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The Effect of Iodine Restriction on Thyroid Function in Patients with Hypothyroidism Due to Hashimoto's Thyroiditis

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Lifelong thyroid hormone replacement is indicated in patients with hypothyroidism as a result of Hashimoto's thyroiditis. However, previous reports have shown that excess iodine induces hypothyroidism in Hashimoto's thyroiditis. This study investigated the effects of iodine restriction on the thyroid function and the predictable factors for recovery in patients with hypothyroidism due to Hashimoto's thyroiditis. The subject group consisted of 45 patients who had initially been diagnosed with hypothyroidism due to Hashimoto's thyroiditis. The subjects were divided randomly into two groups. One group was an iodine intake restriction group (group 1) (iodine intake: less than 100 μg/day) and the other group was an iodine intake non-restriction group (group 2). The thyroid-related hormones and the urinary excretion of iodine were measured at the baseline state and after 3 months. After 3 months, a recovery to the euthyroid state was found in 78.3 % of group 1 (18 out of 23 patients), which is higher than the 45.5% from group 2 (10 out of 22 patients). In group 1, mean serum fT4 level (0.80 $\pm$ 0.27 ng/dL at the baseline, 0.98 $\pm$ 0.21 ng/dL after 3 months) and the TSH level (37.95 $\pm$ 81.76 μIU/mL at the baseline, 25.66 $\pm$ 70.79 μIU/mL after 3 months) changed significantly during this period (p <0.05). In group 2, the mean serum fT4 level decreased (0.98 $\pm$ 0.17 ng/dL at baseline, 0.92 $\pm$ 0.28 ng/dL after 3 months, p < 0.05). In the iodine restriction group, the urinary iodine excretion values were higher in the recovered patients than in non-recovered patients (3.51 $\pm$ 1.62 mg/L vs. 1.21 $\pm$ 0.39 mg/L, p=0.006) and the initial serum TSH values were lower in the recovered patients than in the non-recovered patients (14.28 $\pm$ 12.63 μIU/mL vs. 123.14 $\pm$ 156.51 μIU/mL, p=0.005). In conclusion, 78.3% of patients with hypothyroidism due to Hashimoto's thyroiditis regained an euthyroid state iodine restriction alone. Both a low initial serum TSH and a high initial urinary iodine concentration can be predictable factors for a recovery from hypothyroidism due to Hashimoto's thyroiditis after restricting their iodine intake.

Key Words: Hypothyroidism, hashimoto's thyroiditis, restriction of iodine intake, spontaneous remission of thyroid function

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INTRODUCTION

Autoimmune thyroiditis with hypothyroidism consists of chronic goitrous thyroiditis (Hashimoto's thyroiditis) and chronic atrophic thyroiditis.[1]

Hashimoto's thyroiditis is believed to be a disease causing the progressive destruction of the thyroid follicular epithelium. At the early stages, due to the increased TSH concentration, a goiter develops and the thyroid function remains in the euthyroid state. However, as the disease progresses, lymphocytes and fibrotic tissues infiltrate into the thyroid, which leads to the destruction of the thyroid. Consequently, hypothyroidism develops and this requires life long thyroid hormone replacement.[2] However, it has been reported that hypothyroidism due to Hashimoto's thyroiditis might resolve spontaneously without thyroid hormone replacement, which suggests that it is sometimes reversible.[3,4] However, little is known regarding the mechanism causing the spontaneous remission of hypothyroidism.[5-8] Recently, Yoshinari et al. reported that more than half of the

patients with newly diagnosed hypothyroidism with a goiter regain the euthyroid spontaneously after dietary iodine restriction without thyroid hormone replacement.[9] Epidemiological studies have shown a higher frequency of thyroid autoantibodies in the residents of iodine-sufficient areas compared to the residents of iodine-deficient areas.[10,11] Therefore, this study hypothesized that excessive dietary iodine intake plays an important role in triggering or exacerbating hypothyroidism in Hashimoto's thyroiditis, and that the thyroid functions could recover partially with only dietary iodine restriction in patients with hypothyroidism due to Hashimoto's thyroiditis.

