

Serum prolactin concentration and severity of depression symptoms in climacteric women

R. Słopeń¹, A. Słopeń², A. Warenik-Szymankiewicz¹

¹ Department of Gynecological Endocrinology, Poznań University of Medical Sciences, Poznań

² Department of Child and Adolescent Psychiatry, Poznań University of Medical Sciences, Poznań (Poland)

Summary

Objective: The study was conducted to elucidate the problem of prolactin (PRL) serum concentration in menopausal women and its possible relations with climacteric and depressive symptoms. **Materials and Methods:** The study included 202 women aged 40-65 years admitted to the Department of Gynecological Endocrinology, Poznań University of Medical Sciences, because of climacteric symptoms. The authors assessed the intensity of climacteric and depressive symptoms with the Kupperman index and the Hamilton depression scale, measured BMI index, serum PRL, FSH, LH, 17 β -estradiol, total testosterone, and dehydroepiandrosterone sulfate (DHEAS) levels in all studied women. **Results:** They found a correlation between serum PRL concentration and result of M. Hamilton depression scale ($R=0.21$; $p=0.005$) and a between serum PRL concentration and serum 17 β -estradiol concentration ($R=0.21$; $p=0.003$). **Conclusion:** The authors concluded that serum PRL concentration is related to severity of depressive symptoms in menopausal women.

Key words: Prolactin; Menopause; Climacterium; Depression.

Introduction

Prolactin (PRL) is a 23 kDa protein secreted by the pituitary gland and has many actions in the reproductive system and metabolism [1]. PRL secretion depends on various neurotransmitters and its serum concentration differs in various somatic and psychological conditions [1].

The most common medical problem of climacteric women are vasomotor and depressive symptoms [2]. Etiology of these symptoms still is not clear with hormonal background suggested.

This study was conducted to elucidate the problem of serum PRL concentration in menopausal women and its possible relations with climacteric and depressive symptoms.

Material and Methods

The study included 202 women aged 40-65 years admitted to the Department of Gynecological Endocrinology, Poznań University of Medical Sciences, because of climacteric symptoms. The mean age of the studied women was 54.2 ± 4.9 years. 74 of them were still menstruating or the time since last menses was no longer than 12 months, whereas 128 were at least one year after last menstrual period. Conditions unrelated to menopause that usually influence the PRL secretion like renal failure, cirrhosis, epilepsy, cranial irradiation, chest wall trauma, and medications like: phenothiazines, antihypertensives, antihistamines, neuroleptics, anticonvulsants, antidepressants, opiates and estrogens constituted the exclusion criteria.

The intensity of climacteric and depressive symptoms was evaluated with the Kupperman index (Table 1) [3] and the Hamilton depression scale (Table 2) [4], respectively, for all study par-

ticipants. The BMI index was calculated with the use of the BMI = body mass/height² formula. Serum PRL, FSH, LH, 17 β -estradiol, PRL, total testosterone, and dehydroepiandrosterone sulfate (DHEAS) levels were evaluated in all studied women. FSH, LH, 17 β -estradiol and total testosterone concentrations were tested by immunoenzymatic methods. Intra- and interassay coefficient of variation (CV) ranges were 1.2-3.3% and 2.0-5.6%, respectively. DHEAS level was evaluated with the radioimmunological method: intraassay CV and interassay CV ranges were 5.1% and 11%, respectively. In the statistical analysis Spearman's test for the correlation between variables was used.

The study was approved by the Ethics Committee, Poznań University of Medical Sciences, and financed by the State Committee for Scientific Research (project no: 50305-01109136-12261-08039).

