NOTE

Low T₃ Syndrome in Cancer Patients in Relation to Weight Loss, Intravenous Hyperalimentation Therapy and Age.

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Abstract

In order to investigate the relation of weight loss and intravenous hyperalimentation therapy to low T₃ syndrome, serum T₃, T₄, rT₃ and TBG were determined by radioimmunoassay in 105 cancer patients.

The cancer patients were classified into 3 groups, Group I, II and III depending on the grade of weight loss, ranging up to a 5% change in weight loss from a healthy condition, from 5 to 9%, and more than 10%, respectively. Cancer patients under age 59 showed no significant difference in serum T₃, T₄, rT₃ and TBG among these 3 groups. However serum T₃ and T₃/T₄ in cancer patients at age 60 and over were significantly reduced in group III, compared to groups I and II. Serum rT₃ values were significantly elevated in group III of elderly cancer patients. The incidence of low T₃ syndrome in group III of elderly cancer patients was also significantly higher than in groups I and II.

In three out of 5 cancer patients with low T₃ syndrome, serum T₃ values increased after the intravenous hyperalimentation therapy, whereas no significant change in serum T₃ values was observed in two patients who died within one day after the final examination.

It is concluded that weight loss produced different effects on peripheral conversion of T₄ to T₃ between cancer patients under age 59 and over age 60 and glucose plays an important role in the pathogenesis of low T₃ syndrome except cases with very poor prognosis.

It is already known (Sullivan et al., 1973) that many serious systemic diseases are characterized by an unusual change in circulating thyroid hormones. In these cases, a decrease in total and free 3, 5, 3'-triiodothyronine (T₃ and FT₃), an increase in 3, 3', 5'-triiodothyronine (reverse T₃, rT₃), normal total thyroxine (T₄) and normal, low or high free thyroxine (FT₄) are frequently observed.

A change in the deiodinative mechanism leads to the clinical situation known as low T₃ syndrome characterized by a reduced peripheral conversion of T₄ to T₃ and a rise in rT₃ levels. Low T₃ syndrome has been also described in the undernutrition states such as fasting (Croxson and Ibberton, 1977), anorexia nervosa (Miyai et al., 1975; Spencer

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et al., 1983) and cancer (Kamijo et al., 1981a). Studies of low diet therapy in obesity have also demonstrated that carbohydrate plays a very important role in the pathogenesis of low T₃ syndrome (Spaulding et al., 1976; Burman et al., 1979). The present study was undertaken to investigate the relationship of weight loss and hyperalimentation therapy to low T₃ syndrome in cancer patients.

**Materials and Methods**

One hundred and five cancer patients including 58 gastric, 25 colonic, 7 hepatocellular, 7 pancreatic, 5 pulmonary and 3 esophageal cancers were investigated. None of the patients was pretreated with steroid. Serum T₃, T₄, rT₃ and TBG were measured by radioimmunoassay, as previously reported (Kamijo et al., 1981b). T₃/T₄ ratio was used to evaluate a peripheral conversion of T₄ to T₃ because of highly significant correlation with its true conversion (Nomura et al., 1974; Kato and Kamijo; in preparation).

Weight loss was expressed as percent changes from the body weight in a healthy condition of individual patients. Serum T₃ and T₄ values were measured before and about 2 weeks after intravenous hyperalimentation therapy with 900 to 1200 cal of glucose administered to 3 patients with pulmonary cancer and 2 patients with gastric cancer presenting low T₃ syndrome.

Low T₃ syndrome was defined as low T₃ values (less than 62 ng/dl) and normal T₄ values (5.4 to 11.4 μg/dl) (Kato and Kamijo, in preparation).

**Results**

(1) Relationship between weight loss in serum T₃, T₄, T₃/T₄, rT₃, and TBG values (Fig. 1, 2, 3, 4 and 5) (Table 1).

Cancer patients were classified into 3 groups i.e. groups I, II and III, depending on the grade of weight loss ranging up to a 5% change in weight loss from a healthy condition, from 5 to 9%, and more than 10%, respectively. The mean ages of group

<table>
<thead>
<tr>
<th>% body weight loss</th>
<th>Serum T₃ values</th>
<th>Under age 60</th>
<th>Age 60 and over</th>
</tr>
</thead>
<tbody>
<tr>
<td>(0 ～ 4%)</td>
<td>100 (n=12)</td>
<td>150 (n=7)</td>
<td>110 (n=11)</td>
</tr>
<tr>
<td>(5 ～ 9%)</td>
<td>50 (n=40)</td>
<td>150 (n=16)</td>
<td>110 (n=35)</td>
</tr>
<tr>
<td>(10 ~ %)</td>
<td></td>
<td></td>
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</tbody>
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* p<0.01: compared to (0 ～ 4%) and (5 ～ 9%) at the age 60 and over

![Fig. 1. Effect of body weight loss on serum T₃ values in cancer patients.](image)
Fig. 2. Effect of body weight loss on serum T4 values in cancer patients.

