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Original Research Article

Effect of High-Dose Cabergoline Therapy for Hyperprolactinemic Infertility among Bangladeshi Women

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Abstract

Background: Cabergoline is effective in the treatment of hyperprolactinemic hypogonadism. It is a highly effective and long-acting inhibitor of prolactin secretion. The rate of cabergoline-induced pregnancy in women with prolactinoma, is unknown. ***Objective:*** The aim of present study is to evaluate the efficacy and safety of high-dose cabergoline therapy for hyperprolactinemic infertility among Bangladeshi women. ***Method:*** This descriptive cross- sectional study was conducted among 50 patients from January, 2020 to January, 2022 in at The Medinova Diagnostic Centre, Sylhet, Bangladesh. ***Results:*** In our study, maximum (14) patients belong to the age group of 19 to 23 years, and minimum number of patients (4) was between 39 to 43 years. Maximum (52%) patients had the primary infertility and 48% had secondary infertility. The mean values of thyroid stimulating hormone (TSH), Follicle-stimulating hormone (FSH), *luteinizing hormone (*LH) and prolactin PRL is 3.93±6.58, 10.96±13.58, 9.83±6.8, and 12.46±14.39 respectively and these were significant. 12% patients had PCO and 88% patients were normal in our study. 78% semens were normal, 4% semen showed Azzospermia, 14% semens showed Oligo Astheno Spine and 4% semens showed Astheno spine. ***Conclusion:*** In infertile women with prolactinoma, cabergoline can achieve a high pregnancy rate with uneventful outcomes. The findings demonstrated that cabergoline can be used safely to improve menstrual cycles in hyperprolactinemia.

Keywords: Hyperprolactinemia, Infertility, Cabergoline.

INTRODUCTION

The most common type of pituitary tumor is a prolactin-secreting adenoma [1, 2]. Most prolactinomas in women are microadenomas (10 mm), and prolactin hypersecretion causes amenorrhea, galactorrhea, and infertility. Men, too, can suffer from hypogonadism and infertility. Infertility is caused by gonadotropin secretion suppression, which manifests as hypogonadotropic hypogonadism (HH) [3]. The treatment's goals are to normalize prolactin, shrink tumors, reverse hypogonadism, and restore fertility. The dopamine receptor agonist's bromocriptine and cabergoline are the most commonly used treatments. In 80%-90% of patients with microadenomas, bromocriptine normalizes prolactin and reduces tumor size. Nausea, orthostatic hypotension, headache, and fatigue are some of the side effects. Cabergoline, a more selective D2 receptor agonist, is more effective and well tolerated than bromocriptine. While cabergoline is the most commonly used medical therapy and can be used in women who are trying to conceive, bromocriptine has been used more extensively during pregnancy and thus has a better safety record. In women with hyperprolactinemia, cabergoline corrects hyperprolactinemia and restores the ovulatory cycle more effectively than bromocriptine [4, 5]. In terms of its use in treating infertility, available evidence indicates that cabergoline has no negative effects on mothers or fetuses [6]. The number of cabergoline-induced pregnancies currently exceeds 441 [7, 8], but there have only been 324 pregnancies in prolactinoma patients, who typically require higher cabergoline doses than those with idiopathic hyperprolactinemia [9]. Furthermore, there have been no reports of cabergoline's pregnancy induction rate. Cabergoline contracts prolactinomas more effectively than bromocriptine and frequently extinguishes them [10],

potentially eliminating the need for pregestational surgery or radiotherapy.

OBJECTIVE

The aim of present study is to evaluate the efficacy and safety of high-dose cabergoline therapy for hyperprolactinemic infertility among Bangladeshi women.

METHODOLOGY

Type of study	Descriptive cross-sectional study
Place of study	The Medinova Diagnostic Centre, Sylhet, Bangladesh.
Study period	January, 2020 to January, 2022
Study population	A total of 50 female patients were included in the study
Sampling technique	Purposive sampling

Study Procedure

This study was done on50 female patients with increased serum prolactin concentration [1.5 fold more than normal level], who referred to The Medinova Diagnostic Centre of Bangladesh. Informed consent was obtained from all participants. Our participants were selected from patients with clinical symptoms of hyperprolactinemia and pcos such as obesity, menstrual irregularity and other causes of increased prolactin levels such as TSH test, pituitary magnetic resonance imaging (MRI) for detection of prolactineoma and other disorders or tumors that can increase prolactin. Patients who had other endocrine disorders (such as thyroid disorders), history of cardiovascular disease, history of using the increasing prolactin drugs, women who wanted to be pregnant, and who couldn't tolerate the cabergoline were excluded from the study. Demographic characteristics including age, history of drug usage, and the menstrual situation were asked and recorded.

