Original Article

Outcome of Treatment with Lisuride in Hyperprolactinemic Infertile Women

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ABSTRACT

OBJECTIVE: To determine the treatment response with lisuride in Hyperprolactinemic women.
STUDY DESIGN: Observational
PLACE AND DURATION: Department of Gynecology / Obstetrics, Peoples Medical College, Nawabshah from 1st October 2002 to 30th September 2004
PATIENTS AND METHODS: 25 patients with amenorrhea, oligomenorrhea, galactorrhea and infertility with raised levels of serum prolactin, lisuride treatment was given.
RESULTS: Serum prolactin levels decreased to normal in 19(76%) patients resumption of regular menses in 20(80%) patients and cessation of galactorrhea in 24(96%) and 6(24%) patients become pregnant. Side effects attributed to lisuride were minimal transient and usually well tolerated.
CONCLUSION: Our study suggests that lisuride is an appropriate therapeutic modality for hyperprolactineamia and prolactin secreting adenomas.

KEY WORDS: Lisuride, Hyperprolactinemia, Infertile Women.

INTRODUCTION

Hyperoprolactinemia is a condition with increased levels of prolactin in the blood, which in women is associated with amenorrhea[1] and galactorrhea[2] and in men[3] has been reported to cause hypogonadism and impotence and in some cases, gynecomastia[4] often but not invariably associated with microadenoma[5] of the anterior pituitary gland. Hyperprolactinemia is commonest pituitary cause of amenorrhea. There are many other causes of a mildly elevated serum prolactin concentration such as stress, physical and breast examination. If the serum prolactin levels are continuously raised[6] at high levels then it is necessary to image the pituitary fossa (CT or MRI scan)[7] Hyperprolactinemia may result from a prolactin secreting adenoma[8,9] or from a non-functioning disconnection, tumuor in the region of the hypothalamus or pituitary, which disrupts inhibitor influence of dopamine on prolactin secretion. Hyperprolactinemia could also be because of hypothyroidism, polycystic ovarian syndrome and several drugs, i.e. the dopaminergic antagonists like phenothiazines, domperidone and metoclopramide. Prolactin secreting pituitary micoradenoma is usually associated with a moderately elevated prolactin and is unlikely to result in abnormalities on a lateral skull x-ray film. Conversely, a macroadenoma, associated with quite high concentration of prolactin and by definition greater that 1 cm in diameter, may cause typical radiological changes that is an asymmetrically enlarged pituitary fossa, with double contour to its floor and erosion of the clinoid processes[10]. CT and MRI[11] scans allow detailed examination of the extent of the tumour. Prolactin is an excellent tumour marker[12, 13] and so the higher the serum concentration the larger the size of the tumour.[4] The management of hyperprolactinemia centers around the use of dopamine agonists[14, 15] Most patients show a fall in prolactin levels within a few days to few weeks of commencing the therapy[10, 16]. Side effects can be troublesome i.e. nausea, vomiting, headache and postural hypotension and are minimized by commencing the therapy at bed time at night for few days and taking the tablets in the middle of a mouthful of food. The purpose of this study as planned to see effectiveness of lisuride hydrogen maleate (Dopeagin) in resolving the problem of hyperprolactinemia and infertility related to it.

MATERIAL AND METHODS

This study in infertile and hyperprolactinemic women has been done in the department of Obstetrics and Gynecology at People's Medical College Hospital Nawabshah from 1st October 2002 till 30th September 2004. During this period of two years about 25 patients had come with the complaints of galactorrhea, infertility, oligomenorrhea and amenorrhea. All patients were investigated for serum prolactin levels, Serum thyroxine, tri-iodothyronin and thyroid stimulating hormones, serum gonadotrophin levels, Serum estradiol levels, X- ray films of the skull, and computerized tomographic scanning.

TREATMENT: All of the patients in this series were given the dopamine agonist called Dopergin i.e. lisuride hydrogen maleate ½ tablet, means 0.1 mg at bed time alongwith some food for one week and by increasing it gradually i.e. ½ tablet twice a day for another week and then one tablet i.e. 0.2mg two times a day onwards along with the meals in order to reduce the side effects and to increase the tolerance of the drug. Each patient was seen initially at monthly intervals for 3 months then at 2-3 months intervals.

DATA ANALYSIS: The Data were evaluated in SPSS version 11.0. Simple frequencies and percentages were calculated on 95% confidence interval. Mean and standard deviation was also calculated for continuous variables i.e. age and weight.