Fig. 3. Effect of body weight loss on T3/T4 values in cancer patients.

* p<0.01: compared to (0–4%) and (5–9%) at the age 60 and over
Fig. 4. Effect of body weight loss on serum rT₃ values in cancer patients.
* p<0.01: compared to (0-4%) and (5-9%) at the age 60 and over

Fig. 5. Effect of body weight loss on serum TBG values in cancer patients
Table 1. Incidence of low T₃ syndrome in cancer patients

<table>
<thead>
<tr>
<th>Group</th>
<th>% Body weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0–4%</td>
</tr>
<tr>
<td>II</td>
<td>5–9%</td>
</tr>
<tr>
<td>III</td>
<td>10%</td>
</tr>
<tr>
<td>Under age 60</td>
<td>2/12</td>
</tr>
<tr>
<td>Age 60 and over</td>
<td>3/40</td>
</tr>
<tr>
<td>Total</td>
<td>5/52</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>% Body weight loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0–4%</td>
</tr>
<tr>
<td>II</td>
<td>5–9%</td>
</tr>
<tr>
<td>III</td>
<td>10%</td>
</tr>
<tr>
<td>Under age 60</td>
<td>0/7</td>
</tr>
<tr>
<td>Age 60 and over</td>
<td>3/16</td>
</tr>
<tr>
<td>Total</td>
<td>3/23</td>
</tr>
</tbody>
</table>

* 3 cases were examined at 2 different points of % body weight loss.

I, II and III in the elderly cancer patients were 72±7 (±S.D.) years, 71±5 and 70±6, respectively. Cancer patients under age 59 showed no significant difference in serum T₃, T₄, rT₃ and TBG among these 3 groups. It was noted, however, in cancer patients at the age 60 and over that serum T₃ and T₃/T₄ were significantly lower in group III (p<0.01) than in group I or group II. Serum rT₃ values were significantly higher in group III of elderly cancer patients than in group I (p<0.01) or group II (p<0.01). No significant changes in serum T₄ or TBG were observed among three groups of elderly cancer patients. The incidence of low T₃ syndrome is summarized in Table 1. No significant difference in the incidence of low T₃ syndrome was found among three groups of cancer patients under age 59, although group III of elderly cancer patients showed a significantly higher incidence (17/35: 48.6%) of low T₃ syndrome than group I (3/40: 7.5%; p<0.01) or II (3/16: 18%; p<0.05) of them.

(2) Influence of intravenous hyperalimentation therapy on serum T₃ and T₄ values (Fig. 6).

In three out of 5 cancer patients, serum T₃ values increased after the intravenous hyperalimentation therapy, whereas no significant changes in serum T₄ values were observed after the therapy. Two patients who died within one day after the final examination showed no significant changes in serum T₃ levels before and after hyperalimentation.

![Fig. 6. Effect of hyperalimentation for about 2 weeks on T₃ and T₄ values in cancer patients with low T₃ syndrome. (○—○): died within 1 day after the final examination (●—●): died 22±17 days after the final examination](image-url)
Discussion

We have demonstrated that weight loss produced different effects on peripheral conversion of T4 to T3 in cancer patients under age 59 and those over age 60. The results of clinical studies on the influence of hyperalimentation on the serum T3 concentrations lead to the conclusion that glucose plays an important role in the pathogenesis of low T3 syndrome in cancer patients except cases with very poor prognosis who died within one day after the examination.

Spaulding et al. (1976) reported that unlike protein and lipid, only carbohydrate maintained normal T3 values during low calory diet in obese subjects. Not only glucose, but fructose also has a similar effect on serum T3 values (Burman et al., 1979). In contrast, it is pointed out that in cancer patients with weight loss, low T3 syndrome is not based on abnormal metabolic changes in carbohydrate because the blood free fatty acid and alanine decreased but the blood glucose, ketone body, lactic acid, pyruvate as well as insulin and glucagon were all within the normal range (Axelrod et al., 1983). However our results indicated that the low T3 syndrome in cancer patients was associated with metabolic changes in glucose since the intravenous hyperalimentation therapy induced the normalization of serum T3 values.

It has been also reported that low T3 or low T4 syndrome is closely associated with poor prognosis (Kaptein et al., 1982; Vierhapper et al., 1982). In the present study, no significant changes in serum T3 were induced by hyperalimentation in cancer patients with very poor prognosis. The results suggests that low T3 syndrome may also be caused by a certain metabolic change associated with poor prognosis in cancer patients.

Acknowledgements

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References


