Research Journal of Biological Sciences 6 (10): 493-495, 2011
ISSN: 1815-8846

A Comparison Between Serum Prolactin in Patients with Amenorrhea/Oligomenorrhea and Normal Women

[1]Alireza Azargoon, [1]Mojhgan Kaviani, [2]Nahid Lorzadeh, [3]Ezzatollah Rafiee Alavi,
[4]Mohammad Javad Tarrahi, [4]Yadollah Pournia and [5]Vahid Almasi
[1]Department of Internal Medicine, [2]Department of Gynecology, [3]Department of Pathology,
[4]Department of Biostatistics, [5]Clinical Research Center,
Lorestan University of Medical Sciences, Khorramabad, Lorestan, Iran

Abstract: The aim of this study was the assessment and comparison of serum prolactin level in the women with amenorrhea or oligomenorrhea and with normal mensturation period. In this cross sectional study, serum prolactin was assessed in two groups of 15-44 years women in Khorramabad. They did not use any drug, they were not pregnant or lactate and they had no chronic disease. One group had normal mensturation periods (control group) and another group had amenorrhea or oligomenorrhea. Fasting serum prolactin was assessed by Radioimmunoassay Method. The data were analysed with using SPSS software and Mann-Whitney test. Total 31 women with normal periods and 32 women with amenorrhea or oligomenorrhea were evaluated. Mean of serum prolactin in the control group was 538/6±351/6 and in the case group was 422/8±79/7. There was no significant difference between serum prolactin and development of amenorrhea or oligomenorrhea. In this study, there was no significant difference between serum prolactin and development of amenorrhea or oligomenorrhea. In the other hand, various conditions can develop pseudo hyperprolactinemia. Thus, researchers do not advise the routine evaluation of serum prolactin in the patients with amenorrhea or oligomenorrhea.

Key words: Prolactin, hyperprolactinemia, amenorrhea, oligomenorrhea, serum, Iran

INTRODUCTION

Prolactin is secreted by anterior pituitary and its normal range is 10-25 μg L^{-1} in women (<580 mIU L^{-1}) with a pulsatile secretion. The peak serum prolactin levels (up to 30 μg L^{-1}) occur between 4:00 and 6:00 a.m. The half-life of prolactin is about 50 min. The serum level may increase after exercising, eating, sexual activities and acute stress. During pregnancy and lactation prolactin serum level can increase to 10 times of normal range. Its predominant central control mechanism is inhibitory (by dopamine) (Melmed and Jameson, 2005). The most common syndrome of pituitary hormones hypersecretion in both males and females is an increase in prolactin level so that if it is >100 μg L^{-1} (>5000 mIU L^{-1}), adenoma is its most prevalent cause while lower amounts may be created by microprolactinoma, pituitary stalk compression, taking antipsychotics and antidepressants, methyldopa, verapamil, metoclopramide and cimetidine.

Moreover, disorders in other organs including renal failure, primary hypothyroidism, sarcoidosis and ovarian disorders (e.g., polycystic ovarian syndrome) also lead to an increase in serum prolactin (Mancini *et al*., 2008). However, the causes of hyperprolactinemia are not known in many persons and a disorder in the hypothalamus-pituitary axis regulation (idiopathic hyperprolactinemia) may be considered as the cause (Melmed and Jameson, 2005).

Increased prolactin secretion reduces Gonadotropin Releasing Hormone (GnRH), pituitary gonadotropins and sexual steroids. Oligorrhea, amenorrhea, galactorrhea, infertility, weight gain, mild hirsutism and even in the long term, a decrease in Bone Mineral Density (BMD) are among the characteristics of pathologic increase of prolactin in women (Melmed and Jameson, 2005) and account for 14% of secondary amenorrhea cases that is more prevalent in women younger than 25 years old (Devoto *et al*., 1998).

