Do we treat hypothyroidism properly? A survey of 2488 patients from University Hospital Center, Zagreb, Croatia

Nous traitons l’hypothyroïdie correctement ? Un sondage de 2488 patients du centre hospitalier de l’université, Zagreb, Croatie

Darko Solter, Miljenko Solter

Department of Otorhinolaryngology, Head and Neck Surgery, Sisters of Mercy University Hospital Center, Vinogradska 29, 10000 Zagreb, Croatia

University of Zagreb, School of Medicine, Department of Endocrinology, Sisters of Mercy University Hospital Center, Vinogradska 29, 10000 Zagreb, Croatia

Abstract

Objectives. – The objective was to examine the effectiveness of levothyroxine treatment in hypothyroid patients in achieving normal thyroid stimulating hormone (TSH), T4 and T3. Material and methods. – Results of the treatment of 2448 hypothyroid patients treated with LT4 for at least 12 months between 2006 and 2011 (1920 with spontaneous hypothyroidism and 528 with hypothyroidism following surgery or 131I) are presented. Serum TSH, T4 and T3 were analyzed and referred as normal, increased or decreased. Results. – Normal TSH was found in 75 and 68% of patients respectively. In subgroups with increased TSH, 15% and 14% of patients showed borderline or only mildly increased TSH (4.1–5.5 mIU/L). T4 (94 and 86%) and T3 (93 and 90% respectively) were normal in the majority of patients from both groups. LT4 over-treatment is observed in only 4 and 6% of patients respectively. Conclusion. – The results are less favorable for the group with hypothyroidism following surgery or 131I than in spontaneous hypothyroidism, but in about 90% of patients with spontaneous hypothyroidism and 82% with hypothyroidism following surgery or 131I, the LT4 dose could remain unchanged. It is discussed whether standard LT4 replacement could render normal TSH and thyroid hormone patterns in all hypothyroid patients.

Résumé

Objectifs. – L’objectif était d’examiner l’efficacité du traitement de lévothyroxine chez les patients hypothyroïdiens dans la réalisation de normales de thyroid stimulating hormone (TSH), T4 et T3. Matériel et méthodes. – Résultats du traitement de patients hypothyroidiens 2448 avec LT4 pendant au moins 12 mois entre 2006 et 2011 (1920 avec l’hypothyroïdie spontanée et 528 avec hypothyroïdie après chirurgie ou 131I) sont présentés. Sériques TSH, T4 et T3 ont été analysés et appelé à la normale, une augmentation ou une diminution. Résultats. – TSH normale a été trouvé dans le 75 et 68 % des patients respectivement. En sous-groupes avec TSH accrue, 15 % et 14 % des patients ont montré la limite ou seulement TSH légèrement accru (4,1–5,5 mIU/L). T4 (94 et 86 %) et T3 (93 et 90 % respectivement) étaient normaux dans la majorité des patients des deux groupes. Traitement excessif des LT4 est observé dans seulement 4 et 6 % des patients respectivement. Conclusion. – Les résultats sont moins favorables pour le groupe avec l’hypothyroïdie après chirurgie ou 131I que dans l’hypothyroïdie spontanée, mais dans environ 90 % des patients avec l’hypothyroïdie spontanée et 82 % avec l’hypothyroïdie après chirurgie ou 131I, les LT4 dose pourrait rester inchangés. Il est discuté si LT4 remplacement pourrait rendre TSH, T4 et T3 normale chez tous les patients hypothyroïdiens.

Replacement therapy for hypothyroidism, although apparently simple, is facing challenges and complexities, especially when combined levothyroxine (LT4) and liothyronine (LT3) treatment is opposed to LT4 alone [1], and the search for optimal replacement is still going on.

Ideal therapy for hypothyroidism should aim to restore physical and mental fitness and to normalize (optimise) thyroid hormones and thyroid stimulating hormone (TSH). To obtain both simultaneously is not always simple.

We present results of serum TSH, T4 and T3 in 2488 patients with an overt hypothyroidism (1920 with spontaneous 0
hypothyroidism and 528 with hypothyroidism following surgery or \(^{131}I\) treated with LT4 between 2006 and 2011 in the Thyroid referral center, Sisters of Mercy University Hospital Center, one of the largest (863 beds) Teaching Hospitals in the City of Zagreb (population: 0.8; metropolitan area: 1.1 million), Croatia.

The results indicate that a standard LT4 therapy failed to produce normal hormone patterns in a significant proportion of patients. The results in hypothyroidism following surgery or \(^{131}I\) are less favorable than those in spontaneous hypothyroidism.

