytes. Most of the blood count alterations were mild and reversible (grade I or II). Grade III (persistent severe blood count suppression) and grade IV (bone marrow aplasia or acute myeloid leukemia) were less

commonly observed. In this cohort of 107 patients with bone metastasis, blood count alterations in those aged ≤45 were mild, usually grade I or II. However, in patients with high uptake in bone metastasis, it was observed that 8 out of 107 patients died of bone marrow problems[26,27]. Acute myeloid leukemia is the commonest observed type of leukemia after RAI treatment. Only a few cases of chronic myeloid leukemia are reported [28, 29]. A French report by de Vathaire et al revealed no instances of leukemia, at a mean follow-up of 10 years, in 1497 patients who received an average of 7.2 GBq of RAI [30]. In their cohort of 1348 patients (the majority Chinese) in Queen Elizabeth Hospital, they did not observe a single case of acute leukemia after a mean dose of 3.4 GBq in papillary thyroid carcinoma and 4.14 GBq in follicular thyroid carcinoma. The risk of leukemia was not elevated in several large studies including patients with RAI treatment for thyrotoxicosis or diagnostic scans [31].

This study include patients of both causes thyrotoxicosis and thyroid cancer, which they were treated with radio active iodine I^{131} RAI (diagnostic and therapeutic doses) to show the effect of these doses on the normal values of liver enzymes (GOT, GPT , ALP , Billurbian) ,Kidney function (K+,Na+,Urea Creatinine)and thyroid hormones (T3,T4)and thyroid stimulating hormone (TSH) and blood picture before and after RAI-treatment.

Materials and Methods

Twenty patients divided in to two main groups according to administered dose:

1-Group 1: Patients suffering from thyroid disease which they orally administered iodine-^{131}I dose (6-18 mCi) ,

2-Group 2: Patients suffering from thyroid disease which they orally administered iodine-^{131}I dose (100-150 mCi) .

The tested values measured before dose for each group represent the control group .

Four kinds of tests were performed for each group of patient (kidney function, liver enzymes, blood picture and thyroid hormones tests). All these tests conducted before and after iodine dose administration to investigate the effect of different iodine doses on the indicated parameters. All these tests achieved in AL-Nadaer AL-Moshia Clinical Laboratory, Baghdad, Iraq. According to International Methods and International diagnostic kits .

Statistical analysis:

Data were statistically analyzed using SPSS statistical software. Level of significant was assessed by using the Analysis of Variance (ANOVA) test. The level of significance was shown using the Least Significant Difference (LSD) test. Values are given as mean $\pm$ standard error (mean ± S.E.) P values <0.05 were considered statistically significant.

Results and Discussion

The results and discussion were achieved on accordance that results before radioactive iodine (control group)is the fundamental factor for comparison due to the various causes of disease (different thyroid diseases)and to compliances accompanied these causes [32].

1-Kidney function:

Table 1 clear the results of different values of kidney tests before and after RAI dose administration. The values of serum creatinine and urea were shown a significant decreasing level ($p \leq o.o5$) after high(100-150) and low (6-18) doses of administration and non significant increasing level of serum potassium and sodium at high dose with significant increasing level of serum potassium and sodium at low dose($p \leq o.o5$) , when compared with the same value before RIA administration.. On a sight of the results obtained for kidney tests, RIA affect the glomerilar part of the kidney (responsible of urea and creatinine filtration). Mean while the renal tubules (responsible for ions filtration and ionic salts balance have nearly shown a constant values after RIA administration.

2-Liver enzymes:

The results in table 2 represent the values of liver enzymes before and after RAI administration for both low & high doses. The values evident a significant increasing level($p \leq o.o5$)of total bilirubin, indirect bilirubin,GOT and ALP for high dose and total bilirubin in low dose in a comparison to the base line or pretherapy (control group). The results shown that non significant increasing level of bilirubin direct and GPT enzyme in high dose and also non significant increase of bilirubin direct, indirect bilirubin, GPT,GOT and ALP enzymes in low dose when compared control group. The evaluation of the values is may be due to hydrophobic factor that lauding to an increase in the secretion of bile in the intestine then in the circulation blood [33,34]. It is supposed that these increasing level may be due to high enzymatic release from the liver cell membrane of that induced by high radiation dose of iodine .These enzymes entered the circulation and caused high level values .Where as low RIA doses did not induce damage for the liver membrane consequently lead to invariant values of liver enzymes.

