Hyperprolactinemia and Its Comparison with Hypothyroidism in Infertile Women

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Research Article

Abstract: Infertility is a growing problem among women. Hyperprolactinemia is one of the important factors in pathogenesis of anovulation, amenorrhea galactorrhea syndrome and other menstrual disorders. Hypothyroidism may also cause failure to ovulation in women of reproductive age group. Thus this study has been conducted to correlate prolactin and thyroid stimulating hormone (TSH) levels in infertility. Two groups of women comprising of 50 infertile cases as study group and 50 with normal fertility female controls were thoroughly examined and subjected to investigation for prolactin and thyroid factor. The serum levels of hormones prolactin and TSH were measured by using ELISA method. We found that the serum prolactin in infertile group (67.90±20.05ng/ml) was found to be high as compared to the control group (11.60±5.19ng/ml) with incidence of hyperprolactinemia in infertility was found to be 38%. The incidence of hypothyroidism in infertility was found to be 18% , with mean serum TSH to be significantly increased in infertile group (10.25±5.21µlU/ml) as compared to control (2.5±0.61µlU/ml). Thus our study showed that there is high incidence of hyperprolactinemia in infertile women as well high increased incidence of hypothyroidism in these women emphasizes importance of screening of prolactin and TSH levels in these women.

Keywords: Hyperprolactinemia, Hypothyroidism, Infertility, ELISA (Enzyme linked immunosorbent assay)

Introduction

Hyperprolacemia is a common problem which is encountered in reproductive disorder.[1] Hyperprolactinemia is usually associated with menstrual and ovulatory disorders like amenorrhea, oligomenorrhea, anovulation, ovulatory cycle with short or inadequate luteal phase and galactorrhea.[2] The ovulation can be affected by hormonal imbalance, thyroid disorders or chronic diseases such as diabetes.[3] Some women with galactorrhea and hyperprolactinemia might have primary hypothyroidism. This disease is characterized by low serum levels of thyroxine (T4) and decreased negative feedback on the hypothalaopituitary axis. The resulting increased secretion of thyrotropin releasing hormone (TRH) stimulates thyrotropes and lactotrophs, thereby increasing the levels of both TSH and prolactin.[2] Primary hypothyroidism is commonly associated with hyperprolactinemia due to the stimulatory effect of TRH on lactotrophs.[4] Women with hyperprolactinemia are often associated with hypothyroidism which is characterized by high TSH levels in serum. Hypothyroidism is one of the causes of ovulation failure in reproductive age group, resulting in infertility. [5] Thus this study has been undertaken to find out possible role of prolactin in female infertility and to find out its compairison with serum TSH levels.

Material and Methods

50 women with infertility (both primary and secondary) attending the gynecology OPD of GMC Nagpur were selected as cases and 50 age matched women with normal menstrual cycle and fertility were selected as control group. The exclusion criteria was male factor infertility and female tubal factor, any congenital anomaly of urogenital tract or any obvious organic lesions, patients with H/o thyroid diseases and those on thyroid medication. A detailed history was taken, information regarding past oral contraceptive use, lactation, major weight changes, symptoms like headache, visual impairment, drug history, any chest trauma or surgery were elicited. This was followed by general and gynecologic examination. Informed written consent was obtained for venepuncture.5 ml fasting venous blood sample was withdrawn for investigations taking all aseptic precautions. Serum was separated and investigated either immediately or it was preserved at 2-8 C for up to three days. Serum prolactins, TSH were measured by enzyme immunoassay on ELISA Reader using ERBA FERTIKIT and ERBA Thyrokits by ERBA Diagnostics Mannheim GmbH, Germany.

Results

Results are given in tables 1 to 4.

Table 1: Infertility pattern in study group (n = 50)

Type of infertility	No. of cases	Percentage
Primary infertility	29	58 %
Secondary infertility	21	42 %

Table 2: Abnormal hormonal status in cases of infertility

Infertility (n)	Hyperprolactinemia		Hypothyroidism	
	No.	Percent	No.	Percent
Primary (29)	8	27.58 %	6	20.68 %
Secondary (21)	11	53.38 %	3	14.28 %
Total (50)	**19**	**38 %**	**9**	**18 %**

Table 3: Serum prolactin and TSH levels in study group

Subjects	Prolactin (2 to 22 ng/ml)	TSH (0.4 to 6.0 µlU/ml)
INFERTILITY	67.90±20.05	10.25±5.21
CONTROL	11.60±5.19	2.5±0.61

Table 4: Incidence of galactorrhea in patients with hyperprolactinemia and hypothyroidism

Hormonal status	No. of cases	Galactorrhea	Percentage
Hyperprolactinemia	19	5	26.31 %
Hypothyroidism	9	1#	11.11 %

One case having galactorrhea had both hypothyroidism and hyperprolactinemia.

