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jbiolchemres@gmail.com
info@jbcr.in

RESEARCH PAPER

Role of Hyperprolactinemia in Spontaneous Abortions

Uma Singh, S. Pandey, Sumita Arora, Anju Mudra and Rajesh Arora
Department of Obstetrics and Gynaecology, K.G's Medical College, Lucknow, U.P., INDIA

ABSTRACT

A number of studies in recent years have shown an association between hyperprolactinemia and recurrent spontaneous abortions. This study is an effort to establish the role of hyperporlactinemia as one of the causes of spontaneous abortion. It was done by comparing the levels of prolactin in pregnant and non-pregnant cases with history of one or more spontaneous abortion (study group, n=50) with normal healthy pregnant women and those who had delivered healthy full term infants previously (control group n=30). It was observed that 34% of patients in the study had hyperprolactinemia while only 2% of cases in control group had the abnormality. No significant association was observed between the number of abortions and hyperprolactinemia. The incidence was similar in both control and study groups. Therefore there was a significant association between hyperprolactemia and recurrent spontaneous abortions while, no association could be drawn between recurrent spontaneous abortions and luteal phase defect, thyroid abnormality and blood sugar abnormality.

Key words: Hyperprolactinemia, Abortions, Luteal phase, Pregnancy, Thyroid and Blood sugar.

INTRODUCTION

Prolactin disorders have been found to be an important cause of infertility and early pregnancy loss. Prolactin is a polypeptide hormone of the anterior pituitary and plays an essential role in milk secretion and hyperprolactimenia is associated with suppression of the hypothalamic pituitary gonadal axis. The role of prolactin in the corpus luteum during early pregnancy has been studied extensively in the rodent until at least 24 hours after nidation takes place in a rat. This along with other evidence suggests an important role of the hormone in promoting early corpus luteum function.

Various studies have been undertaken to assess the role of hyperprolactinemia as one of the causes in spontaneous abortions. This study is an effort to evaluate the role of hyperprolactinemia in patients of spontaneous abortions.

MATERIAL AND METHODS

Women registered in OPD or admitted in wards of Queen Mary's Hospital with history of one or more consecutive miscarriages were worked up in our study. A detailed history was taken and a detailed examination was carried out on them. Investigations done were Hb%, blood group, blood sugar- fasting and PP, VDRL and hormonal investigations like T_3, T_4, TSH and serum progesterone on 22^{nd} day of cycle, serum prolactin (during mid morning in mid follicular phase); ultrasonography and hysterosalpingography (in pregnant patients) were done.

The patients were divided into study group and control group. Study group comprised of pregnant and non-pregnant cases that had a history of one or more spontaneous abortions. The sample size was 50. Control group consisted of normal healthy pregnant women those who had delivered healthy full term infants previously. The sample size was 30.

Serum prolactin was assayed by Coat A count procedure which is a solid phase I^{125} radiommunoassay designed for quantitative measurement of serum prolactin in human seru. The basal values in nanograms/ml for non-pregnant women and women in each trimester of pregnancy and one day postpartum are tabulated in table 1.

The prolactin kit used for estimation of serum prolactin was Diagnostic Products Corporation (DPC) 5700, West 96^{th} Street, Los Angeles, CA 90045-5597.

RESULTS

When patients in study group and control group were compared for age, socioeconomic status and domicile nature it was observed that there was no significant difference between the two groups. 76% of patients in study group and 83.33% of patients in control group were in 21-30 years of age. In study group, 76% patients were of urban and 24% of rural background while in control group, 83.33% were of urban and 16.66% were of rural background. Maximum number of cases belonged to middle class, 56% in study group and 73.33% in control group. All these differences were insignificant.

When the incidence of hyperprolactinemia was observed in the two groups, it was seen that among the 50 patients in study group, 17 had hyperprolactinemia which was 3%.

In the control group out of 3 patients, 2 had hyperprolactinemia wahich was 6.6% the number of cases with hyperprolactinemia was significantly higher in study group than control group. X^2=7.7354, p=<0.001 (Table 2).

A comparison was done to see the relation of number of abortions with the presence of hyperlactinemia. It can be sent out that out of 3 cases in group of isolated abortions, none had hyperprolactinemia, while out 26 cases which had two abortions, and 11 had hyperprolactinemia which was 42.30%. In cases with 3, 4, 5, 6 abortions the number cases were 4, 0, 1 and 1 respectively which amounted to 30.76%, nil, 100% and 50% respectively. There is no significant difference in the number of cases with hyperprolactinemia having one or two abortions than those having three or more than three abortions. Thus there is no significant association between incidence of hyperprolactinemia and number of abortions (Table 3).

When hyperprolactinemia cases in both groups were compared for distribution according to age of cases, domicile nature and socioeconomic status it was observed that the distribution was similar in control and study groups thereby showing that incidence of hyperprolactinemia is not affected by age, domicile nature and socioeconomic status.

Other endocrinological markers like serum progesterone for detecting luteal phase defect, thyroid function tests and blood sugar levels were compared. (Table 4).

