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Thyroid Function Studies of Healthy Koreans and Patients with Thyroid Disease by means of I^{131}-Triiodothyronine*,**.

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Since Hamolsky and his coworkers[1] had introduced the erythrocyte uptake of I^{131}-labeled triiodothyronine (I^{131}-TRI) as a new thyroid function test, this simple and rapid in vitro test was used and discussed by some other investigators[2,4,11]. On the basis of these clinical data, triiodothyronine in vitro test was known as a method with good diagnostic accuracy in thyroid disease.

The results of the study reported in here primarily concern the use of the red blood cell in vitro incorporation of I^{131}-labeled triiodothyronine from whole blood as an index of thyroid function status in Koreans. The accuracy of this study was compared with other currently used methods such as I^{131} thyroid uptake, PBI^{135} conversion ratio, BMR, serum cholesterol level etc. This report also deals with the summary of thyroid function of normal Koreans from various districts in an effort to find the standard level. Besides, attempts were made to find whether there exist any significant difference in the erythrocyte uptake of I^{131}-TRI according with geographical areas using the in vitro triiodothyonine method.

Materials and Methods

Materials

Blood samples were taken from healthy physicians, medical students, technicians and nurses of Seoul National University and out and in-ward patients of Seoul National University Hospital. Independently thyroid status was determined by clinical evaluation including clinical response to therapy and one or more standard laboratory procedures such as the measurement of BMR, chemical PBI level, 24 hour thyroid-uptake of radioiodine (I^{131}), PBI^{131} conversion ratio and blood cholesterol concentration. Blood samples taken from healty inhabitants in various districts also were received by male.

Methods[1]

a) Tracer amounts($50\times10^{-4}\mu g/0.1ml.$) of I^{131}-TRI were added to aliquots in duplicate of the heparinized whole blood in a 15ml. pyrex tube.

b) The tubbe was then incubated in water bath at 37°C. and constantly shaken for 2 hours.

c) With a well-type scintillation counter, the radioactive content of each tube was determined by counting for sufficiently long period as to obtain 2% accuracy.

d) The aliquots were centrifuged, supernatant plasma remeved, and red cells were washed 3 times with 5~6 times volumes of isotonic saline.

e) The radioactivity remaining in the r.b.c. fraction was then determined by the method as described in c).

f) The percentile r.b.c. uptake was then calculated as

$$\text{Erythrocyte uptake in \%} = \frac{\text{net counts in rbc/3ml}}{\text{net counts/3ml of whole blood}} \times 100$$

The values were corrected to hematocrit reading of 100.

$$\text{Corrected erythrocyte uptake} = \frac{\text{erythrocyte uptake}}{\text{hematocrit}} \times 100$$

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Results

1. Summary of the red blood cell uptake of I^{131}-triiodothyronine from whole blood of normal Koreans and geographical relations

Table 1. The 2 hr. in Vitro r.b.c. uptake of I^{131}-TRI from whole Blood of Healthy Koreans

	Men		Women	
	r.b.c. uptake (%)	No. of case	r.b.c. uptake (%)	No. of case
Range	9.7—24.8		8.5—21.8	
Average	15.7	154	14.4	143
S. D.	3.24*1		3.56*2	
Less than Normal Range	<10% <11%	1 (0.64%) 7 (4.54%)	<10% <11%	3 (2.10%) 8 (5.59%)
Abovethan Normal Range	>17% >19%	44(28.57%) 7 (4.54%)	>17% >19%	18(12.59%) 4 (2.80%)

※ 1:s.e.o.296 2:s.e.o.261 t:3.826

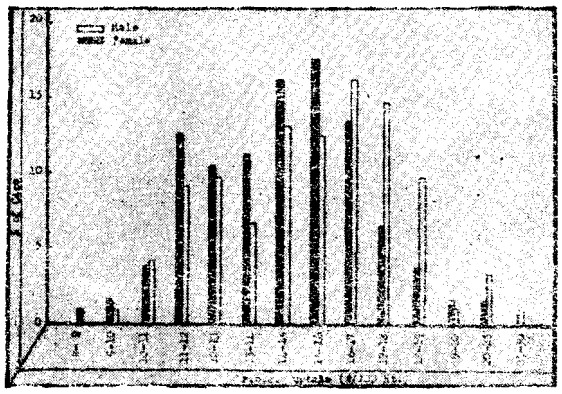


Fig. 1. Distribution of the r.b.c. uptake of I^{131}-TRI in vitro from whole blood of normal Koreans

