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Original Research Article

Effectiveness of Cabergoline therapy in hyperprolactinemic infertility

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ABSTRACT

Background: Hyperprolactinemia may be associated with ovulatory dysfunction and resultant subfertility. Hyperprolactinemia affects the pulsatile release of GnRH, which in turn impairs the secretion of FSH and LH. It may also affect the endocrine activity of ovarian follicles, resulting into luteal phase defect and ovulatory dysfunction. Hyperprolactinemia may be associated with infertility in up to one-third of women undergoing infertility workup. Women with hyperprolactinemia are generally treated with dopamine receptor agonists to reduce serum prolactin levels and regularisation of menses. The aim of this study was to study the effectiveness of cabergoline therapy in hyperprolactinaemic infertility.

Methods: This prospective study was performed from June 2017 to July 2018 in women with Hyperprolactinemic infertility attending the infertility clinic at INHS Patanjali. In this study, 20 women with hyperprolactinemic infertility who satisfied the inclusion and exclusion criteria were started on four week cabergoline therapy. The effectiveness of therapy was evaluated on the basis of normalization of prolactin levels, regularization of menses, reduction in galactorrhea, successful conception and adverse effects if any.

Results: The women on Cabergoline therapy showed marked improvement in menstrual irregularity, near normal prolactin levels and reduced galactorrhea. After the four week Cabergoline therapy the frequency of galactorrhea and irregular menses was reduced in 8 (80%) and 14 (93.3) per cent, of women respectively. Successful conception was achieved in 17 (85%) women after regularization of menses with no any major adverse effects.

Conclusions: This study shows the effectiveness of cabergoline therapy both on lowering the serum prolactin levels and successful Conception with no any major adverse effects. Cabergoline therapy is a cost effective and safe option in hyperprolactinaemic infertility.

Keywords: Cabergoline, Hyperprolactinemia, Infertility

INTRODUCTION

Prolactin, a pituitary-derived hormone has a pivotal role in a variety of reproductive functions.[1] Hyperprolactinemia can be defined as the presence of abnormally high level of prolactin in the blood. Normal levels are in range of 10-35 ng/ml.[1,2]

Hyperprolactinemia may be associated with ovulatory dysfunction and resultant subfertility.

Hyperprolactinemia affects the pulsatile release of GnRH, which in turn impairs the secretion of FSH and LH. It may also affect the endocrine activity of ovarian follicles, resulting into luteal phase defect and ovulatory dysfunction.[2] Hyperprolactinemia may be associated with infertility in up to one-third of women undergoing infertility workup. Women with hyperprolactinemia are generally treated with dopamine receptor agonists to reduce serum prolactin levels and regularisation of menses.[1,3]

The main aim of hyperprolactinemia treatment is to correct the biochemical consequences of the hormonal excess.[4] Dopamine receptor agonists currently available for the treatment of hyperprolactinemia are bromocriptine and Cabergoline.

Bromocriptine has been used for a number of years for this purpose. However, patient compliance and its side effects led doctors to search for a better alternative. Studies have shown Cabergoline to be an important advance in the treatment of hyperprolactinemia.[5,6]

The available evidence about its use in infertility shows that cabergoline therapy has no deleterious effects on mothers and fetuses.[7]

In patients with Hyperprolactinemic infertility, fertility may be promoted with protocol based use of dopaminergic drugs like Cabergoline. The effective therapy normalizes (PRL) Prolactin level and thus improves ovulatory dysfunction and luteal phase defect.[1,2]

The aim of this study was to study the effectiveness of Cabergoline therapy in hyperprolactinemic infertility.

METHODS

This prospective study was performed from June 2017 to July 2018 in women with Hyperprolactinemic infertility attending the Infertility Clinic at INHS Patanjali. A detailed history and complete physical examination were performed along with basic infertility workup on all such patients.

Inclusion criteria

- Primary or secondary infertility
- Hyperprolactinemia with or without galactorrhea (prolactin >35 ng/ml).

Exclusion criteria

- Patients with other causes of infertility such as tubal factor, male factor and unexplained infertility

Patients were fully informed of the conduct and consequences of the study. A total of 20 women with hyperprolactinemic infertility who satisfied the inclusion and exclusion criteria were included in this study.

They were treated with oral Cabergoline 0.25 mg twice a week for four weeks and adverse effects if any were noted. Serum Prolactin level was measured after completion of four week therapy.

