Thyroid Function in Patients with Fibromyalgia Syndrome

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Abstract. **Thyroid function was tested in 13 female patients with primary fibromyalgia syndrome (FS) and 10 healthy age matched controls by intravenous injection of 400 μg thyrotropin-releasing hormone (TRH). Basal thyroid hormone levels of both groups were in the normal range. However, patients with primary FS responded with a significantly lower secretion of thyrotropin and thyroid hormones to TRH, within an observation period of 2 h, and reacted with a significantly higher increase of prolactin. Total and free serum calcium and calcitonin levels were significantly lower in patients with primary FS, while both groups exhibited parathyroid hormone levels in the normal range. (*J Rheumatol 1992;***19:1120–2)**

Key Indexing Terms:
FIBROMYALGIA SYNDROME TRH TSH PROLACTIN CALCIUM
THYROID HORMONES CALCITONIN PARATHYROID HORMONE

Primary fibromyalgia syndrome (FS) is a noninflammatory rheumatic disease with muscular aching, fatigue and multiple fibrositic tender points. Primary FS is predominantly observed in women and is often combined with various neurovegetative disorders such as constipation, chilliness, low blood pressure, dermatographia, headaches and sleep disturbances, and the patients often suffer from mental depression[1-3]. Little is known about the pathogenic mechanism of primary FS. Since it is frequently observed in patients with Hashimoto's thyroiditis[4], and since many of the neurovegetative symptoms of primary FS are also typical for hypothyroidism, deficiency of thyroid hormones has been implicated to be causally related to primary FS. However such a coincidence has been detected in only a small number of patients with primary hypothyroidism[5,6]. Calcium homeostasis may also be disturbed in patients with primary FS and the lowered serum calcium levels have been thought to aggravate pain[7]. Our aim was to compare the function of the hypothalamic-pituitary-thyroid axis in patients with primary FS with that of a group of healthy volunteers, using the classic approach of iv injection of thyrotropin releasing hormone (TRH), together with the estimation of serum calcium, parathyroid hormone and calcitonin.

MATERIALS AND METHODS

Thirteen female patients (mean age 48 ± 2 years) with primary FS according to the recently proposed classification[8], and 10 healthy female volunteers (mean age 45 ± 2 years) were studied. Neither group had taken any medication for the 3 months before the study. All investigations were performed between 1 and 3 pm. With the exception of calcitonin and parathyroid hormone (PTH) which were determined only prior to TRH stimulation, blood was taken through an indwelling cannula before and 30, 60, 90 and 120 min after the iv injection of 400 μg TRH (Hoechst, Germany), centrifuged at +4°C and kept frozen until assayed. Thyrotropin (TSH), total thyroxin (TT4), total triiodothyronine (TT3), free thyroxin (fT4), free triiodothyronine (fT3), prolactin (PRL), calcitonin and PTH were estimated by commercially available radioimmunoassays: TSH-IRMAclon, Henning, Berlin, Germany, (sensitivity 0.03 μU/ml); Prolactin RIA, Amersham, Braunschweig, Germany, (0.3 ng/ml); Serozym T4, Serono, Freiburg, Germany (2.5 ng/ml); FT4 RIAsol, Henning, Berlin, (0.3 pg/ml); Serozym T3, Serono, Freiburg (0.1 ng/ml); Amerlex-M FT3, Amersham, Braunschweig (0.025 ng/ml); RIA-mat PTH, C-terminal, Byk-Sangtec, Dietzenbach (0.3 ng/ml); RIA-mat Calcitonin II, Byk-Sangtec, Dietzenbach (0.5 pg/ml). Care was taken that samples from volunteers and patients were run in the same assay. Total serum calcium was measured by flame photometry and free serum calcium was estimated with an ion selective electrode.

Statistics. Variables were checked for group homogeneity with the Bartlett test. The statistical significance of changes in the variables was estimated by paired t tests using the modified t statistic calculated by Bonferroni's method[9] or using the Wilcoxon matched pairs signed ranks test. The value of p required for significance was taken as 0.05/n or 0.01/n, where n = the number of comparisons made. All data are given as mean ± SEM.