The results of thyroid function test in 154 euthyroid males and 143 females were shown in Table 1. The invitro red blood cell uptake of I^{131}-triiodothyronine in males ranged from 9.7% to 24.8% averaging 15.7±3.24 percent. In females, the uptake ranged from 8.5% to 21.8%, averaging 14.4±56 percent The data indicates that the erythrocyte uptake in males was significantly higher than in females.

In Fig. 1, the distribution of each valus was shown. In males, one case(0.64%) was less than 10.0percent of I^{131}-TRI erythrocyte uptake and 7 cases(4.54%) less than 11.0 percent of I^{131}-TRI erythrocyte uptake. In the upper range of normal spectrum, 44 cases of males' value(28.57%) were above 17 percent of I^{131}-TRI erythrocyte uptake and 7 cases(4.54 %) above 19 percent of I^{131}-TRI erythrocyte uptake. On the other hand, 3 cases of euthyroid females (2.10%) were less than 10.0 percent of I^{131}erythrocyte uptake and 8 cases(5.59%) less than 11.0 percent of I^{131}-TRI erythrocyte uptake. Values above 17.0% of I^{131}TRI erythrocyte uptake were found in 18 cases(12.5%), and those above 19.0 percent were found in 4 cases(2.50%).

Table 2. Age Distribution of r.b.c. Uptake in Normal Koreans

Sex / Age	Male		Female	
	Average (%)	S.D.	Average (%)	S.D.
10~19	15.30	2.49	13.98	1.66
20~29	15.90	3.26	14.60	2.27
30~39	16.90	4.14	14.50	4.72
40~49	15.30	1.82	12.70	2.09
50~59	14.50	2.19	11.60	1.25
60~69	11.80		11.40	

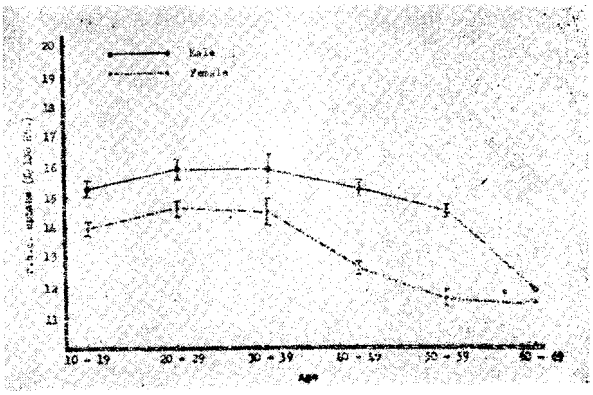


Fig. 2. Age Distribution of r.b.c. uptake in Normal Koreans

The effect of age upon thyroid function was shown in Table 2 and Fig. 2. In both sexes, the uptake was low in the older individuals. The decline of erythrocyte uptake in euthyroid females just before menopause was significant.

Data from various areas are summarized in Table 3. Except two areas of islands, Jaeju and Jindo, blood samples were taken from inhabitants in urban areas. No significant differences in r.b.c. uptake according with geographical areas were found either in males or females. In Jindo, blood samples were