Out of 50 patients , 29 (58%) had primary infertility and 21 (42%) had secondary infertility.(Table 1) All the women were in age group of 25 – 29years in both the groups. The incidence of hyperprolactinemia (PRL>22ng/mL) was 38% (19/50). Out of these hyperprolactinemia present in primary infertility was 27.58% (8/29) and those in secondary infertility was 52.38% (11/21). (Table 2) The incidence of hypothyroidism (TSH > 6) was 18% (9/50). Out of these 20.68 % (6/29) were primary infertile and 14.28 % (3/21) were having secondary infertility. (Table 2) The mean serum PRL concentration was increased in infertile group 67.90±20.05 as compared to the control group 11.60±5.19 and it was found to be statistically highly significant. (p value < 0.001) (Table 3) The incidence of galactorrhea was found to be 26.31%among hyperprolactinemia. (Table 4) Similarly the mean serum TSH in the infertile group was 10.25±5.21and in control group it was 2.5±0.61 which was also highly significant. (p value < 0.0001). (Table 3)

Discussion

Hyperprolactinemia is a common problem encountered in reproductive disorders. [1, 4] The understanding that PRL hypersecretion not only causes galactorrhea and amenorrhea but also gonadal dysfunction & infertility led to wider use of prolactin estimation. In our study there were 58% women with primary infertility & 38% with secondary infertility. In a study by Kumkum et al[2] they found patients with primary infertility to be 60% while those of secondary infertility to be 40%. Somewhat similar results were obtained by other authors [1, 4] The incidence of hyperprolactinemia in our study was found to be 38%. Kumkum et al[2] reported the incidence of hyperprolactinemia to be 46% in infertility while Mishra et al[6] reported it to be 20%. The mean PRL levels in infertility in our study is 67.90±20.05 whereas it was 76.33±55.97 in a study by Kumkum et al[2]& Mishra et al[6] found to be 128.28±12.74. The incidence of hypothyroidism in our study is 18% with mean TSH in patients with infertility was 10.25±5.21. The Kumkum et al[2] found it to be 19.6%. The incidence of galactorrhea in our study was 26.31%, whereas Kumkum et al[2]found it to be 18% and it was 25% in a study by Mishra et al.[6] Hyperprolactinemia causes infertility by two mechanisms – 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. [7]

The cause of infertility and menstrual irregularities is said to be anovulation resulting from hyperprolactinemia. Raised levels of serum prolactin inhibit GnRH (Gonadotropin Releasing Hormone) levels which are necessary for ovulation. The low GnRH levels causes decreased secretion of FSH and LH hormones, thus affecting gonadal steroid synthesis,resulting in infertility. [8-10] It is observed that the prevalence of hyperprolactinemia associated hypothyroidism which is characterized by high levels of serum TSH & low levels of thyroid hormones T3 and T4 is high in infertile women as compaired to normal fertile females.[11] Infertility due to hyperprolactinemia has been found to be associated with abnormal menstrual pattern as well as anovulatory cycles. Hyperprolactinemia is often the cause of amenorrhea occurring in hypothyroid patients. This hyperprolactinemia is said to be resulting from defective positive feedback of oestrogen on LH and FSH suppression. Ovulation is affected by impaired pulsatile secretion of GnRH because of hyperprolactinemia, thus ultimately resulting in menstrual and ovulatory dysfunctions. [12] Hyperprolactinemia is quite an important cause of 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. Since there is increased TSH in infertile women as compared to controls emphasizes importance of estimation of thyroid hormones in infertility.

Conclusion

The incidence of hyperprolactinemia in infertile women is found to be significant. Since the incidence of hyperprolactinemia is very high in women with galactorrhea and quite high in infertility, a search for

galactorrhea and measurement of serum prolactin levels is important screening procedure in infertility. The relatively high occurrence of high TSH levels in these patients emphasized the importance of TSH screening in infertility.

References

1. Choudhary SD, Goswami A. Hyperprolactinemia and reproductive disorders – a profile from north east. J Assoc Physiacians India 1995; 43: 617-8.
2. Avasthi Kumkum. Hyperprolactinemia and its correlation with hypothyroidism in infertile women. J Obstet Gynecol India. 2006; 56: 68-71.
3. Anwar Sultana, Shehnaz Nadir. Pituitary gonadotropic hormones in women with oligo/amenorrhea. J.Ayub Med Coll Abbottabad. 2008:20.
4. Patel S S, Bamigboye. Hyperprolactinemia. J of Obstetrics and Gynecology, July 2007;27(5):455-459.
5. M. Bals-Pratsch. Episodic variation of prolactin, thyroid stimulating hormone, luteinsing hormone, melatonin and cortisol in infertile women with subclinical hypothyroidism. Human Reproduction. 1997; 12: 896-904.
6. Mishra R, Baveja R, Gupta V et al. Prolactin levels in infertility with menstrual irregularities. J Obstet Gyynecol India 2002; 52:40-3.
7. Pratap Kumar, Amar R, Meenakshi Dua et al. Hyperprolactinemia – infertility and beyond. Obs and Gynae today May 2006; Vol XI(5): 295-98.
8. Koutras DA. Disturbances of menstruation in thyroid disease. Ann N Y Acad Sci. 1997; 816: 280-4.
9. Cramer DW, Sluss PM, Powers RD. et al. Serum prolactin and TSH in an in vitro fertilization population: is there a link between fertilization and thyroid function? J Assist Reprod. 2003; 20:210.
10. Poppe K, Velkeiners B. Thyroid and infertility. Verh K Acad Geneeskd elg. 2002; 64(6): 389-99.
11. Affia Tasneem et al. The incidence of hyperprolactinemia and associated hypothyroidism.: local experience from Lahore Center for Nuclear Medicine, Mayo Hospital Lahore, 2government College for Boys Gulberg Lahore. PJNM. 2011, 1:49-55.
12. Binita Goswami et al. Correlation of prolactin and thyroid hormone concentration with menstrual pattern in infertile women. J Reprod Infertil. 2009; 10 (3):207-12.