Statistical Analysis

Collected data was collated and appropriate statistical analysis was done using SPSS (Statistical Program for scientific study) version 23 statistical package. P-value <0.05 was considered significant in our study.

RESULTS

Figure 1 is showing the age distribution of the female patients of our study. Here, maximum (14) patients belong to the age group of 19 to 23 years. And minimum number of patients (4) was between 39 to 43 years. See the figure 1 below-

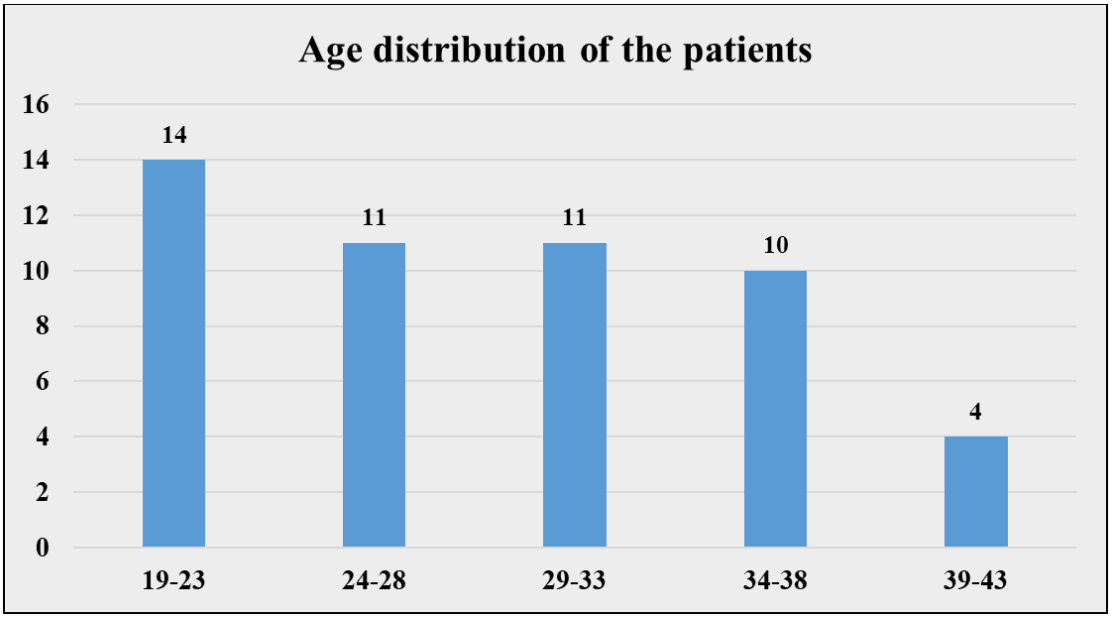

Figure 1: Distribution of the age of the patients.

Figure 2 shows the type of infertility among the patients of our study. Here, maximum (52%) patients had the primary infertility and 48% had secondary infertility. See the figure 2 below-

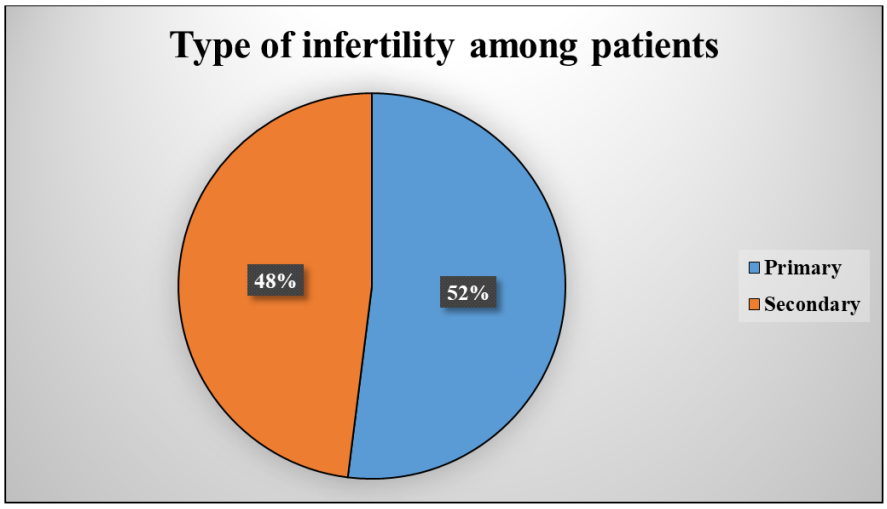

Figure 2: Type of infertility among patients.