In order to investigate the effect of iodine intake on the thyroid function in patients with hypothyroidism due to Hashimoto's thyroiditis, the thyroid function of 45 patients with hypothyroidism due to Hashimoto's thyroiditis was investigated for 3 months. The patients were divided into two groups. One group consisted of 23 patients whose iodine intake was restricted to $<100\,\mu$g per day (group 1), and the other group consisted of 22 patients whose iodine intake was not restricted (group 2).

MATERIALS AND METHODS

Subjects

Between June 1998 and March 1999, 45 patients who were initially diagnosed with hypothyroidism due to Hashimoto's thyroiditis were enrolled in this study. Hashimoto's thyroiditis was defined as a chronic goiter history, a firm and diffuse palpable goiter, hypothyroidism (serum TSH $\geq 5\,\mu$IU/mL), and the presence of antimicrosomal or antithyroglobulin antibodies.

Methods

Prior to initiating this study, the daily dietary iodine intake of all patients was evaluated, and the size of the goiter, the antimicrosomal, antithyroglobulin and TSH receptor antibody titers, thyroid function, 24 hour radioactive iodine uptake were measured. After the initial diagnosis of hypothyroidism due to Hashimoto's thyroiditis, the thyroid function was reevaluated 3 months later without thyroid hormone replacement. In 23 patients, the iodine intake was restricted to < 100 μg per day (group 1), and in the other 22 patients iodine intake was not restricted (group 2).

Thyroid function test and thyroid autoantibodies

The serum total T4, total T3, free T4, TSH concentration were determined using Elecsys 2010 (Boehringer Mannheim, Mannheim, Germany). The range of normal values was 5.2 - 12.9 μg/dL for T4, 84 - 157 ng/dL for T3, 0.8 - 1.7 ng/dL for fT4 and 0.41 - 4.43 μIU/mL for TSH. The serum antimicrosomal and antithyroglobulin antibody titers were measured by a passive agglutination immunoassay using SERODIA AMC (FUJIREBIO INC., Tokyo, Japan) and SERODIA ATG (FUJIREBIO INC., Tokyo, Japan). The TSH receptor antibody titers were measured using a RIA kit (RSR LIMITED, Cardiff, U.K.).

Thyroid weight

Thyroid weight was calculated using Spencer's method as follows:[12]

Thyroid weight (g)=0.12 × (height of left lobe + height of right lobe) × (height of left lobe × width + height of right lobe × width)

Measurement of daily iodine intake

A semi-quantitative food frequency method was used to investigate the usual iodine intake of the subjects.

The dietary iodine intake level was calculated as follows:

$$I = F \times Q \times N$$

(I: dietary iodine intake, F: frequency per day, Q: one-time consumption amount, N: iodine content in the food).

The data of the iodine content in common Korean food was obtained by neutron activation analysis.[13]

Measurement of urinary iodine excretion

The morning spot urine from the first urination before breakfast was examined for the urinary

iodine excretion measurements. The iodine concentration in the urine samples was measured by an iodide-selective ion electrode method (model 9653 champion series iodide electrode: Orion Research Inc, Boston, MA, U.S.A.).[14-16] Standard solutions were prepared by a serial dilution of a Iodide Standard solution at 20-25℃. The response characteristics of the electrode were evaluated by exposing it to different standard iodide solutions. The standard solution was 0.1 M NaI, and the ionic strength adjuster was 5 M $NaNO_3$ in a mixing rate of 1 : 10 for urine.

Statistical analysis

All the results are expressed as mean ± standard deviation. Chi-Square tests were used for the categorical data and non-paired t-tests were used for the continuous data. A paired t-test was used to compare the initial thyroid functions with those 3 month later. The Pearson chi-square test was used to compare the gender differences. A p-value < 0.05 was considered significant.