RESULTS

The basal thyroid hormone values of both the volunteers and patients were found in the normal range (Table 1), but the responsiveness of the pituitary to TRH was altered in the latter group. As shown by the data depicted in Figure 1, the patients demonstrated a lesser TSH response and a greater PRL response than the controls. The group with primary FS also exhibited lower levels of fT3 and fT4 during the TRH stimulation test.

A highly consistent finding ($p < 0.005$) in patients with primary FS was that the total and free serum calcium levels were lowered, although the PTH levels (61.7 ± 7.5 ng/dl) do not differ from those of the volunteers (58.4 ± 9.7 ng/dl). Calcitonin was too low to measure in 9 patients, with a mean value of 2.99 ± 1.6 pg/ml in the group with primary FS and 19.7 ± 4.7 pg/ml in the volunteers.

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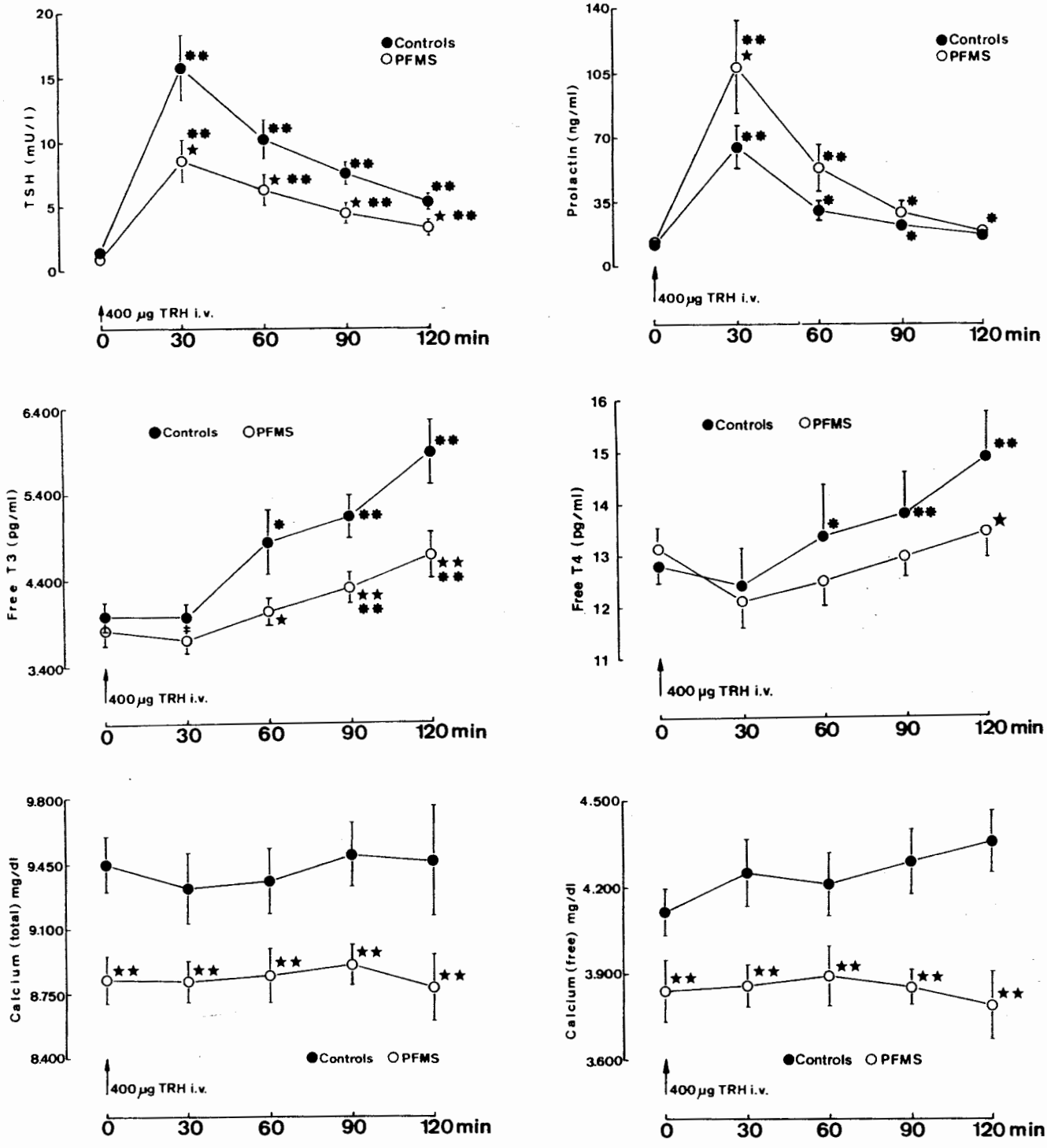

