World J. Surg. 5, 855–857, 1981

World Journal of Surgery

Prophylaxis of Recurrent Goiter by High-Dose L-Thyroxine

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In a prospective, randomized, controlled study of 64 patients after bilateral subtotal thyroidectomy, a high dosage of 1.0 mg L-thyroxine taken once a week was compared to the usual intake of 0.1 mg L-thyroxine daily for prevention of recurrent goiter. During a follow-up study for 52 weeks, the effectiveness and acceptability of an intermittent high dosage was assessed clinically and also by measuring basal TSH, stimulated TSH, iT_4, and iT_3. In both groups, postoperative elevated TSH levels could be reduced to subnormal levels by L-thyroxine intake. iT_3 and iT_4 levels remained in the normal range after either daily or intermittent therapy. The weekly high dosage of 1.0 mg L-thyroxine has proved to be at least as effective as the usual therapy with no apparent disadvantage.

Recurrence after removal of simple goiter represents a major problem in operative treatment of this condition. Thorough postoperative control with increased patient compliance with regard to L-thyroxine intake could reduce recurrent goiter from 15% to 1.5% [1]. Since some patients still find the daily intake of L-thyroxine a burden, we investigated the acceptability of high-dose L-thyroxine intake once a week as an alternative to daily medication. Our investigations were stimulated by studies of Sekadde et al. [2] and Bernstein et al. [3], who administered L-thyroxine in intermittent high dosages but could refer only to very few individual patients with varying underlying diseases and operative procedures. Therefore, a prospective, randomized, controlled study was performed in a homogeneous group of patients with standardized surgical treatment.

Materials and Methods

Ninety-four patients were operated on for simple goiter between February and July, 1978 at Bethesda Hospital, Duisburg, West Germany. All patients with bilateral subtotal thyroidectomy (n = 64) were included in the study. These patients were randomly divided into 2 groups (Table 1). For the first 5 weeks postoperatively, none of the patients received any prophylaxis against goiter recurrence. Thereafter, the patients took either 1.0 mg L-thyroxine (L-T_4) once a week (group I) or 0.1 mg L-thyroxine (L-T_4) daily (group II) over a period of 12 weeks, succeeded by a 4-week interval free of therapy. Again there followed a therapeutic period over 21 weeks. iT_3, iT_4, basal, and stimulated TSH (after injection of 200 mg TRH) were measured at the end of 1, 5, 17, 21, and 52 weeks after surgery by the radioimmunoassay technique (Henning Corp., Berlin).

Results

Basal and stimulated TSH values are commonly used to prove stimulating influences on the growth of the goiter, especially after bilateral subtotal thyroidectomy [4, 5]. Figure 1 shows the basal and stimulated TSH values of both groups related to therapeutic regimen at different times. After periods without medication (5th and 21st weeks), the basal and stimulated TSH values (Fig. 1) are elevated above normal range in both groups, while after 12

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0364-2313/81/0005-0855 $01.00

Table 1. Course of the study on postoperative therapy for recurrent goiter in 94 patients.

Postoperative weeks	Group	Treatment
1–5	I	No therapy
	II	No therapy
5–17	I	1.0 mg/week L-T_4
	II	0.1 mg/day L-T_4
17–21	I	No therapy
	II	No therapy
21–52	I	1.0 mg/week L-T_4
	II	0.1 mg/day L-T_4

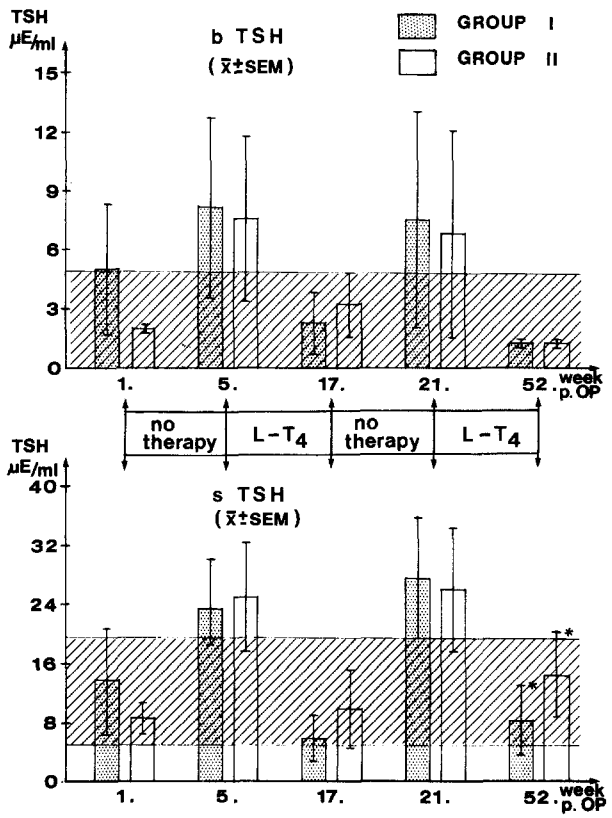

Fig. 1. TSH-values (b = basal, upper part; s = stimulated, lower part) at different times indicated by the arrows. Group I: 1.0 mg L-T_4 weekly; group II: 0.1 mg L-T_4 daily; * statistical significance, $P < 0.05$ by Wilcoxon rank test. Normal range indicated by shaded area.

and 21 weeks of medication (17th and 52nd weeks postoperatively), TSH values showed a statistically significant decrease in both groups, respectively. Simultaneous comparison of the TSH values of groups I and II indicated moderate differences, not significant up to 52 weeks postoperatively.