Results

A clinical and hormonal characteristic of the study group is presented in Table 3. The mean serum PRL concentration was 11.7 ± 5.7 ng/ml. Mean serum PRL concentration in women who were still menstruating was 11.9 ± 4.4 ng/ml, and mean serum PRL concentration in women after one year since last menstruation was 11.1 ± 4.9 . The difference was not statistically relevant. There was no correlation between serum PRL concentration and age, time since last menstruation, and BMI. There was no correlation between serum PRL concentration and result of Kupperman index whereas There was a correlation between serum PRL concentration and result of M. Hamilton depression scale ($R=0.21$; $p=0.005$). In relation to the hormonal parameters, there was a

Revised manuscript accepted for publication July 3, 2014

Table 1. — *Kupperman index.*

Climacteric symptom	Points*
Hot flashes	4
Sweating	2
Insomnia	2
Nervousness	2
Low mood	1
Vertigo	1
General weakness	1
Arthralgia	1
Headaches	1
Palpitations	1
Paresthesia	1

Table 2. — *M. Hamilton depression scale.*

Depression symptom	Points
1) Depressive mood	0-4
2) Feeling of guilt	0-4
3) Suicidal thoughts and tendencies	0-4
4) Insomnia	0-2
5) Shallow sleep	0-2
6) Waking up early	0-2
7) Loss of interest in activities	0-4
8) Slowness of movement	0-4
9) Sensorimotor anxiety	0-3
10) Psychic symptoms of anxiety and fear	0-4
11) Somatic symptoms of anxiety and fear	0-3
12) Symptoms from the digestive tract	0-2
13) General somatic symptoms	0-2
14) Symptoms from the genital system	0-2
15) Hypochondria	0-4
16) Weight loss	0-2
17) Self-criticism	0-2

correlation between serum PRL concentration and serum 17β -estradiol concentration ($R=0.21$; $p=0.003$). There was no other correlation between serum PRL concentration and other hormonal parameters of the study group.

Discussion

Mean serum PRL concentration in menopausal women in the present study ($13.8 \text{ ng/ml} \pm 10.2 \text{ ng/ml}$) was in the normal range ($4.8 - 23.3 \text{ ng/ml}$). Serum prolactin concentration is reported to be lower by about 40% in postmenopausal women than in premenopausal women [5]. This is probably not an effect of aging but menopause as in men after fifty there is an 18% increase of PRL serum concentration in comparison with younger men [5]. In the present study there was no effect of age and time since last menstruation on serum PRL concentration.

The present authors did not observe any correlation between serum PRL concentration and BMI. Such a correlation is reported by other authors [5, 6]. The explanation for this correlation is a positive impact of leptin on PRL secretion [7].

Table 3. — *Clinical and hormonal characteristics of the study group.*

Parameter	Result \pm Standard deviation
Age (years)	54.2 ± 4.9
Time since last menstruation (years)	3.9 ± 4.6
BMI (kg/m^2)	26.8 ± 4.6
Kupperman index	26 ± 13.1
Hamilton scale	11.1 ± 6.6
FSH (IU/l)	67.1 ± 35.8
LH (IU/l)	34.9 ± 17.5
E2 (pg/ml)	48.1 ± 97.5
PRL (ng/ml)	11.7 ± 5.7
Total testosterone (ng/ml)	0.28 ± 0.2
DHEAS (mg/dl)	1.36 ± 0.82

There was no correlation between serum PRL concentration and climacteric symptoms severity. There are no studies on possible relationship between serum PRL concentration and severity of climacteric symptoms. Studies referring to impact of hormonal replacement therapy on the severity of climacteric symptoms revealed that improvement in hot flashes was connected with increase of PRL serum concentration [8].

In the present study there was a correlation between serum PRL concentration and depressive symptoms severity. Similar results were obtained in the study referring to the patients with clinic hypothyroidism and subclinical hypothyroidism. These patients had hyperprolactinemia and depression together with sexual dysfunction [9]. There are also studies which reveal normal serum PRL concentration in depression [10]. Patient with improvement of depressive symptoms during treatment had higher serum PRL concentration [8] and increase of PRL serum concentration during antidepressant therapy was suggested to be a positive prognostic factor of beneficial effect of such a therapy [11].

There was a correlation between serum PRL concentration and serum 17β -estradiol concentration. Such a correlation is reported also by other authors [8]. 17β -estradiol acts on the level of pituitary stimulating synthesis and secretion of PRL [12], proliferation of lactotrophs [13], and sensitizing lactotrophs to respond to neuropeptides and growth factors [14].