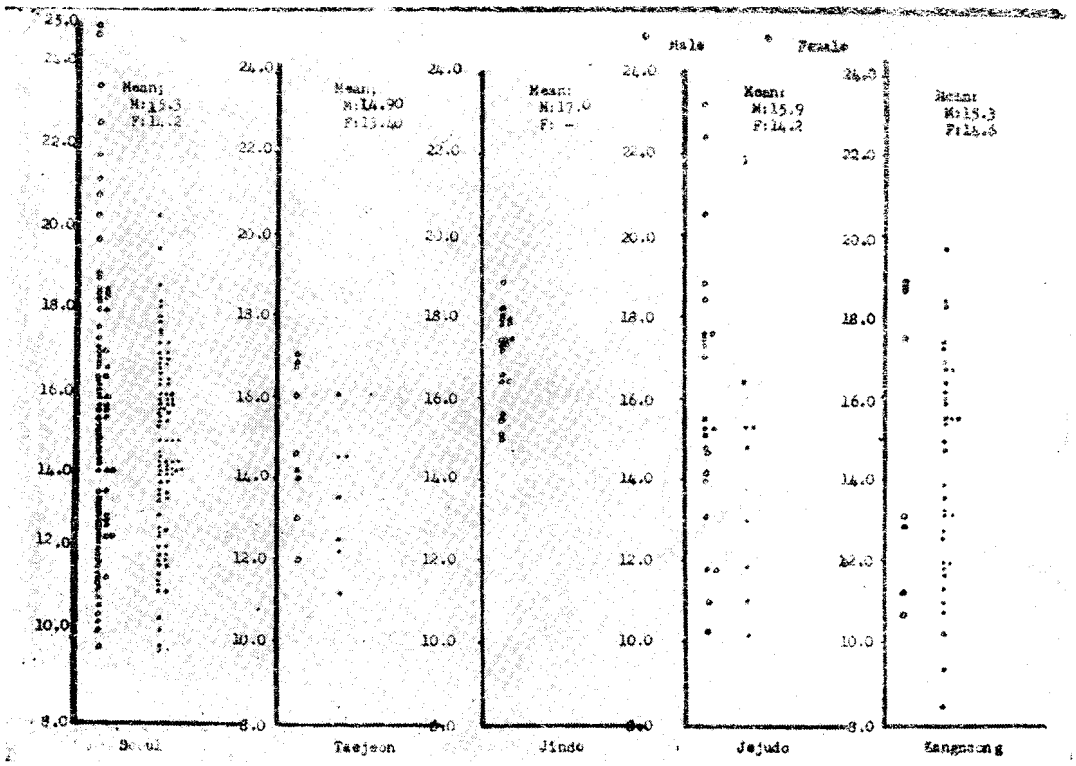
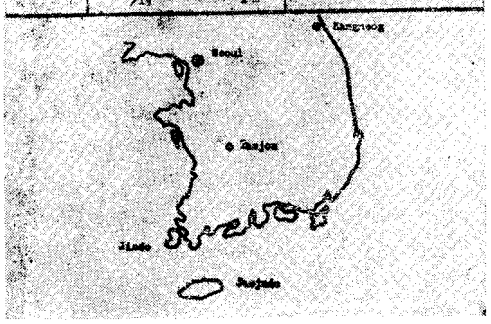


Fig. 3. Comparative values of r.b.c. uptake of I^{131}-TRI with Various Districts of Korea

Table 3, Summary of comparative values of I^{131}-TRI, r.b.c. uptake with various districts of Korea.

Sex / Dist. Subj.	Male		Female	
	r.b.c. Uptake	No. of Case	r.b.c. Uptake	No. of Case
Seoul	9.7 ~ 25.6 % (15.3±3.39)	91	9.7 ~ 20.3 % (14.6±2.27)	91
	<11	4	<11	5
	>19	5	>17	12
			>19	3
Kangneung	10.7 ~ 18.9 % (15.3±3.74)	8	8.5 ~ 19.2 % (14.2±4.79)	14
	<11	1	<11	5
	>19	0	>17	5
Taejeon	12.0 ~ 20.2 % (16.90±1.98)	10	11.2 ~ 16.0 % (13.4±1.69)	7
	<11	0	<11	0
	>19	1	>17	0
Jejudo	10.2 ~ 20.2 % (15.9±3.37)	23	10.2 ~ 21.8 % (17.4±1.65)	9
	<11	1	<11	1
	>19	2	>17	1
Jindo	15.0 ~ 23.5 % (17.0±1.8)	21		
	<11	0		
	>19	2		



taken only from approximately 20 years old males. Although the r.b.c. uptakes of male inhabltants in various areas appeared to be slightly higher than of females, the differences were not significant in the series as presented in this report. The distribution of values of each sex was summarized in Fig. 3.

