

# Metformin decreases thyrotropin in overweight women with polycystic ovarian syndrome and hypothyroidism

Diabetes & Vascular Disease Research  
8(1) 47–48  
© The Author(s) 2011  
Reprints and permission: sagepub.  
co.uk/journalsPermissions.nav  
DOI: 10.1177/1479164110391917  
dvr.sagepub.com  


S. Morteza Taghavi, Hale Rokni and Sedigeh Fatemi

## Abstract

**Objective:** To assess the effect of metformin administration on thyroid function in overweight women with polycystic ovarian syndrome (PCOS).

**Methods:** Twenty-seven overweight women with PCOS and hypothyroidism were selected. Fifteen patients (group I) were treated with metformin 1500 mg/day for 6 months and 12 patients (group II) with placebo. Serum thyrotropin (TSH), free T3 and free T4 were measured at baseline and 6 months after the beginning of the study.

**Results:** A significant decrease ( $p < 0.001$ ) in TSH levels was observed in group I but not in group II subjects after 6 months of metformin treatment. No significant change in free T3 and free T4 was observed throughout the study in any group.

**Conclusion:** In obese PCOS patients with primary hypothyroidism, metformin results in a significant fall and sometimes normalisation of TSH, without causing any reciprocal changes in other thyroid function parameters.

## Keywords

Hypothyroidism, metformin, polycystic ovarian syndrome (PCOS), thyrotropin (TSH)

## Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrinopathy occurring in five to seven per cent of women of reproductive age and primary hypothyroidism is also very prevalent in women and occurs more commonly in PCOS.<sup>1</sup> Metformin has been used for the treatment of type 2 diabetes and PCOS for many years. Recently there have been some reports that metformin is able to influence thyroid function tests, mainly by a decrease in serum levels of thyrotropin (TSH).<sup>2</sup> We evaluate the interplay between metformin and thyroid tests by following thyroid hormone levels in overweight PCOS patients with hypothyroidism after treatment with metformin or placebo.

## Patients and methods

This study performed in 27 overweight women with PCOS and primary hypothyroidism. PCOS was diagnosed in accordance with the Rotterdam consensus diagnostic criteria. Hypothyroidism in all patients was subclinical and was diagnosed for the first time. Fifteen patients (group I) were treated with metformin 1500 mg/day for 6 months and 12 patients (group II) with placebo. The patients did not receive any other medications for treatment of PCOS. Serum TSH, free T4 (FT<sub>4</sub>) and free T3 (FT<sub>3</sub>) were measured once at baseline and 6 months after the beginning of the

study. All statistical analysis was performed using SPSS 14. Data are shown as mean  $\pm$  standard deviation. Paired *t*-tests were used to analyse changes in thyroid function tests and BMI. *P* values less than 0.05 were considered significant.

## Results

Clinical characteristics and thyroid function tests in the two groups of patients are summarised in Table 1. There was no significant difference between mean age and BMI in the two groups. Mean basal TSH levels decreased significantly in group I after 6 months of metformin treatment ( $p < 0.001$ ). In five patients in this group (30%) serum TSH levels reached normal range. Mean basal TSH levels in patients in group II did not change significantly after placebo treatment. In one patient in this group serum TSH levels reached normal range, that can be seen in the natural course of

---

Endocrine Research Center, Mashhad Medical University, Iran

### Corresponding author:

S. Morteza Taghavi, Endocrine Research Center, Mashhad Medical University, Ahmad Abad Street, Ghaem Hospital, Mashhad, Iran.  
Email: taghaviMR@mums.ac.ir

**Table 1.** Clinical characteristics and thyroid function tests in two groups of patients (mean  $\pm$  SD)

	Group I before treatment	Group I after treatment	Group II before treatment	Group II after treatment
BMI (kg/m <sup>2</sup> )	29.7 $\pm$ 2.5	28.59 $\pm$ 2.56	28.2 $\pm$ 2.2	27.96 $\pm$ 1.73
TSH (mIU/L)	7.78 $\pm$ 1.74	6.14 $\pm$ 2.47	8.02 $\pm$ 2.21	8.82 $\pm$ 2.89
FT4 (pg/ml)	16 $\pm$ 2.26	15.6 $\pm$ 2.45	15.8 $\pm$ 2.2	16.5 $\pm$ 3.8
FT3 (pg/ml)	4.8 $\pm$ 0.99	4.83 $\pm$ 1.26	4.6 $\pm$ 1.1	4.67 $\pm$ 1.28

