



ISSN: 0975-833X

RESEARCH ARTICLE

SERUM PROLACTIN ASSAY IN SECONDARY AMENORRHEA AND INFERTILITY

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ARTICLE INFO

Article History:

Received 16th October, 2013
Received in revised form
10th November, 2013
Accepted 17th December, 2013
Published online 26th January, 2014

Key words:

Secondary amenorrhea,
Galactorrhea,
Serum prolactin.

ABSTRACT

Amenorrhea is the absence or abnormal cessation of the menses. Secondary amenorrhea is defined as the absence of menses for a length of time equivalent to a total of at least 3 of previous cycle intervals or 6 months of amenorrhea. Recent advances in reproductive endocrinology has incriminated the anterior pituitary polypeptide hormone prolactin (PRL), in pathogenesis of anovulation in amenorrhea galactorrhea syndrome. The study was undertaken to estimate the serum prolactin level by ELISA technique to evaluate prolactin status in patients with secondary amenorrhea. Two groups of female comprising of 50 secondary amenorrhea cases as study group and 50 normal menstruating females as control were thoroughly examined and subjected to investigations for prolactin factor. Study showed that PRL levels should be kept in consideration during the diagnosis and management of secondary amenorrhea as the PRL values were found to be significant (22%). The estimation should be done in cases with H/o anovulation, infertility, secondary amenorrhea and abnormal menses. Thus the role of endocrinological PRL evaluation by ELISA appears to be a very sound and plausible answer for evaluation.

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INTRODUCTION

Secondary amenorrhea is a distinct clinical entity due to derangement in function of the hypothalamo-pituitary-ovarian axis thereby resulting in absence of menstruation for a variable period. But to locate the site of dysfunction and as well as to search for the cause of the disorder has been a matter of great concern and challenging task before clinicians. Recent advances in reproductive endocrinology has incriminated the anterior pituitary polypeptide hormone prolactin (PRL) in pathogenesis of anovulation in amenorrhea galactorrhea syndrome. Long term effects associated with amenorrhea are primarily osteoporosis and increased risk of cardiovascular diseases. This risk is increased with amenorrhea associated with hyperprolactinemia. Association of hyperprolactinemia with osteopenia is most likely because of accompanying decrease estrogen. (Morey Schachter *et al.*, 1994; Beverly MK Biller *et al.*, 1992) Raised prolactin leads to infertility due to luteal phase defect and anovulation. Thus unawareness of the problems of hyperprolactinemia will results in unsuccessful treatment of secondary amenorrhea and anovulation. Even clomiphene citrate fails to induce ovulation where there is hyperprolactinemia. Thus the role of endocrinological PRL evaluation by ELISA appears to be a very sound and plausible answer for evaluation. In the view of this context this study has been carried out with the purpose to evaluate the secondary amenorrhea cases and to find out incidence of abnormal serum prolactin in secondary amenorrhea after excluding pregnancy.

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MATERIALS AND METHODS

The present study is conducted in the department of biochemistry, government medical college and hospital Nagpur. A total 50 willing cases of secondary amenorrhea of at least 6 months duration attending gynecology OPD were enrolled in the study group. Exclusion criteria was those with primary amenorrhea, physiological amenorrhea, pregnancy, chronic illness, those on drugs like antipsychotics and antidepressants and oral contraceptive pills. 50 healthy normal females in the age group of 20 -40 were taken as controls. Complete menstrual and obstetric history along with thorough clinical examination was done. Other information collected was regarding prolonged lactation, major weight changes, infection, radiations, any trauma, headache and visual impairment etc. Serum prolactin is estimated by ELISA method using ERBA FERTIKIT by ERBA diagnostic MANNHEIM GmbH Mannheim Germany.

RESULTS

Table 1 and 2 shows hyperprolactinemia was present in 22% (11) cases. The mean levels of serum prolactin among control group was found to be 7.184 ± 0.584 ng/ml, whereas in the secondary amenorrhea the mean level was found to be 23.43 ± 3.611 ng/ml which is above the normal range (Normal range 2-22 ng/ml). Increase in prolactin level was found to be statistically highly significant with P value < 0.0001 . The overall incidence of bilateral galactorrhea was found to be 27.27% among women with hyperprolactinemia. (Table 3)

Table 4 and 5 shows the incidence of infertility among secondary amenorrhea was found to be 28% (14 out of 50). Out of these 57.14% (8 out of 14) had primary infertility and 42.85% (6 out of 14) had secondary infertility. The incidence of hyperprolactinemia was 35.71% among infertility cases.