2. The effect of pregnancy

Of 26 pregnant females, the r.b.c. uptake of triiodothyronine was consistently decreased throughout the entire period of pregnancy, as shown in Table 4. and Fig. 4.

The r.b.c. uptake averaged 9.1±1.71 percent, ranging from 7.8 to 15.0 percent. In one woman, measurements of r.b.c. uptake were performed before and during pregnancy, and in another woman during and after pregnancy. In the former, the value was decreased from 12.6 perecent before pregnancy to 9.3 and 9.7 percent after the first and 3rd month of gestation respectively. In the latter, r.b.c. uptake during pregnancy(8.6%) was restored to 13.6 percent two weeks after delivery. Besides, one patient with eclampsia showed 15.0 percent of r.b.c. uptake at the 6th month of pregnancy.

Table 4 Relation between r.b.c. uptake of I^{131}-triiodothyronine and Pregnancy

months of pregnancy	1	2	3	4	5	6	7	8	9	10
I^{131} TRI	9.3	10.9	9.7	9.2	9.3	15.0	8.5		9.5	9.8
uptake	8.8	8.5	10.2	8.1	10.0	10.6	9.5		10.3	8.6→13.6
at	10.2	9.8	9.1	9.9		11.9		7.8		
randon						8.2		10.3		

Total Mean:9.1±1.71%

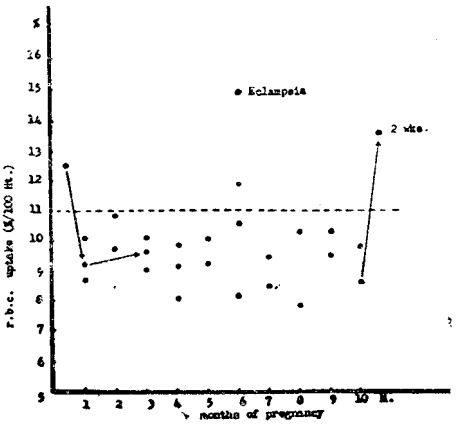


Fig. 4. Relation between r.b.c. uptake of I^{131}-TRI and Pregnancy

thyroid uptake of 24 hours, PRI^{131} conversion ratio of 24 hours, BMR and serum cholesterol were 54.1 percent, 56.0 percent, 37.4 percent and 109.6mg percent respectively.

The value that fell within normal range was one in I^{131}-TRI test, one in I^{131}-thyroidal uptake of 24 hours, one in PBI^{131} conversion, one in BMR and none in cholesterol level.

Average value of r.b.c. I^{131}-TRI uptake of 36 cases of female hyperthyroidism was 23.5 percent, and average values of I^{131}-thyroidal uptake, PBI^{131} conversion ratio, BMR, cholesterol level were 65.3 percent, 62.6 percent, 28.0 percent and 123.8mg percent respectively. The values that fell within normal ranges were one in I^{131}-TRI test, in I^{131}-

Table 5 The r.b.c. uptake of I^{131}-TRI Compared with the other Thyroid Function Tests in Thyrotoxic Patients

sex	T.F.T. / Subjects	r.b.c. uptake of I^{131}TRI	I^{131} thyroid uptake (24hr.)	P.B.I.CR (24hr.)	B.M.R.	cholesterol (total)
Male	No. of cases	7	7	7	7	6
	range	19.1~40.5	8.6~92.5	26.0~85.0	+3~+69	95.6~127.8(mg)
	mean Value	27.6	54.1	56.0	37.4	109.6(mg)
	S.D.	4.63	16.3	16.7	14.9	9.5(mg)
	No of cases. fell in normal spectrum	<19% 1(14.3%)	<40% 1(14.3%)	<45% 1(14.3%)	<+15% 1(14.3%)	>140mg 0(0%)
Female	No. of cases	36	36	36	36	36
	range	15.1~44.0	10.4~99	6.5~91	−6~+79	62.8~215(mg)
	mean Value	23.5	65.3	62.6	28	123(mg)
	S.D.	5.80	18.3	17.9	18.3	25.8
	No of cases. fell in normal spectrum.	<17% 1(2.8%)	<40% 5(13.9%)	<45% 3(8.3%)	<+15% 7(19.4%)	>140mg% 4(11.1%)

3. Comparative study of r.b.c. uptake test with other currently used methods in toxic and nontoxic goiter

The results are summarized in tables 5. and 6. In seven hyperthyroid males, average value of r.b.c. I^{131}-TRI uptake was 27.6 percent, mean values of I^{131}-thyroidal uptake, in 3 PBI^{131} conversion ratio, 7 in BMR and 4 in cholesterol level.