RESULTS

Patient characteristics

Among the 45 patients, there were no significant differences in terms of gender, age, duration, size of the goiter, the serum antimicrosomal, antithyrogloburin and TSH receptor antibody titers, the 24 hr radioactive iodine uptake, the iodine intake, urinary iodine excretion level, and initial serum total T3, total T4 and TSH concentration. Initial serum fT4 from group 2 was significantly higher than that of group 1. However, the TSH level, which is a more predictable value of hypothyroidism than fT4, was similar in the two groups (Table 1).

Table 1. Clinical Characteristics in the 45 Patients with Hypothyroidism Due to Hashimoto's Thyroiditis

	Group 1	Group 2
Number (patients)	23	22
Sex (male:female)	0 : 23	3 : 19
Age (years)	40.70 ± 10.49	43.50 ± 11.88
Duration of disease (months)	25.26 ± 25.22	32.50 ± 66.23
Goiter size (g)	15.19 ± 11.08	9.96 ± 5.18
Initial T3 (ng/dL)	110.63 ± 35.40	109.70 ± 25.77
Initial T4 (μg/dL)	7.02 ± 2.41	7.16 ± 0.73
Initial fT4 (ng/dL)	0.80 ± 0.27*	0.98 ± 0.17*
Initial TSH (mIU/mL)	37.95 ± 81.76	11.25 ± 11.42
MSAb (U/mL)	205.65 ± 137.54	186.36 ± 143.58
TGAb (U/mL)	86.09 ± 119.42	42.73 ± 73.56
TRAb (U/mL)	0.69 ± 2.37	4.79 ± 12.15
24 hr RAIU (%)	24.77 ± 19.16	29.23 ± 17.29
24 hr iodine intake (μg)	486.45 ± 318.40	716.60 ± 1113.83
Urine iodine excretion (mg/L)	2.96 ± 1.73	3.72 ± 1.56

Data are means ± SD.
*$p<0.05$ by t-test between Group 1 and Group 2.
Group 1: hypothyroidism due to Hashimoto's thyroiditis with restriction of iodine intake.
Group 2: hypothyroidism due to Hashimoto's thyroiditis without restriction of iodine intake.
MSAb, antimicrosomal antibody; TGAb, antithyroglobulin antibody; TRAb, TSH receptor antibody; RAIU, radioactive iodine uptake.

Recovery rate of thyroid function according to iodine restriction

Eighteen out of the 23 patients (78.3%) from group 1 recovered euthyroid, 4 patients (17.3%) had sustained hypothyroidism, and 1 patient (4.3%) had aggravated hypothyroidism after 3 months. In the 22 patients from group 2, 10 patients (45.5%) recovered to the euthyroid state, 2 patients (9.0%) sustained hypothyroidism, and 10 patients (45.5%) had aggravated hypothyroidism (Fig. 1).

Changes of thyroid function after 3 months of iodine restriction

In group 1, the mean total T3 and total T4 levels were not changed, but the fT4 level increased from 0.80 ± 0.27 ng/dL to 0.98 ± 0.21 ng/dL, and the TSH levels decreased from 37.95 ± 81.76 μIU/mL to 25.66 ± 70.79 μIU/mL: they had recovered from their hypothyroidism ($p< 0.05$; Table 2).

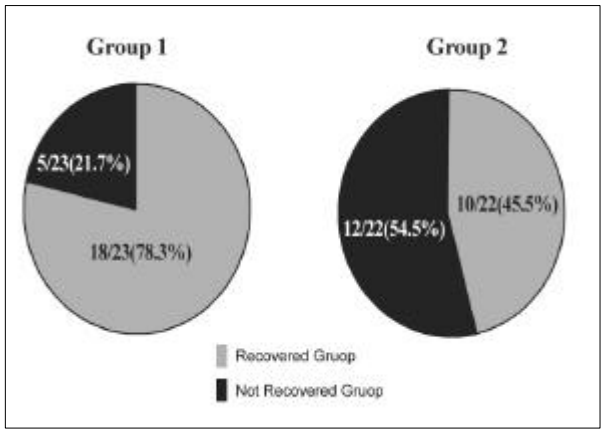

Fig. 1. Recovery rate of the thyroid function. Group 1: hypothyroidism due to Hashimoto's thyroiditis with a restriction of the iodine intake. Group 2: hypothyroidism due to Hashimoto's thyroiditis without a restriction of the iodine intake.