In table 1, the clinical characteristics of the patients are shown. Here, the mean values of TSH, FSH, LH and PRL is 3.93±6.58, 10.96±13.58, 9.83±6.8, and 12.46±14.39 respectively and these were significant. See the detailed information in the table 1 below-

Table 1: Clinical characteristics of the patients

Clinical characteristics	Test results (Mean±Std)	P-value
TSH	3.93±6.58	0.031
FSH	10.96±13.58	0.044
LH	9.83±6.8	0.067
PRL	12.46±14.39	0.002

Figure 3 is showing the distribution of the USG test results among the female patients. It shows that, maximum (88%) patients were normal and minimum (12%) patients had PCO in our study. See the figure 3 below-

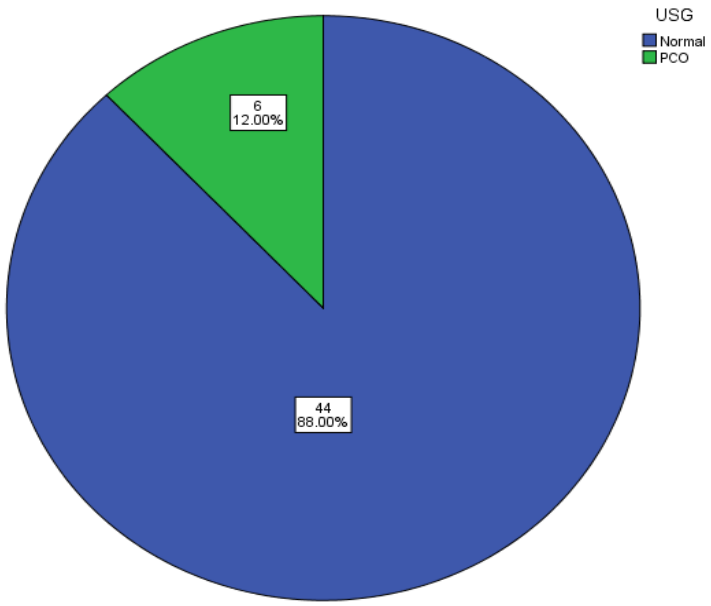

Figure 3: The USG test results among the female patients.

Figure 4 shows the bar chart of outcome of semen analysis in our study. Here, maximum (78%) semens were normal, 4% semen showed Azzospermia, 14% semens showed Oligo Astheno Spine and 4% semens showed Astheno spine. See the detailed figure 4 below-