Monomeric prolactin (23 kDa) normally includes 95% of serum prolactin level in adults (Sadideen and Swaminathan, 2006) but two types of prolactin with higher molecular weights have also been detected in serum using gel filtration chromatography method: a-macroprolactin (big big PRL) with a molecular weight of <100 kDa; b-big

Corresponding Author: Aliraza Azargoon, Department of Internal Medicine, Lorestan University of Medical Sciences, Clinical Research Center, Ashayer Hospital, Enghelab Street, Khorramabad, Lorestan, Iran

Prolactin (big PRL) with a molecular weight of 40-60 kDa (Fahie-Wilson *et al*., 2005). Macroprolactin usually is a combination of gathered prolactin accompanied by Immunoglobulin G (IgG) which has a longer half-life and cannot be connected to the prolactin receptor. It is measured as prolactin in immunoassay methods, resulting in reporting high false values of prolactin and even as a major element of prolactin in some persons, it can result in idiopathic hyperprolactinemia (Strachan *et al*., 2003). Most of the evidence often indicates that it does not have any prominent biological activities and is not considered pathologically important and the person is asymptomatic (Fahie-Wilson *et al*., 2005). However, the resulted hyperprolactinemia in these persons leads to diagnostic mistakes, unnecessary evaluations and even improper treatment. An increase in prolactin serum can appear in three ways. A mild increase indicates a prolactin serum level of 20-50 μg L^{-1} and can cause infertility without any disorders in the monthly cycle. A moderate increase shows a prolactin serum level of 50-100 μg L^{-1} and can result in amenorrhea and oligomenorrhea while a severe increase indicates a prolactin serum level of >100 μg L^{-1} and appears with hypogonadism signs including amenorrhea, infertility and hot flashes.

MATERIALS AND METHODS

This cross sectional study included 31 women with normal periods in the age range of 15-44 who did not consume any drugs did not lactate and were not pregnant. Furthermore, it included 32 women from 15-44 years of age with amenorrhea/oligomenorrhea, referring to clinics with these complaints who did not take any medications that increased serum prolactin did not lactate and were not pregnant. A systematic sampling method was utilized and after the persons were selected they were referred to a laboratory in Khorramabad (West of Iran). The Radioimmunoassay Method (IRMA) was applied to measure the serum prolactin of the subjects. The samples were investigated in terms of normality of frequency distribution using Kolmogorov-Smirnov. The distributions of the two groups were not normal based on a $p \leq 0.001$ therefore, the nonparametric test of Mann-Whiteny was applied. Subsequently, the mean and median of serum prolactin were calculated for each group. The $p<0.05$ were considered as statistically significant in the study.

RESULTS AND DISCUSSION

This study was conducted on 31 women with normal periods from 15-44 years of age and 32 women with amenorrhea/oligomenorrhea in the age range of 15-44. The mean age in the control and case groups were 34±12 and 32±8, respectively. The mean body mass index in the control and case groups were 29±12 and 26±11, respectively. The means of serum prolactin in the control and case groups were 538.6±351.6 and 422.8±79.7, respectively. The difference was not statistically significant ($p = 0.99$). In the control group, the highest amount of prolactin was 1570 mIU L^{-1}, the lowest was 151 mIU L^{-1} and the median was 400 mIU L^{-1} while the highest and lowest amounts of prolactin and the median were 650, 282 and 418, respectively in the case group. About 2 patients with high serum prolactin were excluded from the study due to primary hyperthyroidism.

The present study was carried out considering the fact that in some clinics, serum prolactin is sometimes requested routinely for assessing infertility, hirsutism, bigness of breasts, etc., in women with normal monthly periods, resulting in high serum prolactin reports despite normal monthly periods. In this study, several cases of increased prolactin were observed in the normal persons and even the mean of prolactin in the women with normal monthly periods was higher than the mean in the group with amenorrhea/oligomenorrhea (despite of excluding the patients with chronic diseases and those who consuming drugs, etc.).

Nawroth (2005)'s study revealed that in some asymptomatic patients with high prolactin, the serum in fact, contained prolactin with high molecular weight (macroprolactinemia) which did not stimulate the negative feedback mechanism of dopamine did not reduce monomeric prolactin secretion and did not affect the secretion of gonadotropin. It was recommended that unnecessary tests and treatments had to be avoided by detecting macroprolactinemia cases. Although in this group, prolactinoma was also reported, it was considered as accidental event (Nawroth, 2005). Sadideen introduced macroprolactinemia as one of the causes of hyperprolactinemia which was not accompanied by a specific pathology.