3- Blood: The results of table 3 represent complete blood count (CBC) for the patients before and after RAI dose (low& high doses). The values shown a significant increase ($p \leq o.o5$) of blood components total protein, , Globulin and Bas% in high dose and total protein), Mon% and Eos% in low dose and non significant increase values of blood components albumin , Neu#,Mon#,Eos#,Neu%,Mon%,Eos%, HCT and MCH for high dose) and non significant increase of albumin, Globulin,Mon#,Eos#,Lym%,Bas%,MCT,MCH and PDW in low dose. The results obtained shown a significant ($p \leq o.o5$) decreasing levels of Lym% and MCHC in high dose and WBC, Neu#,Lym#,Neu%, MCV, RDW-SD and PLT in low dose and non significant decreasing levels of WBC , Lym# , Bas# ,RBC% , HGB , MCV , RDW-CV, RDW-SD ,PLT , MPV and PDW in high dose and Bas# ,RBC , HGB , MCHC , RDW-CV, MPV in low dose when compared with the same value before RIA administration. These results agreed with previous reports as published by other authors[35,36,37].

4-Thyroid hormones & Thyroid stimulated hormone:

The results of table 4 indicated to obvious changes to the thyroid hormones levels for patients that have been administered with both high and low doses of RIA. The values of hormones shown a significant increase values ($p \leq o.o5$) of T4 hormone in high and low dose and T3 hormone in low dose with non significant increasing values of T3 in high dose. Also the results shown a significant decreasing values ($p \leq o.o5$) of TSH hormone in high and low doses when compared with the same values before RAI administration.

Table 1 Values of kidney function for thyroid diseases patients before and after administration of high dose (100-150 mCi) and low dose (6-18 mCi)of iodine-131.

Type of test	Control	High dose(100-150 mCi)		Low dose (6-18 mCi)	
		Value before Iodine dose	Value after Iodine dose	Value before iodine dose	Value after iodine dose
urea	≤ 50 mg/dl	25.75±1.106	$24.83 \pm 1.105^{N.S}$	32.00±1.106	28.16±1.105*
creatinine	0.4 - 1.4 mg / dl	1.9±0.126	0.95±0.055 *	0.85±0.055	0.60±0.055*
Serum potassium	3.6 - 5.2mmol/l	4.38±0.11	$4.48 \pm 0.011^{N.S}$	4.36±0.022	4.46±0.11*
Serum sodium	137.0–148.0 mmol/l	140±0.65	$140.6 \pm 0.11^{N.S}$	138.2±0.118	139.0±0.22*

Mean ± S.E. , n= 10 , NS= Non significantly different , * Significantly different ($p \leq o.o5$)

Table 2 Values of liver function for thyroid diseases patients before and after administration of high dose (100-150 mCi) and low dose (6-18 mCi)of iodine-131.

Type of test	Control	High dose(100-150 mCi)		Low dose (6-18 mCi)	
		Value before Iodine dose	Value after Iodine dose	Value before iodine dose	Value after iodine dose
Bilirubin Total	0.30 - 1.20 mg/dl	0.46±0.026	0.58±0.039*	0.50±0.041	0.59±0.02*
Bilirubin Direct	0.10 - 0.50 mg/dl	0.144±0.005	$0.155\pm0.015^{N.S}$	0.13±.007	$0.14\pm0.006^{N.S}$
Bilirubin InDirect	0.10 - 0.80 mg/dl	0.322±0.02	0.43±0.036 *	0.37±0.023	0.39 ± 0.011^{NS}
ALT(GPT)	≤ 32 u/l	27.8±0.577	28.5 ± 0.63^{NS}	22.66±0.632	22.66 ± 0.47^{NS}
AST(GOT)	≤ 31 u/l	29.66±0.577	33±0.60*	27.93±0.58	28.00 ± 0.63^{NS}
ALP	42 – 131 u/l	118.33±0.58	143.83±0.92*	79.00±0.81	79.2 ± 0.82^{NS}

Mean ± S.E. , n= 10 , NS= Non significantly different , * Significantly different (p≤o.o5)

Table 3 Values blood picture for thyroid diseases patients) before and after administration of high dose (100-150 mCi) and low dose (6-18 mCi)of iodine-131.