Table 1. Prolactin status in secondary amenorrhea (n = 50)

Prolactin status	Cases		Control	
	No.	Percent	No.	Percent
Euprolactinemia	39	78 %	50	100 %
Hyperprolactinemia	11	22 %	-	-
Total	50	100 %	50	100 %

Table 2. Prolactin levels in secondary amenorrhea (n = 50)

Test	Cases	Control	P value
Sr. Prolactin (ng/ml)	23.43 ± 3.611	7.184 ± 0.584	<0.0001*

Values are shown as Mean ± SEM, SEM = Standard Error of Mean.

* P value – significant

Table 3. Incidence of galactorrhea in patients with hyperprolactinemia

Hormonal status	No. of cases	Galactorrhea	Percentage
Hyperprolactinemia	11	3	27.27 %

Table 4. Infertility pattern in secondary amenorrhea (n = 14)

Type of infertility	No. of cases	Percentage
Primary infertility	8	57.14 %
Secondary infertility	6	42.85 %
Total	14	100 %

Table 5. Abnormal prolactin status in cases of infertility

Infertility (n)	Hyperprolactinemia	
	No.	Percent
Primary (8)	2	25 %
Secondary (6)	3	50 %
Total (14)	5	35.71 %

DISCUSSION

1. In our study, hyperprolactinemia was present in 22% (11) cases with the serum prolactin level ranging from 29 to 120 ng/ml. Our results are in agreement with those of Sujata Mohanty *et al.* (1993) They observed hyperprolactinemia among 23.91% (11 out of 46) cases of secondary amenorrhea with serum prolactin level ranges between 35 to 150 ng/ml. Our results are also in accordance with the reports of Geeta Sinha *et al.* (1989). According to them, the incidence of hyperprolactinemia among secondary amenorrhea was 24.4%. In another study conducted by Rashmi Mishra *et al.* (2002) the incidence of hyperprolactinemia in secondary amenorrhea was 30.7%. In our study we found 3 cases of galactorrhea and the incidence of galactorrhea among hyperprolactinemic cases was found to be 27.27%. Incidence of galactorrhea was found to be 25% of hyperprolactinemic cases; in a study conducted by Rashmi Mishra *et al.* (2002). Avasthi Kumkum *et al.* (2006) quoted incidence of galactorrhea to be 18% among hyperprolactinemia. Galactorrhea is a typical marker of hyperprolactinemia, but it is not present in all the patients. Hence serum prolactin estimation is mandatory to diagnose hyperprolactinemia. In the present study the incidence of infertility among secondary amenorrhea was found to be 28% (14 out of 50). In a study by Rashmi Mishra *et al.* (2002) the

incidence of infertility among secondary amenorrhea was 37.2% (13/35). Out of these 53.8% (7/13) cases had primary infertility and 46.2% (6/13) had secondary infertility. In another study conducted by Geeta Sinha *et al.* (1989) the incidence of primary infertility among secondary amenorrhea was 51.21% and that of secondary infertility was 48.78%. The exact mechanism by which hyperprolactinemia causes suppression of menstruation is unclear. But it probably involves suppression of normal feedback on GnRH, either directly or indirectly, by changes in neurotransmitter function. (Michelle P Warren 1996) Prolactin suppresses hypothalamic GnRH and pituitary gonadotropin secretion, ultimately impairing gonadal steroidogenesis. Prolactin also blocks folliculogenesis and inhibits granulosa cell aromatase activity, leading to hypoestrogenism and anovulation and thus inhibiting reproductive function (Shlomo Melmed, *et al.*, 2005). Hyperprolactinemia causes infertility by two mechanism – anovulation accompanied by amenorrhea and luteal phase defect. Prolactin alters the hypothalamic neurotransmitters content through direct feedback mechanism resulting in a decrease GnRH and decrease in LH pulsatility. It has been postulated that PRL may also have a direct effect on the capacity of gonadotrophs and a direct action at gonadal level. (Pratap Kumar *et al.*, 2006) Hyperprolactinemia is a common problem encountered in reproductive disorders. The prolactin hypersecretion not only causes amenorrhea but also galactorrhea and gonadal dysfunction including infertility. Measurement of serum prolactin levels is mandatory in all secondary amenorrhea women. Since the incidence of hyperprolactinemia is very high in women with galactorrhea and quite high in women with secondary amenorrhea, a search for galactorrhea and measurement of serum prolactin levels are important screening procedures in all women who have amenorrhea.

Conclusion

Hyperprolactinemia is commonly encountered in secondary amenorrhea, galactorrhea and infertility. Presence of hyperprolactinemia in patients of secondary amenorrhea (22%) and galactorrhea (27.27%) as seen in this study suggests that PRL estimation is mandatory in all secondary amenorrhea patients. Hyperprolactinemia is quite an important cause of secondary amenorrhea and infertility. Galactorrhea which is a typical clinical marker of hyperprolactinemia is not present in all the patients hence Serum prolactin estimation is mandatory for diagnosis.

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