Long Term Results of Treating Hyperthyroid Patients with $^{131}$I

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Present status of the patients over 10 years after therapy of hyperthyroidism with radioiodine several factors which might influence the outcome of therapy were investigated. Accurate information was obtained in 512 cases out of 1620 patients treated with $^{131}$I from 1963 to 1967 at Ito Hospital. Radiation absorbed doses delivered thyroid were measured in all cases. Hypothyroidism was diagnosed in the presence of a serum T4 of $<5.3$ ng/dl and T3 of $<80$ ng/dl. When either serum T3 or T4 is within normal range, it was diagnosed clinically referring to metabolic index. The incidence of hypothyroidism was 28.9%, euthyroidism 65.9% and hyperthyroidism 5.1% in 512 cases. Considering these results from a standpoint of pituitary-thyroid axis, high TSH level was observed in 139 (41.0%) out of 340 euthyroid cases. While TRH tests were performed in 11 cases with normal T3, T4 and TSH levels, TSH response was normal in only 2 out of 11 cases, exaggerated in 7 cases and not observed in 2 cases.

The incidence of hypothyroidism was 15.8% when dose was under 5,000 rads and 43.3% when dose was over 10,000 rads. Since there were no differences in the incidences of hypothyroidism among three groups received 6,001–7,000, 7,001–8,000 and 8,001–9,000 rads, relationship between clinical results and various factors before treatment were investigated in these 245 cases. The incidence of hypothyroidism was high in cases with small goiter, soft goiter, low thyroidal uptake and short half life of $^{131}$I at the time of therapy, short period between the onset of hyperthyroid symptoms and $^{131}$I therapy. The titer of antithyroid antibody before treatment, age or sex of the patients appeared unrelated. In the cases with severe exophthalmus ($\geq 18$ mm), the incidences of both hyperthyroidism and hypothyroidism were high. The degree of exophthalmus increased after therapy in 307 out of 512 cases but it's change had no relation to thyroid function.

At 1 year after therapy, 11.0% of subjects were hypothyroid and the incidence of hypothyroidism increased annually at a rate of 1.9% yearly from the second to the tenth year after treatment.

Three cases of thyroid cancer and 2 cases of leukemia were observed after $^{131}$I therapy. While 0.55 cases of leukemia were expected in person year method of 823 treated cases, incidence of leukemia was high but not significant. There were no cases of which serum calcium level was low.

These findings suggest that it is necessary to regulate the dose of $^{131}$I referring to size and consistency of goiter, thyroidal uptake and half life of $^{131}$I etc.

Receptor Assay of the Thyroid Stimulators

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We examined two methods of the receptor assay. 1) Receptor assay using radioimmunoassay (RIA)
A new receptor assay of thyroid stimulators using TSH radioimmunoassay (RIA) was devised. The principle of this method is RIA determination of displaced HTSH amounts by any other
thyroid stimulators from thyroidal receptor fraction that was bound with unlabelled HTSH.

Practically, 4 μU of HTSH were conjugated with receptor, and then displaced effect by test serum (0.1 ml) was observed. Animal TSH of both bovine and rat showed displacement with HTSH. Patient sera with increased TSH by RIA showed a high correlation with the determined value by the receptor assay. However, 18 sera with a high LATS activity in untreated hyperthyroidism did not show any positive displacement. By this method it could not demonstrated that LATS and TSH bind with the same receptor.

The principle of this radioimmuno-receptor assay may be available to examine the isohormone of other all peptide hormone that can be determined by RIA method.

2) Receptor assay using the radioiodine-labeled long acting thyroid stimulator (LATS)

A new receptor assay that is based on determination of the displacing activity of 125I-LATS from human thyroid receptor by test serum is developed. The purified LATS-IgG was labeled with 125I-LATS was purified by selective absorption with the purified plasma membrane from human thyroid. Although the displacement of 125I-LATS from human thyroid receptor was not occurred by normal human serum, the significant displacement was occured by high Lats positive sera of 17 cases except one.

Twenty-six cases in 38 cases of LATS negative sera in Graves’ disease also showed the displacing activity. All cases of Hashimoto’s sera with the precipitating antibody for thyroglobulin and about a half sera with the haemagglutination antibody for thyroglobulin showed the positive displacing activity. Human and bovine TSH did not show any displacement.

These data mean that the binding of 125I-LATS with thyroid receptor is displaced by the most LATS and some of Hashimoto’s sera with a high thyroidal antibody, but is not displaced by TSH.

It is possible to apply this procedure for the determination of thyroid receptor binding immunoglobulin (TRBI) in test serum with satisfactory reproducibility.