Ovulation induction and follicular monitoring was started after regularization of menses.

Successful conception was documented by transvaginal sonography, at 6-7 weeks of gestational age. Main outcome assessed were normalization of serum prolactin level, reduction of galactorrhea, regularization of menses, successful conception and adverse effects if any.

RESULTS

Of the 20 patients, 10 (50%) had galactorrhea and 15 (75%) had irregular menses.

As shown in Table 1 the mean age of women with hyperprolactinemic infertility was 24 years. The mean duration of infertility 2 years and the mean baseline prolactin level was 54 ng/ml.

Table 1: Demographic characteristics.

Variable	Range	Mean
Age (years)	20-30	24
Duration of infertility (years)	2-5	2
Serum level of prolactin (ng/ml) range mean±SD	35-100	54
Galactorrhea No. (%)	10 (50)	
Irregular menstruation No. (%)	15 (75)	

Raised levels of prolactin can result in suppression of luteinising hormone secretion and inhibition of ovulation and thus be associated with infertility. This usually manifests with oligomenorrhea or amenorrhea.[7]

Major outcomes of the study

Major outcomes of this study are shown in Table 2. After the four week Cabergoline therapy the frequency of galactorrhea and irregular menses was reduced in 8 (80%) and 14 (93.3) per cent, of women respectively. The mean serum level of prolactin was decreased to 18 ng/ml (Table 2).

Finally, after the study period, all women had a near normal serum prolactin level.

This finding are significant and in line with the systemic review and meta-analysis conducted by Wang At et al.[12]

Cabergoline therapy is effective in reducing hyperprolactinemia, amenorrhea/oligomenorrhea, and galactorrhea.

Table 2: Major outcomes of the study.

Outcomes	Number (%)
Regularization of menses	8 (80)
Reduced galactorrhea	14 (93.3)
Near normal serum prolactin	20 (100)

Successful conception

Successful Conception was achieved in 17 (85%) patients as shown in Table 3.

Table 3: Successful conception.

Successful conception	Number (%)
Spontaneous	10 (50)
Ovulation induction	7 (35)
Total	17 (85)

Out of this, 10 patients conceived spontaneously and rest with standard ovulation induction protocol Table 3. This result are comparable to the studies conducted by Ono et al and Robert et al.[8,9]

Safety profile

No any major adverse effect was noted during the therapy. This enabled a better compliance of the patient for the four week Cabergoline therapy in this study.

DISCUSSION

Preeclampsia leads to increased perinatal morbidity and Cabergoline is one of several dopamine agonists that are currently available for the treatment of hyperprolactinemia. In this study, successful Conception was achieved in 85% women. This results are comparable to results achieved by Motazedian et al, pregnancy was occurred in 82 per cent of all infertile women who received cabergoline treatment at the time of study. Moreover, the level of prolactin was decreased to normal range in 84.3 per cent of these women as compared to 100 per cent in the current study.

Similar successful conception rates were achieved by Ono et al and Robert et al which shows that cabergoline can correct hyperprolactinemia, recover fertility, induce pregnancy, and bring about uneventful delivery in such infertile patients. Importantly, cabergoline provides this total care by itself without requiring any aid from gynecological, neurosurgical, and radiotherapeutic modalities.[8,9]

The study conducted by Hamoda et al, shows that Cabergoline is more effective than bromocriptin in lowering prolactin levels, with substantially fewer adverse effects and higher patient compliance.[10] Cabergoline has a very long elimination half-life and can, therefore, be administered once or twice a week. It has been shown to result in resumption of ovulation in 95% of cases.[11] Study conducted by Ricci et al, supports the safety profile of Cabergoline.[6] No data have shown cabergoline to be unsafe for women anxious to conceive.[7]

Wang At et al, meta-analysis shows that Cabergoline is more effective than bromocriptine in reducing persistent hyperprolactinemia, amenorrhea/ oligomenorrhea, and galactorrhea. A large body of non-comparative literature shows dopamine agonists improved major outcomes as shown in our study.[12,13]

CONCLUSION

This study shows the effectiveness of cabergoline therapy both on lowering the serum prolactin levels and successful Conception with no any major adverse effects. Cabergoline therapy is a cost effective and safe option in hyperprolactinaemic infertility.

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