The peripheral hormone levels of iT_3 and iT_4 remain within normal range without any significant difference between groups I and II (Fig. 2). This is

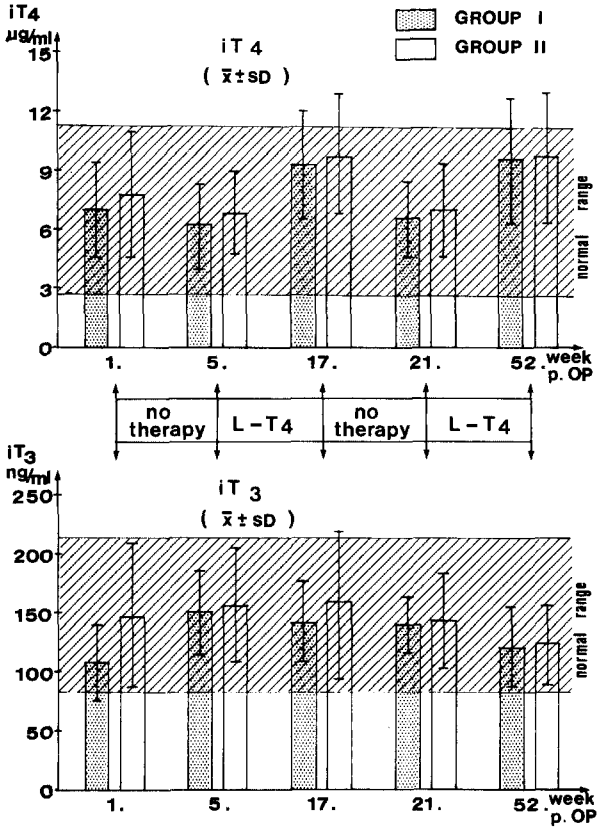

Fig. 2. iT_4 and iT_3 values at different times indicated by the arrows. Group I: 1.0 mg L-T_4 weekly; group II: 0.1 mg L-T_4 daily; normal range indicated by shaded area. No statistical difference between groups I and II (Wilcoxon test).

in accordance with the clinical aspects: no patients, especially in group I, complained of symptoms of hyperthyroidism.

By a more detailed measurement, the iT_3, iT_4, and TSH values within 8 days after repetitive application of 1 mg L-T_4 were investigated in 5 euthyroid healthy probands (Fig. 3). While iT_4 was elevated but within normal range, iT_3 showed a minor tendency to decrease with a marked suppression of TSH values. This provides evidence that peripheral conversion of T_4 into T_3 apparently takes place slowly [6, 7]. In accordance, no clinical symptoms of hyperthyroidism were observed.

Discussion

This study has shown that weekly administration of 1 mg L-T_4 as compared to the daily intake of 0.1 mg L-T_4 has proven to be effective by suppressing elevated TSH levels, and acceptable by attaining peripheral hormone levels within normal range. Furthermore, no clinical symptoms of hyperthy-

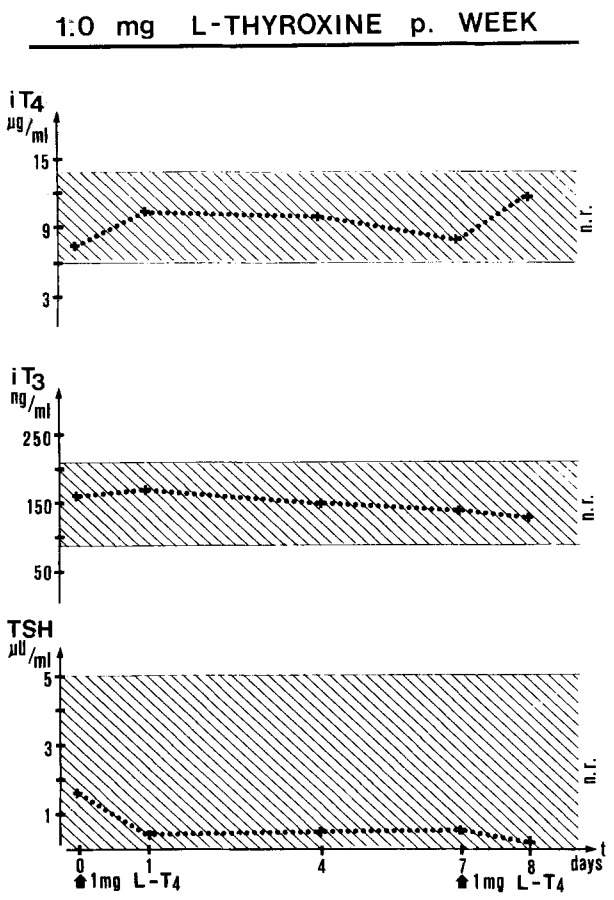

Fig. 3. iT_4, iT_3, and TSH values in 5 healthy euthyroid probands after repetitive application of 1 mg L-T_4 indicated by the arrows; n.r. = normal range, indicated by shaded area.

roidism were observed in any patient. This supports previous findings of Odell et al. [8], Braverman et al. [9], Hays et al. [10], and Wenzel et al. [11], that T_4 is virtually a prohormone which must be converted into the effective T_3 hormone peripherally [7]. Even higher dosages of thyroxine (3.0 mg L-T_4) as used for the thyroid suppression test are generally well tolerated [1, 11, 12].

Concerning the limited capacity of intestinal resorption of L-T_4 and, additionally, a restricted binding capacity on plasmatic thyroglobulin [13], the dosage of 1 mg L-T_4 seems appropriate and effective. Since after a single high dose of L-T_4, TSH suppression could be demonstrated for 12 to 16 days [8, 12, 14], weekly administration appears adequate.

The weekly administration of 1 mg L-T_4 offers a useful alternative to the well-documented effect of daily application of 0.1 mg L-T_4 for prophylaxis against recurrence of goiter [15–17]. It might help to increase the patients' comfort and compliance.

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