In group 2, the mean total T3, total T4, and TSH levels were unchanged, but the fT4 levels decreased from 0.98 ± 0.17 ng/dL to 0.92 ± 0.28 ng/dL: their hypothyroidism remained ($p < 0.05$; Table 2).

Predictable factors for recovery of thyroid function

In a comparison of the clinical characteristics between the recovery group and the non-recovery group, the duration of disease of the recovery group was shorter than that of the non-recovery group (21.36 ± 22.20 months vs. 41.06 ± 74.71 months). However, there was no statistical significance (p=0.197; Table 3) with the exception that the other variables in the recovery group and non-recovery group were similar (Table 3).

In a comparison of the clinical characteristics in the 23 patients with iodine restriction, the iodine intake of recovery group was more likely to be higher than that of the non-recovery group (555.67 ± 302.19 μg vs. 264.92 ± 289.70 μg), but the difference was not statistically significant (p=0.074; Table 4). Iodine excretion, which is an objective indicator of the iodine intake level of the recovery group was significantly higher than that of the non-recovery group (3.51 ± 1.62 mg/L vs. 1.21 ± 0.39 mg/L; $p<0.01$, Table 4). The initial serum

Table 2. Changes in the Thyroid Function after 3 Months Later

	Group 1		Group 2	
	Initial	3 months later	Initial	3 months later
T3 (ng/dL)	110.57 ± 36.23	103.50 ± 27.41	109.70 ± 25.77	102.84 ± 20.09
T4 (μg/dL)	7.02 ± 2.41	6.52 ± 3.79	7.03 ± 1.23	9.15 ± 1.34
FT4 (ng/dL)	0.80 ± 0.27*	0.98 ± 0.21*	0.98 ± 0.17*	0.92 ± 0.28*
TSH (mIU/mL)	37.95 ± 81.76*	25.66 ± 70.79*	11.25 ± 11.42	14.27 ± 19.31

Data are means ± SD.
*p<0.05 by paired t-test between initial and 3 months later thyroid function.
Group 1: hypothyroidism due to Hashimoto's thyroiditis with restriction of iodine intake.
Group 2: hypothyroidism due to Hashimoto's thyroiditis without restriction of iodine intake.

Table 3. Clinical Characteristics in Hypothyroidism due to Hashimoto's Thyroiditis according to the Reversibility of Hypothyroidism

	Recovery group	Non-recovery group
Number (patients)	28	17
Sex (male:female)	3 : 25	0 : 17
Age (years)	40.50 ± 11.01	44.65 ± 11.24
Duration of disease (months)	21.36 ± 22.20	41.06 ± 74.71
Goiter size (g)	12.27 ± 7.37	12.24 ± 11.45
MSAb (U/mL)	180.71 ± 137.84	221.76 ± 141.96
TGAb (U/mL)	67.14 ± 99.47	61.18 ± 106.35
TRAb (U/mL)	3.56 ± 10.82	1.20 ± 3.19
24 hr RAIU (%)	26.64 ±16.48	27.56 ± 21.12
24 hr iodine intake (μg)	521.75 ± 265.47	730.30 ± 1285.51
Urine iodine excretion (mg/L)	3.50 ± 1.42	3.11 ± 2.02
T3 (ng/dL) initial	116.82 ± 30.14	99.22 ± 29.29
3 months later	110.75 ± 15.48*	91.14 ± 29.60*
T4 (μg/dL) initial	7.64 ± 1.05	5.65 ± 3.03
3 months later	8.61 ± 2.53*	5.20 ± 3.18*
FT4 (ng/dL) initial	0.89 ± 0.22	0.88 ± 0.27
3 months later	1.07 ± 0.17*	0.75 ± 0.20*
TSH (mIU/mL) initial	12.05 ± 10.70	46.04 ± 94.38
3 months later	3.07 ± 1.16*	48.12 ± 78.27*

