Bone mineral density in adolescent females treated with L-thyroxine: a longitudinal study

Abstract

It has been suggested that chronic treatment with L-thyroxine (L-T4) could be implicated in reducing bone mineral density (BMD). The purpose of this longitudinal study was to determine whether appendicular and axial BMD is decreased by L-T4 treatment in adolescent girls. Thirteen adolescent girls with subclinical hypothyroidism caused by chronic lymphocytic thyroiditis were enrolled in the study at the median age of 13.4 years (range 9.2–18.1 years). L-T4 was administered in a single dose of 1–5 μg/kg daily. BMD was evaluated at the distal one-third of the non-dominant radius by single photon absorptiometry (SPA) and at the lumbar spine (L2–4) by dual energy X-ray densitometry (DEXA). Osteocalcin levels were measured to assess bone turnover before and during L-T4 treatment. Before the start of therapy, mean BMD at both the radial and lumbar level was not significantly different from that of a control group (median age 13.0 years; range 9.0–18.5 years). During L-T4 therapy for 2–5 years, BMD did not change at any site. Before treatment, osteocalcin levels were not significantly different from those of controls and did not change during follow up.

Conclusion

Long-term L-T4 therapy in adolescent girls has no adverse effect on BMD and bone turnover. Our data indicate that attainment of peak bone mass is not impaired by L-T4 administration.

Key words Bone mineral density · L-thyroxine · Osteocalcin · Subclinical hypothyroidism · Prevention

Abbreviations

BMD bone mineral density · BMI body mass index · CLT chronic lymphocytic thyroiditis · DEXA dual energy X-ray absorptiometry · FT4 free thyroxine · L-T4 L-thyroxine · SDS standard deviation score · SPA single photon absorptiometry · TSH thyrotropin

Introduction

Thyroid hormones have potent effects on skeletal growth and bone turnover, as evidenced by bone loss and increased serum levels of bone markers which may be present in adult as well as in paediatric patients with hyperthyroidism [16, 25]. In recent years, several reports recognised that chronic L-thyroxine (L-T4) therapy may be associated with reduced bone mass [10, 20]. Some degree of L-T4 over-treatment leading to mild hyperthyroidism may be the cause of the decreased bone mass [8–10], but decreased bone density has also been found in premenopausal women with Hashimoto thyroiditis who received physiological doses of L-T4 [15].

The few data on bone mineral density (BMD) in L-T4 treated children and adolescents demonstrated a significant reduction in peripheral BMD in those receiving high
doses [19]. There are no longitudinal studies to assess the impact of L-T4 treatment on BMD during adolescence. The purpose of this study was to determine whether, in adolescent girls, appendicular and axial BMD was affected by long-term administration of L-T4 therapy in physiological doses.

Patients and methods

Patients

We studied 13 adolescent girls with subclinical hypothyroidism aged 9.2–18.1 years (Table 1). Subclinical hypothyroidism was defined by an elevated basal serum thyrotropin (TSH) level (> 6.0 mU/l) (patients mean 21.74 ± 15.6 mU/l, normal range 0.5–5 mU/l) in conjunction with normal serum free thyroxine (FT4) levels (patients 15.79 ± 3.27 pmol/l, normal range 9.0–27.0 pmol/l) [4]. All patients had chronic lymphocytic thyroiditis (CLT) with diffuse, soft thyroidomegaly and elevated titres of thyroglobulin antibodies (≥ 1:1200); some patients (n = 8) had elevated titres of thyroperoxidase antibodies (≥ 1:100) as well. Pubertal stages ranged from prepuberty (B1, Ph1) to full pubertal development (B5, Ph5); in each patient, pubertal stage was appropriate for her chronological age. Three patients were pre-menarcheal, while the others menstruated (age of menarche 11.0–13.5 years); cycle length was normal for adolescent subjects (25-30 days). Height was within 2.0 standard deviation scores (SDS), weight was within 15% for ideal body weight for height and body mass index (BMI) was within 1.5 SDS; bone ages were not significantly different from chronological ages (Table 1). All subjects were ambulatory, had a normal physical activity for their ages, and were non-drinkers and non-smokers; none were affected by other diseases or were taking drugs known to affect bone metabolism. No patient had a past historical or biochemical evidence of thyrotoxicosis.

A group of 15 healthy girls matched for age (range 9.0–18.5 years) and pubertal stage (range B1, Ph1 – B5, Ph5; menstruating n = 14) was used as control (Table 1); thyroid function was normal (TSH 2.65 ± 0.88 mU/l; FT4 18.34 ± 3.90 pmol/l).

Study protocol

Before beginning the L-T4 therapy, peripheral BMD was assessed in all patients by single photon absorptiometry (SPA). In patients recruited after 1990, axial BMD was also assessed by dual energy X-ray absorptiometry (DEXA).

Serum osteocalcin concentrations were measured to evaluate the effect of L-T4 on bone turnover before L-T4 administration and every month during the first 6 months of treatment. Subsequently, BMD and osteocalcin levels were measured on the same day at yearly intervals. L-T4 was administered in a single dose (1-5 μg/kg/day); each patient was instructed to take the drug at least 30 min before food intake. Serum TSH levels were rechecked after 1 month of therapy and, if the test was normal, TSH levels were measured every 6 months. L-T4 was considered appropriate when TSH concentrations were between 0.5–3.0 mU/l. If TSH was above or below the range, the L-T4 dose was modified until the appropriate concentration was achieved.

Informed consent was obtained from each adolescent and from both parents, when appropriate. The study was approved by the ethical committee of our department.

Methods

Height (mean of three measurements using a wall-mounted stadiometer) and weight were measured at the same hour of the day by one of us. In order to compensate for different chronological ages, heights were also expressed as SDS (SDS = individual value – mean normal value for age and sex/SD of normal mean) using published tables [28]. Pubertal maturation was staged by the method of Tanner [27]. Bone age was determined according to the Greulich and Pyle [12]. To obtain the degree of adiposity, BMI was calculated according to the formula: BMI = weight (kg)/height (m²), and expressed as SDS according to the normative data of Prokopec and Bellisle [18]. Peripheral BMD was measured in the distal third of the non-dominant radius by SPA with 125-I as the radionuclide source (Norland Corporation, Fort Atkinson, WI, USA). The results were expressed as absolute bone mineral content di-

Table 1 Clinical data in the 13 girls with CLT at diagnosis

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<tr>
<th>Case</th>
<th>Age years</th>
<th>Bone age years</th>
<th>Height (cm)</th>
<th>Weight (% of ideal)</th>
<th>BMI SDS</th>
<th>Pubertal stage</th>
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Controls

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<tr>
<th>Case</th>
<th>Age years</th>
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<th>Weight (% of ideal)</th>
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* % of ideal body weight for height