1. Material and methods

The replacement therapy for hypothyroidism usually starts with 50–75 \(\mu g\) LT4, exceptionally with a lower dose (25 \(\mu g\) or less) in coronary heart disease patients. The dose is gradually increased to 100 \(\mu g\) within a week or two. Patients are seen in 2- to 3-month periods and LT4 dose is titrated until a normal TSH (0.4–4.0 mIU/L) is achieved. Later, the patients are observed every 6–12 months.

Patients included in this study were treated for at least 12 months (up to several years). TSH is determined before each visit, T4 (n.v. 65–165 nmol/L) and T3 (n.v. 1.1–3.1 nmol/L) less frequently. The values before the last visit are reviewed. TSH and thyroid hormones were analyzed by Immulite 1000 DPC analyzer. The compliance was tested by a short questionnaire and by a direct physician–patient communication during each interview.

2. Results

Table 1 shows the results of TSH, T4 and T3 (in %) referred as normal, increased or decreased.

Three quarters of patients are properly treated and display normal serum TSH. Eighty percent of others have increased TSH (20.7%). However, in many of them (15.2% in spontaneous, and 14.1% in hypothyroidism following surgery or \(^{131}I\)) this increase is borderline or only mild (4.1–5.5 mIU/L). Only a small proportion (4%) of hypothyroid patients had over-suppressed TSH.

Unlike TSH, serum T4 and T3 are normal in a vast majority of hypothyroid patients. There is only about 6% of these patients with increased (over-treatment) and 5% with decreased (under-treatment) either or both thyroid hormones.

The results are less favorable for the group of patients with hypothyroidism following surgery or \(^{131}I\). The proportion of patients with normal TSH, T4 or T3 is significantly smaller and that with increased or decreased TSH and thyroid hormones higher than in spontaneous hypothyroidism. Percentage of patients with increased either or both thyroid hormones, undoubtedly indicating LT4 over-treatment, is three times higher than in spontaneous hypothyroidism.

3. Discussion

In general, these results are superior to those previously reported (Table 2). In the majority of patients with increased TSH, like in both large series [2,3], the values are only borderline or mildly increased. Our results indicate that in about 90% of patients with spontaneous hypothyroidism (75% with normal and 15% with borderline or slightly increased TSH (< 5.5 mIU/L)), the LT4 dose could remain unchanged. This is supported by a normal serum T4 in a vast majority of patients. The treatment is less effective in hypothyroidism following surgery or \(^{131}I\), but the LT4 dose still works in 82% of patients (68% with normal and 14% with borderline TSH).

The results are markedly shifted towards increased TSH group, implying a more cautious approach. Unlike high figures in other series [2–5], only 4% of patients are over-treated, and LT4 dose should be reduced since over-suppressed TSH is considered a significant health hazard [6–8]. Such a difference could emerge due to data obtained in general population [2,3].

Table 2

<table>
<thead>
<tr>
<th>Study</th>
<th>Normal</th>
<th>Increased</th>
<th>Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ross et al., 1990 [4]</td>
<td>68</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Parle et al., 1993 [5]</td>
<td>52</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>Hollowell et al., 2002 [3]</td>
<td>67</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>This study (spontaneous hypothyroidism)</td>
<td>75</td>
<td>21</td>
<td>4</td>
</tr>
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vs. our data from Thyroid referral center, or in smaller series [4,5], but, probably, also reflects the different treatment modality. We believe that gradually titrating LT4 dose produces maybe slower but safer results than 1.7 μg/kg body weight fixed dose as proposed earlier [9].

The results are less favorable in hypothyroidism following surgery or 131I with a significantly higher percentage of both increased and decreased TSH. In this group, considerable number of patients is athyreotic, and some difficulties could appear in trying to reestablish the normal TSH-thyroid hormone feedback control. In order to reach normal TSH, increasing LT4 doses more frequently result in increased T4 and T3 and a higher proportion of patients with over-suppressed TSH. LT4 failed to ensure euthyroidism in all athyreotic patients [10], and, instead of very high doses of LT4 alone, a defined population of hypothyroid patients could benefit from addition of LT3 in achieving normal TSH [11,12].

Several points arise from these results. Closer attention of thyroidologists in choosing LT4 dose is probably required. The compliance is a major problem in therapy for hypothyroidism as in other livelong treatments. However, considerable flows in adherence to LT4 were observed in less than 10% of patients. In others, among other possible causes, problems involving impaired T3 economy, peripheral and intrapituitary, could emerge, pointing to the role of T3 in keeping TSH-thyroid hormone balance [13]. The additional administration of slow-release LT3 in hypothyroidism results in a better hormone profile [14], possibly approaching the issue to the “magic” formula [15].

On the other side, it is questionable whether any treatment could resolve all problems in all hypothyroid patients [16]. Does it also include TSH and thyroid hormone patterns?

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References