Data are means ± SD.
*$p < 0.05$ by t-test between recovery group and non-recovery group.
Recovery group: patients who recovered from hypothyroidism to the euthyroid state spontaneously.
Non-recovery group: patients who did not recover from hypothyroidism to the euthyroid state.
MSAb, antimicrosomal antibody; TGAb, antithyroglobulin antibody; TRAb, TSH receptor antibody; RAIU, radioactive iodine uptake.

total T3 level of the recovery group was higher than that of the non-recovery group (120.28 ± 28.00 ng/dL vs. 75.90 ± 40.40 ng/dL; $p < 0.05$), and the serum TSH level of the recovery group was lower than that of the non-recovery group (14.28 ± 12.63 μIU/mL vs. 123.14 ± 156.51 μIU/mL; $p < 0.01$, Table 4).

In a comparison of the clinical characteristics in the 22 patients without iodine restriction, the patients who did not recover were all female ($p < 0.05$, Table 5).

DISCUSSION

A few forms of thyroiditis such as postpartum thyroiditis, painless thyroiditis, and subacute thyroiditis, as well as an excessive intake of lithium, amiodarone, and iodide can induce transient hypothyroidism.[17] In addition, an abnormal thyroid function can be combined with severe non-thyroidal disease. Therefore, in order to exclude the cases that could cause transient thyroid function abnormalities, patients who had taken drugs, such as lithium, amiodarone, iodine, and glucocorticoids, and patients with a history of delivery within 1 year or a history of severe non-thyroidal disease were excluded. Furthermore, thyroid goiter patients suffering from pain and tenderness over the thyroid region and patients who had symptoms of thyrotoxicosis over recent 6 months were ruled out of this study in order to exclude any patients on a stage of recovery from transient hypothyroidism after suffering from subacute thyroiditis and painless thyroiditis. However, in some patients with painless thy-

Table 4. Clinical Characteristics in the Patients with Iodine Restriction according to the Reversibility of Hypothyroidism

	Recovery group	Non-recovery group
Number (patients)	18	5
Sex (male:female)	0 : 18	0 : 05
Age (years)	40.33 ± 10.23	42.00 ± 12.55
Duration of disease (months)	25.00 ± 25.81	26.20 ± 25.81
Goiter size (g)	13.57 ± 8.04	21.04 ± 18.60
MSAb (U/mL)	208.89 ± 131.99	194.00 ± 172.57
TGAb (U/mL)	74.44 ±102.80	128.00 ± 175.27
TRAb (U/mL)	0.88 ± 2.67	0.00 ±0.00
24 hr RAIU (%)	28.28 ± 20.09	12.82 ± 9.10
24 hr iodine intake (μg)	555.67 ± 302.19	264.92 ± 289.70
Urine iodine excretion (mg/L)	3.51 ± 1.62*	1.21 ± 0.39*
T3 (ng/dL) initial	120.28 ± 28.00*	75.90 ± 40.40*
3 months later	115.0 ± 414.76*	64.30 ± 24.25*
T4 (μg/dL) initial	7.94 ± 1.14	5.20 ± 3.55
3 months later	8.32 ± 3.26*	3.43 ± 2.35*
fT4 (ng/dL) initial	0.82 ± 0.21	0.75 ± 0.46
3 months later	1.05 ± 0.17*	0.70 ± 0.14*
TSH (mIU/mL) initiall	14.28 ± 12.63*	123.14 ± 156.51*
3 months later	3.18 ± 1.22*	106.59 ± 130.75*

Data are means ± SD.
*$p<0.05$ by t-test between recovery group and non-recovery group.
Recovery group: patients who recovered from hypothyroidism to the euthyroid state spontaneously.
Non-recovery group: patients who did not recover from hypothyroidism to the euthyroid state.
MSAb, antimicrosomal antibody; TGAb, antithyroglobulin antibody; TRAb, TSH receptor antibody; RAIU, radioactive iodine uptake.

roiditis, hypothyroidism can occur without an obvious thyrotoxicosis stage. In such cases, the patients with hypothyroidism lasting for 1 - 6 months from painless thyroiditis cannot be completely ruled out because there are no differences between them and the Hashimoto thyroiditis patients in terms of the thyroid function test, thyroid autoantibody level, and radioiodine uptake.