They noted that when the clinical history of a patient or the radiological evidence was not compatible with the amount of prolacin in the patient, the existence of macroprolactin had to be taken into account. They even regarded investigating all hyperprolactinemic cases with respect to the existence of macroprolactin to prevent unnecessary evaluation of hyperprolactinemia (Sadideen and Swaminathan, 2006). Strarchan study revealed a prevalence of 21% for macroprolactin in hyperprolactinemia. In this study, the serum prolactin of the patients was reported to be 1130 (728-5116) mIU L^{-1} that included 240 (50-656) mIU L^{-1} for monomeric

prolactin and 895 (381-4853) mIU L^{-1} for macroprolactin. Although, about 40% of these patients had the classical symptoms of hyperprolactinemia (there were other possible causes for these symptoms) no relationships were found between concentration of macroprolactin and symptoms of hyperprolactinemia or abnormality of brain images. Therefore, brain images were not regarded as useful in persons with an increase in macroprolactin and normal monomeric prolactin (Strachan *et al*., 2003).

To measure serum prolactin, the altitude of an individual's place of living must be taken into consideration as a study carried out by Gonzales and Carrillo (1993) showed that serum prolactin at high altitude (<4000 m above sea level) was significantly lower than that at sea level. Moreover, the prevalence rates of hyperprolactinemia, galactorrhea and oligomenorrhea at high altitudes were much lower than those at sea level. The potential clinical importance of hyperprolactinemia induced by macroprolactin in asymptomatic women requires further investigations (Nawroth, 2005).

Since, macroprolactin in serum can be measured by simple tests such as Poly Ethylene Glycol Precipitation (PEG) (The standard test for this purpose is Gel Filtration Chromatography), it should be regarded as a differential diagnostic measure for hyperprolactinemia (Sadideen and Swaminathan, 2006).

Time and method of serum prolactin sampling is extremely important and if the sampling is performed in a nonfasting condition after severe exercising or after stimulation and stress, high prolactin will be reported. Regarding the way of sampling, it is highly recommended that pooled samples be taken or serum prolactin be repeated several times.

CONCLUSION

The study shows that to prevent reporting prolactin increase falsely, laboratories should use monomeric prolactin measurements and pooled serum samples should be applied to measure prolactin. Moreover, the time of performing the tests and also, activities that increase prolactin temporarily are important and must also be followed by laboratories and patients have to be asked about such activities before prolactin measurement.

Also, the simultaneous performing of thyroid function tests and serum prolactin measurement is recommended (The existence of 2 cases of hyperprolactinemia in the normal group was due to primary hypothyroidism). Additionally, the possibility of renal failure, mild cases of polycystic ovarian syndrome and consumption of drugs that increase serum prolactin should be considered.

ACKNOWLEDGEMENT

The researchers are grateful to the Clinical Research Center of Lorestan University of Medical Sciences.

REFERENCES

Devoto, E., L. Aravena and X. Gaete, 1998. Has Oligomenorrhea a pathological meaning? The importance of this symptom in internal medicine. Rev. Med. Chile, 126: 943-951.

Fahie-Wilson, M.N., R. John and A.R. Ellis, 2005. Macroprolactin; High molecular mass forms of circulating prolactin. Ann. Clin. Biochem., 42: 175-192.

Gonzales, G.F. and C.E. Carrillo, 1993. Low serum prolactin levels in native women at high altitude. Int. J. Gynaecol. Obstet., 43: 169-175.

Mancini, T., F.F. Casanueva and A. Giustina, 2008. Hyperprolactinemia and prolactinomas. Endocrinol. Metab. Clin. North Am., 37: 67-99.

Melmed, S. and J.L. Jameson, 2005. Disorders of the Anterior Pituitary and Hypothalamus. In: Harrisons Principles of Internal Medicine, Kasper, D.L., E. Braunwald, A.S. Fauci, S.L. Hauser, D.L. Longo and J.L. Jameson (Eds.). 16th Edn., McGraw-Hill, New York, pp: 2076-2097.

Nawroth, F., 2005. Hyperprolactinaemia and the regular menstrual cycle in asymptomatic women: Should it be treated during therapy for infertility?. Reprod. Biomed. Online, 11: 581-588.

Sadideen, H. and R. Swaminathan, 2006. Macroprolactin: What is it and what is its importance?. Int. J. Clin. Pract., 60: 457-461.

Strachan, M.W., W.L. Teoh, A.C. Don-Wauchope, J. Seth, M. Stoddart and G.J. Beckett, 2003. Clinical and radiological features of patients with macroprolactinaemia. Clin. Endocrinol., 59: 339-346.