Fig. 1. Changes of TSH, PRL, FT4, FT3 obtained in 13 patients with primary FS (○——○) compared to 10 healthy controls (●——●) by iv bolus injection of 400 µg TRH. Values are means + SEM.
*p<0.05, **p<0.01 as compared with basal values.
★ p<0.05, ★★ p<0.01 as compared with healthy controls values.

Table 1. *Basal values (means + SEM) for TSH, fT4 and TT4, fT3, TT3 and PRL in n = 13 patients with primary FS and n = 10 healthy volunteers before injection of TRH. All differences are statistically not significant on the basis of p < 0.05*

	TSH (μU/ml)	fT4 (pg/ml)	TT4 (ng/ml)	fT3 (pg/ml)	TT3 (ng/ml)	PRL (ng/ml)
Controls	1.42 ± 0.19	12.80 ± 0.74	88.80 ± 9.73	3.98 ± 0.16	1.12 ± 0.08	11.77 ± 2.39
Patients	0.86 ± 0.18	13.13 ± 0.74	77.88 ± 7.78	3.81 ± 0.17	1.04 ± 0.06	13.18 ± 1.61

DISCUSSION

In a review of the literature concerning possible changes in thyroid function in patients with primary FS, Simons and Travell[10] described low normal levels of T3 and T4 without elevations of TSH. Ferraccioli, *et al*[11] recently reported a blunted TSH response and an exaggerated PRL response to TRH in a subset of patients with primary FS compared to rheumatoid patients and patients with low back pain. These results support our data comparing groups of patients with primary FS and healthy controls. The mean values of the basal thyroid hormones in patients with primary FS did not differ significantly from those of the control group in our study. However, with the exception of fT4, there is a tendency to lower thyroid hormone levels in the patient group (Table 1), without elevations of the basal TSH levels. The TRH test exhibits clear differences in the TSH response in the 2 groups: patients with primary FS had a blunted TSH response whereas the healthy control group exhibited a distinct increase of TSH followed by a significant secretion of fT3 and fT4. The lactotrophs of the patients reacted otherwise with a greater stimulation rate of PRL than the controls.

Elevations of glucocorticoids may reduce the TSH response to TRH in man[12]. There is some evidence of elevated cortisol levels in patients with primary FS. McGain and Tilbe[13] found a flattened diurnal pattern of cortisol in patients with FS. McGain, *et al*[14] and Ferraccioli, *et al*[11] found dexamethasone resistance in subsets of patients with primary FS. Therefore the blunted response of TSH to TRH could be a consequence of enhanced secretion of cortisol.

An interesting finding is the lowered levels of calcium (free and total) in the patients with primary FS. It is known that hypocalcemia may cause aggravation of pain[10], a general enhancement of excitability of the nervous system, enhanced skin erythemata response (dermographism)[15], weak but not relaxed muscles, cold hands and feet and paresthesias. Hypocalcemic disorders are usually due to a diminished secretion or action of PTH or abnormalities in vitamin D metabolism. PTH levels in our patients with primary FS were in the normal range and calcitonin was lowered possibly as a consequence of lowered calcium. Vitamin D levels have not been assessed in our patients.

In summary our findings support earlier results of neuroendocrinologic abnormalities of the hypothalamic-pituitary-thyroid axis in patients with FS. Further studies should also examine calcium homeostasis in patients with primary FS.

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