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Original article

Are there any causes for increased thyroid volume in women with prolactinoma?

Y a-t-il des raisons à une augmentation du volume de la thyroïde chez les femmes atteintes de prolactinome ?

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Abstract

Purpose. – The aim of this study was to evaluate thyroid volume in women with prolactinoma and investigate the relationship between anabolic hormones [insulin, insulin like growth factor (IGF-1), estrogen] and thyroid volume in the patients. *Material-method.* – Sixty-three euthyroid women with prolactinoma and 60 healthy euthyroid women were included. Serum prolactin (PRL), thyroid-stimulating hormone (TSH), thyroxine (free T4), free tri-iodothyronine (free T3), insulin resistance (IR) which was estimated by the homeostasis model assessment, thyroidal microsome (anti-TPO), antithyroglobulin antibodies (TgAb), estradiol (E2), and insulin like growth factor (IGF-1) were evaluated, and thyroid volume was calculated by B-mode doppler USG. *Results.* – The mean thyroid volume was significantly higher in women with prolactinoma (82.5 ± 15.1 mL) than in healthy women (76 ± 15.1 mL)($P = 0.014$), but no correlation was found between thyroid volume and serum PRL levels ($P = 0.967$). There were also no differences between thyroid volume, anabolic hormones (E2, IGF-1), and insulin resistance in women with prolactinoma ($P = 0.776$, $P = 0.786$, $P = 0.647$, respectively). *Conclusions.* – Our study did not show an association between anabolic hormones and increased thyroid volume in women with prolactinoma.

Keywords: Anabolic hormones; Prolactinoma; Thyroid volume

Résumé

Objectif. – Le but de cette étude était d'évaluer le volume de la thyroïde chez les femmes avec prolactinome et d'étudier la relation entre les hormones anabolisantes (insuline, IGF-1, estrogènes) et volume de la thyroïde chez ces patientes. *Matériel-méthode.* – Soixante-trois femmes euthyroïdiennes avec prolactinome et 60 femmes euthyroïdiennes en bonne santé ont été incluses. La prolactine sérique (PRL), la TSH, la thyroxine (T4 libre), la tri-iodothyronine (T3 libre), l'insulinorésistance (IR) qui a été estimée par l'évaluation de modèle d'homéostasie, thyroïdienne microsome (anti-TPO), les anticorps antithyroglobuline (TgAb), l'estradiol (E2), et l'IGF-1 ont été évalués, tandis que le volume de la thyroïde a été calculé en mode B doppler USG. *Résultats.* – Le volume moyen de la thyroïde était significativement plus élevé chez les femmes avec prolactinome (82,5 ± 15,1 mL) que chez les femmes en bonne santé (76 ± 15,1 mL) ($p = 0{,}014$), mais aucune corrélation n'a été trouvée entre le volume de la thyroïde et les niveaux de PRL sérique ($p = 0{,}967$). Il n'y avait également aucune différence entre le volume de la thyroïde, les hormones anaboliques (E2, IGF-1) de résistance, et de l'insuline chez les femmes avec prolactinome ($p = 0{,}776$, $p = 0{,}786$, $p = 0{,}647$, respectivement). *Conclusions.* – Notre étude n'a pas montré d'association entre hormones anabolisantes et le volume de la thyroïde a augmenté chez les femmes avec prolactinome.

Mots clés : Hormones anabolisantes ; Prolactinome ; Volume thyroïdien

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1. Introduction

The thyroid gland is an endocrine organ, weight of the gland is nearly 20 grams (15–25 grams) and dimension is 2×3 cm in adult humans, it is formed with two lobes connected by an isthmus. Histologically, it comprises of spherical vesicles separated by connective tissue [1]. Formation of thyroid nodules is a result of extreme enlargement of some follicles that have undergone involution, and of an increase in the zone of epithelial hyperplasia [2].

Thyroid-stimulating hormone (TSH) plays a major role in organizing the growth and differentiation of thyroid cells [3]. Clinical and biochemical changes of the thyroid gland have been indicated in patients with prolactinoma, and it has been reported that hypothyroidism due to the increased inhibition of the TSH release by dopamine could be seen in these patients [4].

In the literature, increased thyroid volume has also been attributed to many anabolic hormones apart from TSH and PRL [5–8]. For instance, IGF-1 plays a significant role in the growth of thyroid cells and is possibly involved in the pathogenesis of thyroid-related diseases [9,10].