Group 1: Fifteen patients treated with metformin 1500 mg/day for 6 months

Group 2: Twelve patients treated with placebo

subclinical hypothyroidism.<sup>3</sup> Serum FT4 and FT3 levels did not change significantly during study in any group (Table 1).

## Discussion

These data show for the first time that metformin administration in overweight PCOS patients with primary subclinical hypothyroidism results in a significant fall in TSH levels. This is an important finding clinically, because hypothyroidism occurs in more than 10% of PCOS patients<sup>1</sup> and metformin is a common prescription in them. There are several possible explanations for the TSH-reducing effect of metformin but they are speculative at the present time. A subtle increase in the gastrointestinal absorption of levothyroxin is the first possible mechanism, but a reduction in thyroid hormone levels was not reciprocal with TSH in patients with hypothyroidism treated with levothyroxin in initial case reports by Vigersky *et al.*<sup>4</sup> This finding was also shown in another study by Cappelli *et al.* He also ruled out any influence of changes in body weight associated with metformin therapy on TSH levels.<sup>2</sup> Our study also confirms these findings.

Enhancement of inhibitory feedback of thyroid hormones on TSH secretion is another mechanism suggested by Cappelli *et al.*<sup>2</sup> Induced constituent activation of the TSH receptor and increased dopaminergic tone has also had been suggested by Vigersky *et al.*<sup>4</sup> Previous studies have suggested that there is a disruption of the neuroendocrine mechanisms in women with PCOS, mainly due to a deficiency in hypothalamic dopamine.<sup>5</sup> Metformin administration improves endogenous hypothalamic dopaminergic tone, simultaneously with decreasing the insulin resistance in obese PCOS patients.<sup>6</sup> The possibility that metformin administration decreases TSH levels by increasing dopamine in the hypothalamus may be the best explanation but needs to be fully elucidated by further studies.

The main limitation of our study was the small number of patients. However, a significant decrease in TSH levels was observed in our patients.

## Conclusion

In overweight PCOS patients with primary hypothyroidism, treatment with metformin resulted in a significant fall in TSH and in some cases improvement of hypothyroidism. We can begin treatment of obese PCOS patients with subclinical hypothyroidism with metformin and reevaluate their thyroid function after six months.

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## Conflict of interest statement

The authors declare that they have no conflicts of interest.

## Acknowledgements

This study was performed with the support of Mashhad Endocrine Research Center. All authors have contributed significantly and are in agreement with the content of the manuscript.

## References

1. Janssen OE, Mehlmauer N, Hahn S *et al.* High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. *Eur J Endocrinol* 2004; 150: 363–369.
2. Cappelli C, Rotondi M, Pirola I *et al.* TSH-lowering effect of metformin in type 2 diabetes. *Diabetes Care* 2009; 32: 1589–1590.
3. Diez JJ, Iglesias P. Spontaneous subclinical hypothyroidism in patients older than 55 years: an analysis of natural course and risk factors for the development of overt thyroid failure. *J Clin Endocrinol Metab* 2004; 89: 4890–7.
4. Vigersky RA, Filmore-Nassar A and Glass AR. Thyrotropin suppression by metformin. *J Clin Endocrinol Metab* 2006; 91: 225–227
5. Quigley ME, Rakoff JS and Yen SSC. Increased luteinizing hormone sensitivity to dopamine inhibition in polycystic ovary syndrome. *J Clin Endocrinol Metab* 1981; 52: 231–234.
6. Ortega-González C, Cardoza L, Coutiño B *et al.* Insulin sensitizing drugs increase the endogenous dopaminergic tone in obese insulin-resistant women with polycystic ovary syndrome. *J Endocrinol* 2005; 184: 233–239.