In this study the serum TSH levels $>5\,\mu$IU/mL were set as the criteria of hypothyroidism by Hashimoto thyroiditis. Patients with a TSH level $<10\,\mu$IU/mL were included. In the group whose thyroid function had returned to normal, the initial TSH was 12.05 ± 10.70 μIU/mL, which has no statistical difference compared to the initial TSH level of 46.04 ± 94.38 μIU/mL which was the value in the group whose thyroid function had not returned to normal. In the group whose thyroid function returned to normal, there is a possibility that subclinical hypothyroidism patients were included. Therefore, if the subject group was limited to a TSH $>10\,\mu$IU/mL, it is believed that the subclinical hypothyroidism patients could be excluded.

This study suggests that in those patients with hypothyroidism due to Hashimoto's thyroiditis, 78.3% had returned to a normal thyroid function with only iodine restriction without thyroid hormone replacement, and this recovery had occurred mostly within 3 months. In the 4 patients with sustained hypothyroidism with iodine restriction, the serum TSH concentration progressively decreased and it is expected that they will return to euthyroid after longer period. In 2

Table 5. Clinical Characteristics in the Patients without Iodine Restriction according to the Reversibility of Hypothyroidism

	Recovery group	Non-recovery group
Number (patients)	10	12
Sex (male:female)	3 : 7*	0 : 12*
Age (years)	40.80 ± 12.87	45.75 ± 11.04
Duration of disease (months)	14.80 ± 12.05	47.25 ± 87.94
Goiter size (g)	9.93 ± 5.58	9.99 ± 5.08
MSAb (U/mL)	130.00 ± 140.16	233.33 ± 134.12
TGAb (U/mL)	54.00 ± 97.09	33.33 ± 49.05
TRAb (U/mL)	8.91 ± 17.80	1.70 ± 3.73
24 hr RAIU (%)	23.86 ± 7.33	33.70 ± 21.88
24 hr iodine intake (μg)	467.48 ± 195.58	924.21 ± 1494.56
Urine iodine excretion (mg/L)	3.49 ± 1.12	3.91 ± 1.89
T3 (ng/dL) initial	110.60 ± 34.31	108.95 ± 17.44
3 months later	103.45 ± 14.54	102.32 ± 24.43
T4 (μg/dL) initial	7.20 ± 0.83	7.00 ± 0.50
3 months later	8.95 ± 1.53	7.85 ± 2.47
fT4 (ng/dL) initial	1.07 ± 0.12	0.93 ± 0.18
3 months later	1.12 ± 0.16*	0.77 ± 0.23*
TSH (mIU/mL) initial	8.05 ± 3.79	13.91 ± 14.84
3 months later	2.88 ± 1.05*	23.76 ± 22.24*

Data are means ± SD.
*$p<0.05$ by t-test between recovery group and non-recovery group.
Recovery group: patients who recovered from hypothyroidism to the euthyroid state spontaneously.
Non-recovery group: patients who did not recover from hypothyroidism to the euthyroid state.
MSAb, antimicrosomal antibody; TGAb, antithyroglobulin antibody; TRAb, TSH receptor antibody; RAIU, radioactive iodine uptake.

of these patients, the initial serum TSH level was above 300 μIU/mL and progressively declined to approximately 200 μIU/mL with iodine restriction. Therefore, and it is expected that the severe hypothyroidism might return to the euthyroid state after long term iodine restriction.