Average value of r.b.c. I^{131}TRI uptake was 14.2 ±2.47 percent in 12 cases of male nontoxic goiter and 14.2±3.12 percent in 43 female cases.

These data have been compared favorably with

Table 6. The r.b.c. Uptake of I^{131}TRI Compared with other Thyroid Function Tests in Non-Toxic Patients.

sex	T.F.T. / Subjects	r.b.c. uptake of I^{131}-TRI	I^{131}-thyroid uptake (24hrs.)	P.B.I. C-R (24hrs.)	B.M.R.	Cholesterol (total)
Male	No. of cases	12	12	12	11	10
	range	10.2~17.9	6.3~64.3	3.2~69.4	−5~+36.5	90.3~200(mg)
	mean Value	14.2	23.9	22.7	+13.2	160.1(mg)
	S.D.	2.47	18.2	19.5	12.7	47.2(mg)
	No. of cases showed above or less than normaspectrum	<11% 1(8.3%)	<10% 2(16.7%)	<10% 2(16.7%)	<−15% 0(0%)	<140mg% 5(50%)
		>19% 0(0%)	>40% 1(8.3%)	>45% 1(8.3%)	>+15% 4(36.4%)	>240mg% 1(10%)
Female	No. of cases	43	43	43	35	35
	range	8.5~17.6	4.7~60.2	2.7~68.5	−19~+52	91.4~232(mg)
	mean Value	14.2	26.1	25.6	13.5	169.6(mg)
	S.D.	3.12	15.8	17.0	19.2	53.9(mg)
	No. of cases showed above or less than normal spectrum	<11% 5(11.6%)	<10% 6(14.0%)	<10% 5(11.6%)	<−15% 3(8.6%)	<140(mg%) 9(25.7%)
		>17% 2(4.7%)	>40% 8(18.6%)	>45% 6(14.0%)	>+15% 15(42.9%)	>240(mg%) 0(0%)