Insulin growth factor 1-signaling pathway has long been known to be part of the organization of thyroid gene expression and might be considered a factor in thyroid cell proliferation [5,6]. Previous studies concluded that insulin hormone is a growth factor and stimulates thyroid cells proliferation concurrently with TSH [7,8]. A previous study showed that patients with insulin resistance (IR) have larger thyroid volumes and higher risk for formation of thyroid nodules [11]. A recent study indicated that increased thyroid volume and frequency of nodule were also reported in patients with IR in an iodine-sufficient area [11].

Lastly, estrogen is an another anabolic hormone which was named in the pathogenesis of thyroid diseases in some epidemiological data [7,8].

2. Material-method

The retrospective study constituted of analyses of records of the euthyroid women with prolactinoma and healthy euthyroid women at a training and research hospital who lived in Ankara in between 2008–2014. Turkey is a country in which legislation for mandatory iodine fortification by iodization of household salt was passed in 1999. Ankara is now an accepted iodine-sufficient area (mean urinary iodine concentration 92 μg/L) [12].

2.1. Ethic committee

Institutional review board approval for the study was obtained, and patients were asked to sign an informed consent before they enrolled in the study.

2.2. Main outcomes

The main outcomes are:

- to determine whether thyroid volume is higher in women with prolactinoma than healthy subjects who have lived in the same country;
- to determine whether there is an association between thyroid volume and anabolic hormones, including estradiol, IGF-1 and insulin resistance in women with prolactinoma.

2.3. Study groups

A total of 60 healthy euthyroid women were enrolled in the study as well as 63 patients who were referred due to menstrual irregularities including oligomenorrhea and secondary amenorrhea and were later diagnosed with prolactinoma after diagnostic testing. Oligomenorrhea was defined as the menses for a duration of greater than 35 days, and secondary amenorrhea was defined as absence of menses for at least six months [13]. Prolactin affects reproductive function generally by inhibiting the secretion of hypothalamic GnRH and gonadotrophin hormones and inhibiting gonadal steroidogenesis. It also causes hypoestrogenism and anovulation by inhibiting aromatase activity in the granulosa cells during ovulation [13]. Besides this, anovulatory menstrual cycles can be seen in prolactinoma unless there is an inhibition of gonadotropic hormones and E2 production [14]. Evaluation of thyroid function of the patients was performed at the same time of the diagnosis of prolactinoma. Euthyroidism was defined as TSH (reference range, 0.35–4.0 mL·U/L), free tri-iodothyronine (fT3; reference range, 2–4.4 pg/mL), and free thyroxine (fT4; reference range, 0.93–1.7 ng/dL) within the normal reference range. Any thyroid disease was not diagnosed before the enrollment of all subjects in the study.

Patients were excluded from the study if they had a history of pregnancy, lactation, malignancy, chronic diseases (hepatic or renal dysfunction, heart failure), or drug use that could affect thyroid function tests.

Patients' weight (kg) and height (cm) were recorded during admission, and their body mass index (BMI) (kg/m^2) was calculated.

In patients with adenomas noted on pituitary MRI, adenomas with size < 1 cm were grouped as microprolactinomas, and adenomas with size ≥ 1 cm were grouped as macroprolactinomas. All patients had normal levels of anterior hypophysis hormones apart from PRL levels.

2.4. Biochemical analyses

A blood sample was drawn in the morning between 08:00 and 09:00 after an overnight fast from all groups to measure the determinant of the following hormones: FSH (mIU/mL), LH (mIU/mL), E2 (pg/mL), TSH (0.35–4.0 mIU/l), fT4 (0.93–1.7 ng/dL), fT3 (2–4.4 pg/mL), anti-TPO (IU/mL) (normal value < 34), Tg-Ab (IU/mL) (normal value < 115), PRL (ng/dL), IGF-1 (ng/mL) (normal reference range adjusted by age: 238–358), and insulin (mcIU/mL). Serum FSH, LH, E2, PRL, and IGF-1 were measured by the chemiluminescent microparticle immune method (paramagnetic particle, chemiluminescent immunoassay) using a Roche Hitachi Cobalt 600 device. Serum TSH (mIU/mL), free thyroxin (T4) (ng/dL),