Type of test	Control	High dose(100-150) mCi)		Low dose (6-18 mCi)	
		Value before Iodine dose	Value after Iodine dose	Value before iodine dose	Value after iodine dose
Total Protein	66.00 - 87.00 g/l	68.89±0.39	73.00±0.47*	68.92±0.39	70.63±0.63*
Albumin	35.0 - 52.0 g/l	45.32±0.57	45.91 ± 0.63^{NS}	43.7±0.58	44.62 ± 0.47^{NS}
Globulin	35.0 - 52.0 g/l	23.58±0.57	27.06±0.57*	25.23±0.57	26.02 ± 0.63^{NS}
WBC	4.00 - 10.00 10^9/l	6.87±0.47	6.28 ± 0.58^{NS}	8.03±0.47	5.88±0.47*
NEU#	2.00 - 7.0010^9/l	3.6±0.40	3.99 ± 0.39^{NS}	4.71±0.47	2.89±0.29*
LYM#	1.50 - 4.0010^9/L	2.22±0.25	2.12 ± 0.28^{NS}	2.56±0.27	1.98±0.15*
Mon#	0.12 - 0.80 10^9/L	0.32±0.03	0.34 ± 0.032^{NS}	0.415±0.04	0.44 ± 0.04^{NS}
Eos#	0.02 - 0.50 10^9/L	0.12±0.008	0.142 ± 0.01^{NS}	0.22±0.023	0.24 ± 0.017^{NS}
Bas#	0.00 - 0.10 10^9/L	0.028±0.002	0.016 ± 0.016^{NS}	0.04±0.005	0.03 ± 0.003^{NS}

Neu%	42. 0-72.0 %	59.37±3.23	61.2±0.577^{NS}	57.35±1.15	51.67±0.63*
LYM%	20.0 - 45.0 %	33.87±0.71	30.9±0.63 *	34.26±0.95	32.81±0.57^{NS}
Mon%	2.0 - 10.0 %	4.57±0.31	5.28±0.33^{NS}	6.4±0.301	8.6±0.229 *
Eos%	0.5 - 6.0 %	1.95±0.068	2.14±0.13^{NS}	2.86±0.032	4.7±0.214*
Bas%	0.0 - 1.0 %	0.3±0.023	0.42±0.023*	0.56±0.034	0.6±0.040^{NS}
RBC	3.80 - 5.80 10^9/L	5.27±0.289	4.86±0.192^{NS}	4.88±0.204	4.61±0.171^{NS}
HGB	12.0 - 15.5 g/dL	13.85±0.405	13.26±0.30^{NS}	13.11±0.43	13.04±0.464^{NS}
HCT	37.0 - 48.0 %	39.76±0.632	40.83±0.57^{NS}	38.71±0.632	39.42±0.576 ^{NS}
MCV	76.0 - 96.0 fL	86.13±3.85	84.16±0.47^{NS}	85.64±0.58	79.76±0.58 *
MCH	27.0 - 32.0 pg	28.53±0.577	28.8±0.58^{NS}	27.03±0.56	28.34±0.577^{NS}
MCHC	300 – 360 g/L	334±0.816	289.18±1.0*	338±1.93	330.6±0.93^{NS}
RDW-CV	11.5 - 14.5 %	12.81±0.63	12.06±0.63^{NS}	13.5±0.58	12.38±0.471^{NS}
RDW-SD	35.0 - 56.0 fL	41.83±0.86	41.63±0.85^{NS}	42.21±0.85	41.2±1.03 *
PLT	140 – 440 10^9/L	297±1.18	275.33±2.9^{NS}	290.5±4.08	193.8±1.31*
MPV	7.0 - 11.0 fL	8.95±.265	8.76±0.28^{NS}	9.32±0.33	8.63±0.438^{NS}
PDW	15.0 -17.0	15.96±0.63	15.81±0.57^{NS}	16.08±0.583	16.24±0.774^{NS}

Mean ± S.E. , n= 10 , NS= Non significantly different , * Significantly different (p≤o.o5)

Table 4 Values of thyroid hormones for thyroid diseases patients before and after administration of high dose (100-150 mCi) and low dose (6-18mCi) of iodine-131.

Type of test	Control	High dose(100-150 mCi)		Low dose (6-18 mCi)	
		Value before Iodine dose	Value after Iodinedose	Value before iodine dose	Value after iodine dose
T3	0.9 - 2.3ng/mL	1.49±0.114	1.52±0.115^{NS}	1.23±0.063	2.73±0.118*
T4	4.6 – 11.8 µg/dL 60 -120 nmol/L	---- 97.6±0.793	---- 111.28±0.816*	7.81 ±0.41 -----	9.43±0.281* ------
TSH	0.25 - 5.0uIU/ml	23.4±0.577	8.17±0.434*	4.76 ±0.057	0.30±0.014*

Mean ± S.E. , n= 10 , NS= Non significantly different , * Significantly different (p≤o.o5)

Conclusions & Acknowledgement

1-On sight the results obtained, we recommend continuations the research in this approach in order to improve the clinical side of Nuclear Medicine services

2-The possibility of patient radiation reduction for the purpose of diagnosis and treatment.

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