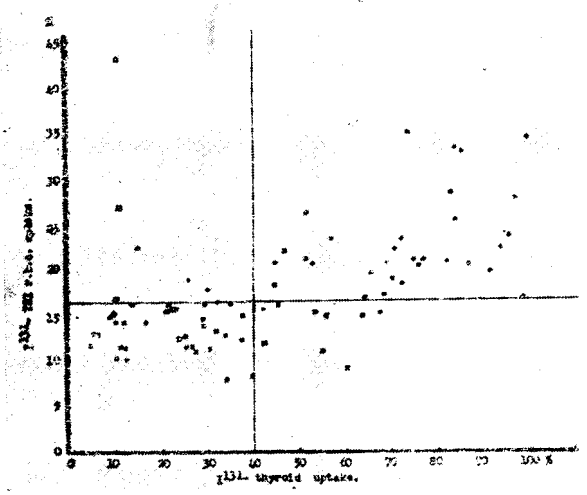


Fig. 5. Relation between r.b.c. Uptake of I^{131}-TRI and I^{131}-thyroid Uptake

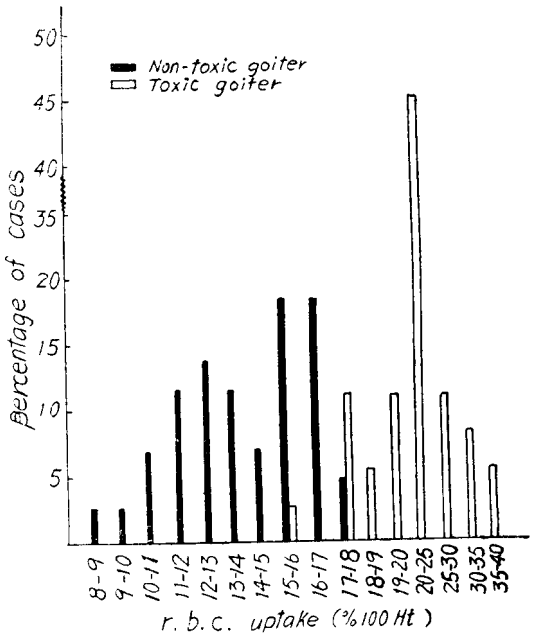


Fig. 6. Distribution of in vitro r.b.c. uptake of I^{131}-TRI from whole Blood in Female Subjects with Toxic and Non-Toxic Goiter

those of currently used methods. As shown in Table 6, the values surpassing the normal range in r.b.c. TRI test was one from 12 male patients(8.35%) and was 7 from 43 female patients(16.3%).

The distribution of TRI test in female subjects with toxic and nontoxic goiter is shown in Fig. 6. Although 2 women (4.7%) with nontoxic goiter showed higher values than normal range, and 5 women (11.6%) showed lower values than normal, most values of TRI test in nontoxic goiter were within normal range. And values in toxic goiter group were significantly high when compared with euthyroid group and nontoxic goiter group. Correlations between the values of TRI test and those of other function test are not apparent except minor

correlation between values of TRI test and I^{131} thyroid uptake as might be seen in Fig. 5.

4. Hypothyroidism and the effect of thyroid administration to hypothyroid subjects

Table 7. The results of thyroid function test compared with various laboratory data in 14 hypothyroid patients.

Pts. \ T.F.T. / treatment		I^{131}-TRI rbc. uptake %	I^{131}-thyroid uptake %	P.B.I. C-r %	B.M.R. %
Pt. A	before	5.4	4	6.1	−5
F: 40	after 1.5M	14.9	6	3.8	+10
Pt. B*	before	10.3	0.1	7.7	3
F: 40	after 1M	22.7	4.4	10.1	25
Pt. C	before	6.8	2.6	5.3	−30
F: 55	after 2M	16.9	9.5	20.0	−11
Pt. D		6.4	15	11.2	−6
M: 53		—	—	—	—

*Sinus tachycardia (Premature beat).

Of 4 hypothyroid cases, red cell uptake of TRI was significantly lower than in euthyroid subjects except that one patient showed 10.3 parcent approaching the lower border of normal spectrum(Table 7). I^{131} thyroid uptake of 24 hours, PBI^{131} conversion ratio and BMR were also significantly decreased in hypothyroidism, but no correlation on the value of r.b.c. TRI uptake was found.

In tests of r.b.c. TRI uptake during the administration of dessicated thyroid tablets, a significant increase in I^{131}TRI erythrocyte uptake were found in all cases.

From the results described above, it may be said that I^{131} thyroid uptake, PBI^{131} conversion ratio and BMR were less reliable as diagnostic tests when compared with RBC-TRI test.

Discussion

As indicated by Robbins[2], laboratory tests of thyroid function have been increasing importance, for the routine examinations in the population at large. There are many parameters of thyroid function currently in use, but the test of the red cell uptake of I^{131}-TRI is simple and rapid in its procedure and is convenient as a screening procedure.

However, it is necessary to evaluate the diagnostic accuracy of this test in comparison with that of other methods. The results of comparative studies were summarized by Bauer[3] and discussed by Hamolsky[1,4] and Robbins[2]. Numerous papers that followed the study dealt with possible mechanism of RBC-TRI and its variance with thyroid status[5~10].

From the results as illustrated in Table 1 to 6, it is apparent that the spectrum of normal range was rather narrow when compared with that obtained by other currently used methods and overlapping of the ranges among euthyroidism, hypothyroidism and hyper-thyroidism were less frequently encountered than that of other laboratory data[11].

In attempts to find whether there exists geogrraphical difference in thyroid function in several area of Korea, no difference among various districts was found. The distribution of thyroid patients that visited the Clinic of Seoul National University Hospital was observed by Kim et al[12] and they concluded that there was no significant variance according with different areas.