Conclusion

Serum PRL concentration is related to severity of depressive symptoms in menopausal women.

References

- [1] Melmed S., Kleinberg D., Ho K.: "Pituitary physiology and diagnostic evaluation". In: Melmed S., Polonsky K.S., Reed Larsen P., Kronenberg H.M. (eds). *Williams Textbook of Endocrinology*. Philadelphia: Elsevier Saunders, 2011.

- [2] Swartzman L.C., Edelberg R., Kemmann E.: "The menopausal hot flush: symptoms reports and concomitant physiological changes". *J. Behav. Med.*, 1990, 13, 15.
- [3] Kupperman H.S., Blatt M.H., Wiesbader H., Filler W.: "Comparative clinical evaluation of estrogenic preparations by the menopausal and amenorrheal indices". *J. Clin. Endocrinol. Metab.*, 1953, 13, 688.
- [4] Hamilton M.: "A rating scale for depression". *J. Neurol. Neurosurg. Psychiatry*, 1960, 23, 56.
- [5] Roelfsema F., Pijl H., Keenan D.M., Veldhuis J.D.: "Prolactin secretion in healthy adults is determined by gender, age and body mass index". *PLoS One*, 2012, 7, e31305. doi: 10.1371/journal.pone.0031305. Epub 2012 Feb 17.
- [6] Kok P., Roelfsema F., Frölich M., Meinders A.E., Pijl H.: "Prolactin release is enhanced in proportion to excess visceral fat in obese women". *J. Clin. Endocrinol. Metab.*, 2004, 89, 4445.
- [7] Isidori A.M., Strollo F., Morè M., Caprio M., Aversa A., Moretti C., et al.: "Leptin and aging: correlation with endocrine changes in male and female healthy adult populations of different body weights". *J. Clin. Endocrinol. Metab.*, 2000, 85, 1954.
- [8] Nappi R.E., Malavasi B., Brundu B., Facchinetti F.: "Efficacy of Cimicifuga racemosa on climacteric complaints: a randomized study versus low-dose transdermal estradiol". *Gynecol. Endocrinol.*, 2005, 20, 30.
- [9] Atis G., Dalkilinc A., Altuntas Y., Atis A., Caskurlu T., Ergenekon E.: "Sexual dysfunction in women with clinical hypothyroidism and subclinical hypothyroidism". *J. Sex. Med.*, 2010, 7, 2583.
- [10] Krogh J., Nordentoft M., Mohammad-Nezhad M., Westrin A.: "Growth hormone, prolactin and cortisol response to exercise in patients with depression". *J. Affect. Disord.*, 2010, 125, 189.
- [11] Faron-Górecka A., Kuśmider M., Solich J., Kolasa M., Szafran K., Zurawek D., et al.: "Involvement of prolactin and somatostatin in depression and the mechanism of action of antidepressant drugs". *Pharmacol. Rep.*, 2013, 65, 1640.
- [12] Watters J.J., Chun T.Y., Kim Y.N., Bertics P.J., Gorski J.: "Estrogen modulation of prolactin gene expression requires an intact mitogen-activated protein kinase signal transduction pathway in cultured rat pituitary cells". *Mol. Endocrinol.*, 2000, 14, 1872.
- [13] Zarate S., Jaita G., Zaldivar V., Radl D.B., Eijo G., Ferraris J., et al.: "Estrogens exert a rapid apoptotic action in anterior pituitary cells". *Am. J. Physiol. Endocrinol. Metab.*, 2009, 296, E664.
- [14] Spuch C., Diz-Chaves Y., Perez-Tilve D., Mallo F.: "Fibroblast growth factor-2, and epidermal growth factor modulate prolactin responses to TRH and dopamine in primary cultures". *Endocrine*, 2006, 29, 317.

Address reprint requests to:

R. SŁOPIEN, M.D.

Department of Gynecological Endocrinology

Polna 33, 60-535

Poznań (Poland)

e-mail: asrs@wp.pl