In the group whose iodine intake was not limited, 45.5% had returned to a normal thyroid function. After observing 20 years of the natural course in Hashimoto thyroiditis patients, Rallison et al. reported that 25% of patients recovered their normal thyroid function.[18] In our study, twice as many patients' thyroid function was recovered. This is because some painless thyroiditis patients who had not been through an obvious thyrotoxic crisis could have been included in the subjects, subclinical hypothyroidism patients with a TSH < 10 μIU/mL could have been included, and it is possible that these patients restricted their iodine intake on their own.

To predict the factor of the recovery to the euthyroid state, recovered patients were compared with the non-recovered patients regardless of iodine restriction. There was no difference in the various factors, such as sex, age, duration, size of the goiter, antimicrosomal, antithyroglobulin and TSH receptor antibody titers, 24 hours radioactive iodine uptake, iodine intake, iodine excretion, and the initial serum total T3, total T4, fT4, TSH concentration between the two groups. Yoshinari et al. reported that the hypothyroid patients with a high radioactive iodine uptake showed spontaneous recovery.[9,19] However, in this study, the radioactive iodine uptake in the

recovery and non-recovery groups were similar. Sato et al. reported that patients with a high titer of antimicrosomal and antithyroglobulin antibodies showed spontaneous recovery.[20] However, there was no difference between the recovery and non-recovery group in this study. Jung et al. reported that a young age might be a predicting factor of a recovery from hypothyroidism.[21] In this study, age did not appear to be a contributing factor.

The recovered patients were compared with non-recovered patients respectively in the total group. In the iodine restriction group, the iodine intake of the recovered patients was higher than that of the non-recovered patients, but this was not significant. However, the iodine excretion from the recovered patients was significantly higher than that of the non-recovered patients. This finding suggests that if the iodine intake were restricted, the patients with a high iodine excretion level would recover spontaneously. In addition, the initial serum TSH concentration was significantly lower in the recovered patients than in the non-recovered patients, which suggests that the possibility of recovery in increasingly rare as the initial hypothyroidism becomes more severe. In the iodine non-restriction group, males had a tendency to recover the euthyroid state more easily. However, there is a report suggesting that males had a 7 times more likelihood of suffering hypothyroidism than females over a long follow-up period.[22] Therefore, this result might be caused by the small number of included patients.

A histological examination of the thyroid tissue was not performed in this study, but it might be a help to correlate the degree of thyroid tissue destruction with the reversibility of hypothyroidism for an evaluation of the predictable factors.

In order to avoid life long thyroid hormone replacement, it is recommend that prior to commencing thyroid hormone replacement therapy, clinicians should allow more time or restrict the iodine intake for several months to determine whether the thyroid function spontaneously will return to the euthyroid state, and then replacement therapy is required for patients who do not recover. In addition, it is believed that in the patients with a high iodine excretion level and mild hypothyroidism, restricting the iodine intake could be a primary option.

This study was conducted to provide the clinical guideline for restricting the iodine intake, considering the severity of symptoms and the initial TSH in the patients with primary hypothyroidism due to Hashimoto's thyroiditis. In addition, this guideline is significant in nations such as Korea where the iodine intake is relatively high. However, the limitation in this study is that it did not provide a cut-off value because the number of subjects was not large enough, and we are planning to provide specific guidelines to restricting the iodine intake by determining a cut off value of the initial TSH levels from a larger number of patients.

In conclusion, 78.3% patients with hypothyroidism due to Hashimoto's thyroiditis had recovered to the euthyroid state within 3 months with only iodine restriction. The patients should be observed continuously over a long period to determine if the patients who had improved gradually from hypothyroidism could recover the euthyroid state, and the recovered patients can remain in the euthyroid state. Although only iodine itself does not cause Hashimoto's thyroiditis, iodine can be an important factor that exacerbates hypothyroidism.