The levels of normal range and decrease in r.b.c. uptake in females as observed in this study well corresponded with the results obtained by other workers. Slightly higher values in this study when compared with data from Hamolsky et al[4]. might have been resulted from thrice washing instead of their four time washings of erythrocytes and other minor differences in experimental procedures.

Effects of pregnancy on the erythrocyte uptake of TRI was observed by Hamolsky[1~4] and Robbins[2] The decrease of erythrocyte uptake during pregnancy has been explained on the basis of an increase in specific binding globuln of plasma[13~16]. In our experiment, the reversal of erythrocyte uptake after delivery and the influence of eclampsia during pregnancy were observed. Other factors that may be concerned with these changes may include alterations of plasma protein pattern, carbon dioxide retension and estrogen level in blood.

The erythrocyte uptake of I^{131}-TRI may prove to be a fairly accurate indicator in the course of follow up studies in hypothyroidism treatment. The effect of thyroxine and triiodothyronine concentrations in the plasma on the uptake of these hormones into erythrocyte and the tissue cells were studied in experimental animals as clinically by several workers[1~6].

In this study, clinical improvement following the

administration of thyroid tissue went parallel with the increased uptake of erythrocyte. With other methods currently in use, however, the tests did not always reveal the favorable results of therapeutic administration of thyroid extract. On the basis of these findings, it may be concluded that the uptake of TRI into erythrocyte best reflects therapeutic effect of thyroid hormone administered against hypothyroidism.

Summary

The in vitro erythrocyte uptake of I^{131}-TRI was determined in normal Korean subjects and patients with thyroid diseases. Concomitantly, other laboratory tests currently in use were performed in patients.

1. Erythrocyte uptake of I-^{131}TRI averaged 15.7±3.24 percent in normal males and 14.4±3.56 percent in normal females. No significant difference in erythrocyte I^{131}-TRI values according with various geographical areas of Korea was found.
2. Erythrocyte uptake of I^{131}-TRI was decreased during pregnancy and restored after delivery.
3. Accuracy of erythrocyte I^{131}-TRI uptake test as a diagnostic aid was compared with that of other currently used methods in patients with toxic and nontoxic goiter.
4. The value of erythrocyte I^{131}-TRI were significantly decreased in hypothyroid patients and administration of thyroid extract resulted with the increase in the value.

국 문 초 록

I^{131}-표식 Triiodothyronine에 의한 正常韓國人 및 甲狀腺患者의 甲狀腺機能에 관한 硏究

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著者들은 I^{131}-triiodothyronine의 赤血球攝取率을 in vitro에서 측정함으로써 甲狀腺의 機能을 평가 하고자 正常韓國人을 대상으로 이 方法을 적용하여 性別, 年齡別 地域別의 관계를 관찰하였으며 甲狀腺患者에 대하여서는 현재 이용되고 있는 I^{131}의 甲狀腺攝取率, 蛋白結合沃素轉化率, I^{131}尿排泄率, 基礎代謝率, 血淸 cholesterol 値에 의한 機能檢査와 比較考察하고 또한 粘液水腫에 대한 甲狀腺製劑 投與 후의 甲狀腺機能의 變化를 이 方法에 의하여 조사하였던바 다음과 같은 結論을 얻었다.

1) I^{131}-triiodothyronine의 赤血球攝取率은 正常韓國人男子에서 15.7±3.24% 이었고 正常韓國人女子에서는 14.4±3.56%이었다. 韓國內의 各地域別 檢査値에서 현저한 差異는 볼수 없었다.
2) 妊娠中에는 I^{131}-triiodothyronine의 赤血球攝取率이 저하되었고 分娩後에는 正常値로 복귀되었다.
3) 甲狀腺腫의 診斷目的으로 현재 응용하고 있는 다른 檢査法과 比較檢討하였는데 그 方法이 간편하고 甲狀腺機能을 가장 正確하게 표시하는 檢査法의 하나라는 것을 알았다.
4) 甲狀腺機能低下症에서는 I^{131}-triiodothyronine의 赤血球攝取率이 正常値에 비하여 현저하게 저하되어있고 甲狀腺製劑의 투여로 攝取率의 증가를 보았다.

REFRENCE

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