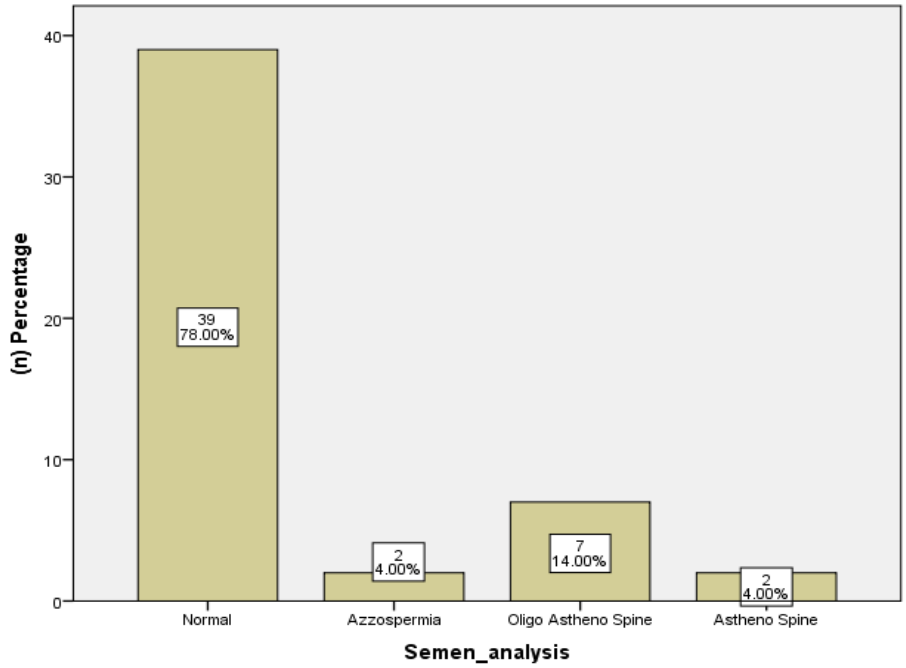

Figure 4: Bar chart showing the outcome of semen analysis

DISCUSSION

According to the findings of this study, cabergoline can induce and promote successful pregnancy in the vast majority of infertile women with prolactinoma, regardless of tumor size or bromocriptine resistance and intolerance. Cabergoline has now been shown to correct hyperprolactinemia, restore fertility, induce pregnancy, control gestational tumor overgrowth, and result in an uneventful delivery in these infertile patients. Importantly, cabergoline provides this total care without the assistance of gynecological, neurosurgical, or radiotherapeutic modalities. Our therapeutic strategy of individualized, high-dose treatment with rapid dose escalation [11] is most likely to blame for cabergoline's remarkable efficacy in this clinical study. There are some serious concerns about using cabergoline to restore fertility in patients with prolactinomas. The first issue, which may be of significant concern, is the efficacy in pregnancy induction because this is the most convincing evidence with which to recommend cabergoline therapy to prolactinoma patients.

The efficacy and safety of high-dose cabergoline therapy for hyperprolactinemic infertility in Bangladeshi women were assessed in a study of 50 patients. Robert *et al.*, [12] reported 226 cabergoline-induced pregnancies in 1996, Ricci *et al.*, [9] reported 61 pregnancies in 2002, and Colao *et al.*, [13] reported 380 pregnancies in 2008. Each study, which treated a mixed population of patients with tumoral and non-tumor hyperprolactinemia, clearly demonstrated no increase in maternal and fetal toxicities, but they did not report pregnancy rates. The current study provides information on the pregnancy rate in cabergoline-treated hyperprolactinemia patients. If cabergoline therapy is used in a typical group of patients with prolactinoma, which typically includes 24% resistant subjects and up to 12% intolerant subjects, the pregnancy rate will rise and pregnancy induction will be accelerated [11].

The second issue is the cabergoline dose used in pregnancy induction. Because patients with prolactinoma do not respond uniformly to dopamine antagonists, the dose of cabergoline should be adjusted appropriately to improve efficacy [11, 13]. Nonetheless, our high-dose cabergoline therapy did not result in an increase in adverse events in mothers or fetuses. These findings, obtained only from patients with prolactinoma in a single institution, add to the evidence that cabergoline is safe to use during pregnancy, even at higher-than-usual doses. Two of the three aforementioned surveys included a maximum of 15 and 12 cabergoline-induced pregnant women with macroprolactinoma, respectively, but they did not address tumor mass control during pregnancy [9].

Cabergoline is likely to be a first-line therapeutic agent that replaces the standard combination therapy of surgery or radiotherapy plus bromocriptine in macroadenomas that are not compressing the adjacent tissues symptomatically at baseline. There is no standard for an appropriate level of melanoma shrinkage that ensures a safe pregnancy course and outcome. According to Molitch's review [14], the likelihood of a small intrasellar macroadenoma enlarging symptomatically following primary bromocriptine therapy is probably only marginally higher than in patients with microadenomas. Some

microadenomas exhibit symptomatic tumor enlargement. Pregnancy, in contrast to its unfavorable effect on tumor growth during gestation, has a favorable effect on both micro- and macroprolactinomas postpartum [15, 16]. In our study, the majority of patients (52%) had primary infertility, while 48% had secondary infertility. Hyperprolactinemia is frequently reduced or even normalized after pregnancy and delivery. Furthermore, a significant proportion of tumors regress, and some of these resolve completely. The underlying mechanisms are unknown, but they could involve changes in estrogen and/or dopamine status. It is necessary to investigate whether cabergoline use during pregnancy could hasten hyperprolactinemia resolution and tumor involution in pregnant women with prolactinoma.

CONCLUSION

In infertile women with prolactinoma, cabergoline can achieve a high pregnancy rate with uneventful outcomes. The findings demonstrated that cabergoline can be used safely to improve menstrual cycles in hyperprolactinemia. Patient acceptability of this approach is higher and therefore it is more effective. However, the data that emerged from this study need further evaluation and confirmation in the form of long term study involving greater numbers of patients.

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