REFERENCES

1. Bottazzo GF, Doniach D. Autoimmune thyroid disease. Annu Rev Med 1986;37:353-9.
2. Lewis EB, Robert DU. Autoregulation. In: Braverman LE, Robert D, editors. The thyroid. 7th ed. Philadelphia: Lippincott-Raven Press; 1996. p.241-7.
3. Rallison ML, Dobyns BM, Keating FR, Rall JE, Tyler FH. Occurrence and natural history of chronic lymphocytic thyroiditis in childhood. J Pediatr 1975;86: 675-82.
4. Yamamoto T, Sakamoto H. Spontaneous remission from primary hypothyroidism. Ann Intern Med 1978; 88:808-9.
5. Carlson HE. Spontaneous remission of hypothyroidism. Arch Intern Med 1980;140:1675-6.
6. How J, Khir ASM, Bewsher PD. Spontaneous remission of hypothyroidism due to Hashimoto's thyroiditis. Lancet 1980;2:427-35.
7. Nikolai TF. Recovery of thyroid function in primary hypothyroidism. Am J Med Sci 1989;297:18-21.
8. Okamura K, Sato K, Yoshinari M, Ikenoue H, Kuroda

T, Nakagawa M, et al. Recovery of the thyroid function in patients with atrophic hypothyroidism and blocking type TSH binding inhibitor immunoglobulin. Acta Endocronol (Copenh) 1990;122:107-14.
9. Yoshinari M, Okamura K, Tokuyama T, Shiroozu A, Nakashima T, Inoue K, et al. Clinical importance of reversibility in primary goitrous hypothyroidism. Br Med J 1983;287:720-2.
10. Reinwein D, Benker G, Koenig MP. Hyperthyroidism in Europe: clinical and laboratory data of a prospective multicenter survey. J Endocrinol Invest 1986;9:1-12.
11. Takasu N, Yamada T, Takasu M, Komiya I, Nagasawa Y, Asawa T, et al. Disappearance of thyrotropin-blocking antibodies and spontaneous recovery from hypothyroidism in autoimmune thyroiditis. N Engl J Med 1992;326:513-8.
12. Spencer RP. Determination of organ volumes by scintillation scanning. J Nucl Med 1964;5:444-52.
13. Moon SJ, Kim JY, Chung YJ, Chung YS. The iodine content in common Korean foods. Korean J Nutr 1998; 31:206-12.
14. Yabu Y, Miyai K, Endo Y, Hata N, Iijimi Y, Hayashizaki S, et al. Urinary iodine excretion measured with an iodide-selective ion electrode; Studies on normal subjects of varying ages and patients with thyroid disease. Endocr Japan 1998;35:391-8.
15. Yabu Y, Miyai K, Hayashizaki S, Endo Y, Hata N, Iijimi Y, et al. Measurement of iodide in urine using the iodide-selective ion electrode. Endocr Japan 1986;33: 905-11.
16. Kim JY, Moon SJ, Kim KR, Sohn CY, Oh JJ. Dietary iodine intake and urinary iodine excretion in normal Korean adults. Yonsei Med J 1998;39:355-62.
17. Hawthorne GC, Campbell NP, Geddes JS, Ferguson WR, Postlethwaite W, Sheridan B, et al. Amiodarone-induced hypothyroidism. A common complication of prolonged therapy: a report of eight cases. Arch Intern Med 1985;145:1016-9.
18. Rallison ML, Dobyns BM, Meikle AW. Natural history of thyroid abnormality: prevalence, incidence and regression of thyroid disease in adolescents and young adults. Am J Med 1991;91:363-75.
19. Tajiri J, Higashi K, Morita M, Umeda T, Sato T. Studies of hypothyroidism in patients with high iodine intake. J Clin Endocrinol Metab 1986;63:412-7.
20. Sato K, Okamura K, Ikenoue H, Shiroozu A, Yoshinari M, Fujishima M. TSH dependent elevation of serum thyroglobulin in reversible primary hypothyroidism. Clin Endocrinol 1988;29:231-7.
21. Jung JH, Kim KW, Ahn KJ, Min YK, Lee MS, Lee MK, et al. Spontaneous recovery from hypothyroidism in autoimmune thyroiditis. J Korean Soc Endocrinol 1996; 11:30-40.
22. Dayan CM, Daniels GH. Chronic autoimmune thyroiditis. N Engl J Med 1996;335:99-107.