RESULTS

Among these 25 patients 9(36%) were medical students, 3(12%) were doctors, 2(8%) were teachers, 2 (8%) were laboratory assistants and the rest of others were house wives by occupation. Their age was in between 18 and 35 years, 9(36%) of them were unmarried and were complaining of oligomenorrhea, amenorrhea and / or galactorrhea. There was no history of taking the drugs, known to stimulate prolactin secretion. Most of them were having more than two symptoms – two were having regular periods but galactorrhea and infertility (**Table I**). All of them were having good general health, and were having body weight between 44 and 50 kilograms. Nineteen (76%) of them were having galactorrhea and 3(12%) were having dry vagina, they were also complaining of dyspareunia and decreased libido. Serum prolactin levels were raised in all of them. Serum prolactin levels were determined at each visit, which had started decreasing in all of them. The interval between the initiation of therapy and the attainment of normal serum prolactin levels varied. There was no evidence that the magnitude of the pre-treatment prolactin levels was related to the length of time required to normalize the serum prolactin during therapy. In one patient the prolactin never reached to normal values and two had sporadic elevated values secondary to their poor compliance. Three women continue to have normal serum prolactin levels 7 months after the discontinuation of Dopergin. Menstrual bleeding resumed in 10 patients within 3 months after Dopergin was started and all women had regular cycles within two years. Breast secretion diminished and eventually stopped in all except one patient in whom the prolactin levels never normalized. Menses returned prior to the cessation of breast secretion in almost all of them. There was no correlation between the serum prolactin levels and the quantity or duration of the breast secretion. Patients with serum prolactin levels of more than 800 IU/ml got their x-ray skull done and had also sella turcica examined by computerized tomography. Six patients had enlarged pituitary fossa – five of them were having microadenoma that is less than 1 cm and one was having macroadenoma that is more than 1 cm in size (**Table II**). The repeated CT scans during the therapy showed, decreased in the size of prolactinoma. Six patients got pregnant about 6 – 8 months after the commencement of Dopergin therapy and Dopergin was discontinued as soon as term pregnancy was confirmed. All of them had full time pregnancy, two were delivered by cesarean section because of the contracted pelvis – one had c. section because of primary breech and the other three were delivered normally vaginally.

Side effects of Dopergin:

Almost all the 25 patients had experienced some side effects while receiving Dopergin but they were able to tolerate these symptoms and continued to take the medication reliably. The principal complaints were nausea in 15 patients i.e. 60%, dizziness in i.e. 40% light headedness in 7 i.e. 28% and tiredness in 4 i.e. 16% (**Table III**).

TABLE I:

PATIENTS CHARACTERISTICS AND PHYSICAL FINDINGS WITH HYPERPROLACTINEMIA

Age(in years), Mean ± SD (Range)	27.3 ± 1.2 (18 to 35)
Weight (in Kg), Mean ±SD (Range)	48.0 + 0.1 (44 to 50Kg)
	n(%)
Profession:	
House wives	09(36%)
Medical students	09(36%)
Doctors	03(12%)
Teachers	02(8%)
Laboratroy Assistants	02(8%)
Clinical features :	
Galactorrhoea	19(76%)
Oligomenorrhoea	5(20%)
Amenorrhoea	18(72%)
Regular Menses	2(8%)

TABLE II:

RADIOLOGICAL FINDINGS (n = 25)

	n(%)
Microadenoma	05(%)
Macroadenoma	1(4%)

TABLE III:

FREQUENCY OF THE SIDE EFFECTS ATTRIBUTED TO DOPERGIN IN THE PATIENTS UNDER THIS STUDY WAS AS BELOW:

	n(%)
Nausea	5(60%)
Dizziness	10(40%)
Light headedness	7(28%)
Tiredness	4(16%)

DISCUSSION

The etiology and pathogenesis[17] of prolactinomas are unknown, indeed it is arguable whether a microprolactinoma is a true neoplasm, as adenoma cells behave like normal lactotrophes and are normally receptive to dopamine over the past few years the major change in the management of patients with prolactin-secreting pituitary tumors had been a tendency to rely increasingly upon dopamine agonists.[18, 19] Dopamine agonists lower circulating prolactin levels and shrink pituitary prolactin secreting tumours through a dopamine mimetic action on the pituitary at two central nervous system loci.

1. The decrease dopamine turn over in the tubers infundibuler neurons of the arcuate nucleus, generating increased hypothalamic dopamine; and
2. Act directly on pituitary dopamine receptors to inhibit prolactin release [20]

Doperminergic drugs are the usually initial treatment for prolectinomas and it requires long term follow up of the patients.[21] Surgery being reserved for the lesions that extend outside the fossa and irradiation being reserved for invasive or recurrent tumors [16, 21] Radiological findings depend very much on the radiological equipment available and on the training of those interpreting the x-rays. The prolactin secreting cells of the pituitary i.e. the lactotrophs are normally concentrated in the lateral portions of the gland that is the acidophil wings and so when an adenoma of the lactotrophs forms, it expands the pituitary fossa asymmetrically which results in characteristic changes in the shape and the size of the fossa and also can cause the compression on adjacent important structures.[22]

CONCLUSION

So in this study is seen that careful collection of the data, radiological studies and reliable reagents for prolactin assays suggest that the dopamine agnonist i.e. Dopergin is an appropriate therapeutic modality for this common and increasingly recognized condition that is hyperprolactinemia and prolactin secreting adenoma giving rise to amenorrheoa and infertility.

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