Out of 50 cases in study group, 8 were in follicular phase. So serum progesterone was measured in only 42 cases. It can be seen that out of total 42 cases, 6 had luteal phase defect which was 14.28% whereas in control group only 3 cases 10% had luteal phase defect. This difference is insignificant. Thyroid abnormality was seen in 1 out 50 patients in study group i.e. 20% while in control group none had thyroid dysfunction. This is also insignificant. Blood sugar derangement was seen in 1 out of 50 patients in study group i.e. 2% while in control group none had blood sugar abnormality. This is an insignificant difference.

By this table it is clear that incidence of LPD, thyroid abnormality and blood sugar abnormality is similar in both control and study group but incidence of hyperprolactinemia is more in study group as compared to control group.

DISCUSSION

Risk of spontaneous abortion for a woman with no history of reproductive wastage is about 15%. After first spontaneous abortion, the chance for a repeat abortion is 19% and with 2 spontaneous abortions the risk increase to 35%. With 3 previous spontaneous abortions, the risk of repeated abortions is 47%.

The main aim of our study was to establish "the role of hyperprolactenimia as one of the causes of spontaneous abortions". It was seen that hyperprolactinemia is found in 17 % of the cases in study group which is higher than that in control group (6.6%). Similar study was done by Hirahara F.,Anodh N et al. They evaluated the role of hyperpoacleimenia in the pathogenesis of recurrent spontaneous abortions and measured the rate of successful pregnancies after restorations of prolactin level with bromocriptine. It was seen that the percentage of successful pregnancies was higher in bromocriptine treated group than in the group that was not treated with bromocriptine (85.7% versus 52.4%, $p<0.05$). Serum prolactin levels during early pregnancy (5-10 weeks of gestation) were significantly higher in patients who miscarried (31.8-55.3 ng/ml) then in patients whose pregnancies were successful (4.6-15 ng/ml, $p<0.01$ or $p<0.05$).

Chung Hua Fu Chan Ko Tsa Chih, 1993 Jan, in their study indicated that prolactin might be associated with luteal function during early pregnancy. Baituraeva T.K. et al. in their study showed that in hyperprolactinemia the level of LH secretion was high the level of LH was moderately increased during all phases of menstrual cycle. Secretion of FSH similar in both groups. Rossi A.M., Vilska S., Hainomen P.K. evaluated the outcome of pregnancies in women with treated or untreated hyperprolactinemia. They found that obstetrical complications like miscarriages and tubal pregnancies are more in women with untreated hyperprolactinemia.

Thus, all these studies indicate that prolactin has a role in recurrent spontaneous abortion indirectly by causing luteal insufficiency or by LH dysfunction.

Day S., Ward S., Burrows E. studied progesterone profile in LPD cycles in patients with recurrent spontaneous abortions. The incidence of luteal phase defect was 40% in women with recurrent abortions in their study and 81% of pregnancies were successful with treatment. In our study the difference between the two groups was insignificant.

Measurement of TSH and free thyroxine are almost routine in patients with a history of repeated pregnancy losses. However, it is rate that a deficiency or an excess of thyroid hormone is the etiology of early pregnancy loss. Patients with thyroid dysfunction are affected instead by preterm labor usually occurring after 24 weeks. No statistically significant difference was seen serum T_3, T_4 and TSH values in study and control groups ($p=0.3156$) in our study.

Controversy surrounds the questions of whether the women with insulin dependent diabetes have a higher than normal risk of spontaneous abortion. Studies by Carne J.P., Wahe N., Stray Peterson B., Stray Peterson S. have shown that diabetes is not a cause of early pregnancy loss.

However, a large multicentre controlled study by Mills J.L., Simpson J.L., Driscoll S.G. et al. found the diabetes with both an elevated blood glucose and haemoglobin A_1C in the first trimester have a significantly increased risk of abortion, whereas those with good metabolic control had a risk similar to that of control subjects. Our study showed no significant difference between the blood sugar values of the study and control subjects (p=0.4656).

Table 1

Reference group	Median (ng/ml)	Central 95% range
Non-pregnant	6.2	ND - 20
1st trimester	17	7-31
2nd trimester	118	31-182
3rd trimester	120	84-232
1 day postpartum	157	20-319

X^2=7.7354; p=<0.001

Table 2

Cases	Study Group A		Control Group B	
	Number of hyper Prolactinemic cases	%	Number of hyper Prolactinemic cases	%
Pregnant cases	14	28	2	6.6
Non pregnant cases	3	6	0	0
Total	**17**	**34**	**2**	**6.6**

Table 3

Pregnancy losses	Total number cases in Group A	Total number of cases with hyperprolactinimia	%
PO+1	3	0	0.00
PO+2	26	11	42.30
PO+3	13	4	30.76
PO+4	5	0	0.00
PO+5	1	1	100.00

X^2 *=0.7923;* p=>0.05 (NS)

Table 4

Endocrinal Markers	Study Group		Control Group		Significance
LPD	6(n=42)	14.28%	3 (n=30)	10.00%	X^2=0.2938 p≥0.05 (NS)
T3, T4 TSH abnormality	1 (n=50)	2%	0	0	X^2=0.61 p=0.3156 (NS)
Blood sugar abnormality	1(n=50)	2%	0	0	X^2=0.0061, p=0.4656 (NS)
Hyperprolactinemia	17 (n=50)	34%	2 (n=30%)	6.60%	X^2=7.7354, p<0.001 (significant)

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