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A COMPARATIVE RESEARCH TO COMPARE AND CONTRAST THE TREATMENT SUCCESS BETWEEN TWO DIFFERENT TREATMENT OPTIONS FOR THE PATIENTS OF HYPERPROLACTINEMIC INFERTILITY

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Abstract:

Objective: *The objective of this research was to compare the success rate of treatment between bromocriptine plus clomiphene citrate and bromocriptine among patients of hyperprolactinemic infertility.*

Materials & Methods: *We conducted this comparative research at Allied Hospital Faisalabad from February 2018 to January 2019 on a total of 180 hyperprolactinemic infertility patients. These patients were shortlisted in the age bracket of (20 – 40) years. The study commenced after ethical review committee permission and informed consent of the patients.*

Results: *In the age bracket of 20 years to 40 years the mean age was (29.68 ± 5.45) years. Patients were divided into two groups respectively Group A & B with respective mean age of (28.47 ± 3.22) years and (27.58 ± 4.52) years. We also compared the rate of treatment success among both groups. The success rate in Group – A was reported in 56 patients (62.22%); whereas, Group – B presented a success rate among 73 patients (81.11%). Study Group – B presented a significantly higher success rate of treatment than the patients of Group – A (P-Value 0.0078).*

Conclusion: *Study outcomes speak for the efficacy of bromocriptine plus clomiphene citrate in comparison to sole bromocriptine as a treatment approach to manage hyperprolactinemic infertility. Therefore, the use of bromocriptine plus clomiphene citrate as a treatment option is suggested over the use of bromocriptine alone for the achievement of the majority of pregnancies among women with the hyperprolactinemic infertile profile.*

Keywords: *Prolactin, Pregnancy, Female Infertility, Efficacy, Bromocriptine, Clomiphene Citrate and Bromocriptine.*

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INTRODUCTION:

Prolactin (PRL) is among various hormones which produce in the pituitary gland and PRL also performs different functions in the human body. PRL is a 23-KD protein (198-amino acid) which is produced in the anterior pituitary gland (lactotroph cells). There is a negative influence of the fat homeostasis and glucose with the pathologically per prolactinoma individuals [1]. Hyperprolactinemia also attributes in infertility among one-third woman facing disorders relating to reproductivity [2]. According to an estimate, about 75% of patients present amenorrhea and galactorrhea also present hyperprolactinemia [3]. Prolactinomas are the common functional type of pituitary tumours and its incidence is six to ten patients out of million people every year and sixty to a hundred patients in every million [1 – 2]. Previous reports estimate 40% to 45% of the pituitary tumours [3, 4]. Gender and age also affect the overall occurrence which is commonly developed among females of 20 years to 50 years of age. The male to female ration was 1:10 [5].

Hyperprolactinemia among women refers to an abnormally higher level of PRL in blood. Whereas, the normal levels are in the range of (10 – 35) ng/ml and 1 ng which equals (21.2 mU/ml) [6]. Most of the patients having micro-prolactinomas, macroprolactinomas and prolactinomas can be effectively managed through dopamine (D2) receptors as recommended treatment option with normal gonadal function and prolactin secretion [7]. Commonly utilized dopamine agonists are pergolide, bromocriptine, cabergoline and quinagolide. In comparison to the half-life plasma, tolerability and efficacy of these drugs vary. The assessment of related risk factor of every drug is also important to know. Nowadays, to treat hyperprolactinemic infertility, we also combine clomiphene citrate with bromocriptine in order to treat anovulatory cycles and menstrual irregularities for the achievement of earlier pregnancies [8].

The objective of this research was to compare the success rate of treatment between bromocriptine plus clomiphene citrate and bromocriptine among patients of hyperprolactinemic infertility.

MATERIAL AND METHODS:

We conducted this comparative research at Allied Hospital Faisalabad from February 2018 to January 2019 on a total of 180 hyperprolactinemic infertility patients. These patients were shortlisted in the age bracket of (20 – 40) years. The study commenced after ethical review committee permission and informed consent of the patients. We did not include those patients who presented related causes of infertility that is tubal factors, unexplained infertility, male factor, polycystic ovarian disease, hyperthyroidism, macroadenoma of the pituitary gland, dopamine-depleting drugs, H-2 blocker, dopamine receptor blocking and verapamil intake by the patients. Patients were divided into two groups after selection in the research as a sample. Group – A received (1.25 mg) dose of bromocriptine with a snack before going to bed and gradually increased the dose from (1.25 – 2.5) mg twice a day with food intake for a period of three to four weeks; the treatment was maintained for a period of six months. Pregnancy waited for one year after the initiation of treatment. Group – B received bromocriptine with the same amount of dose and treatment approach as used in Group – A. With the initiation of menses; on the second and sixth day of the menstrual cycle, a dose of 50 mg of clomiphene citrate was initiated twice a day for the first two menstrual cycle; then dose was increased from twice to thrice a day and 100 mg twice a day after 5^{th} and 6^{th} menstrual cycle. After the achievement of ovulation, the use of Clomiphene citrate was ceased after confirmation through follicular tracking on transvaginal sonography at the 12^{th} day of every menstrual cycle. One year wait time was maintained for pregnancy after initiation of management.

Final outcomes of serum β-HCG were measured at the occurrence of pregnancy and absence of pregnancy respectively (≥5 m IU/ml) and (<5 m IU/ml) for a period of one year after initiation of management. Data were analyzed through SPSS software (P-Value ≤ 0.05).

RESULTS:

In the age bracket of 20 years to 40 years the mean age was (29.68 ± 5.45) years. Patients were divided into two groups respectively Group A & B with respective mean age of (28.47 ± 3.22) years and (27.58 ± 4.52) years. We also compared the rate of treatment success among both groups. The success rate in Group – A was reported in 56 patients (62.22%); whereas, Group – B presented a success rate among 73 patients (81.11%). Study Group – B presented a significantly higher success rate of treatment than the patients of Group – A (P-Value 0.0078). There were two major groups of age which were in the range of 20 – 30 years and 31 – 40 years. Group – A included 90 patients out of which 20 – 30 years and 31 – 40 years age groups respectively included 53 and 37 patients. Group – A included 90 patients out of which 20 – 30 years and 31 – 40 years age groups respectively included 56 and 34 patients. The success rate in 20 – 30 years age group in both Group – A & B were respectively reported in

40 patients (75.47%) and 48 patients (85.71%). There was an insignificant difference between the success rate (P-Value 0.2263). There was a significant statistical difference in success rate between both groups in the age group of 31 – 40 years (P-Value = 0.0157). The respective success rate in both Groups A & B was respectively reported in 16 patients (43.24%) and 25 patients (73.53%).

Detailed outcomes are given in Table – I & II with graphical presentation.

Table – I: Comparison of Success Rate between Groups

Success Rate	Yes		No		P-Value
	Number	Percentage	Number	Percentage	
Group – I (Bromocriptine)	56	62.22	34	37.78	0.0078
Group – II (Bromocriptine Plus Clomiphene Citrate)	73	81.11	17	18.89	

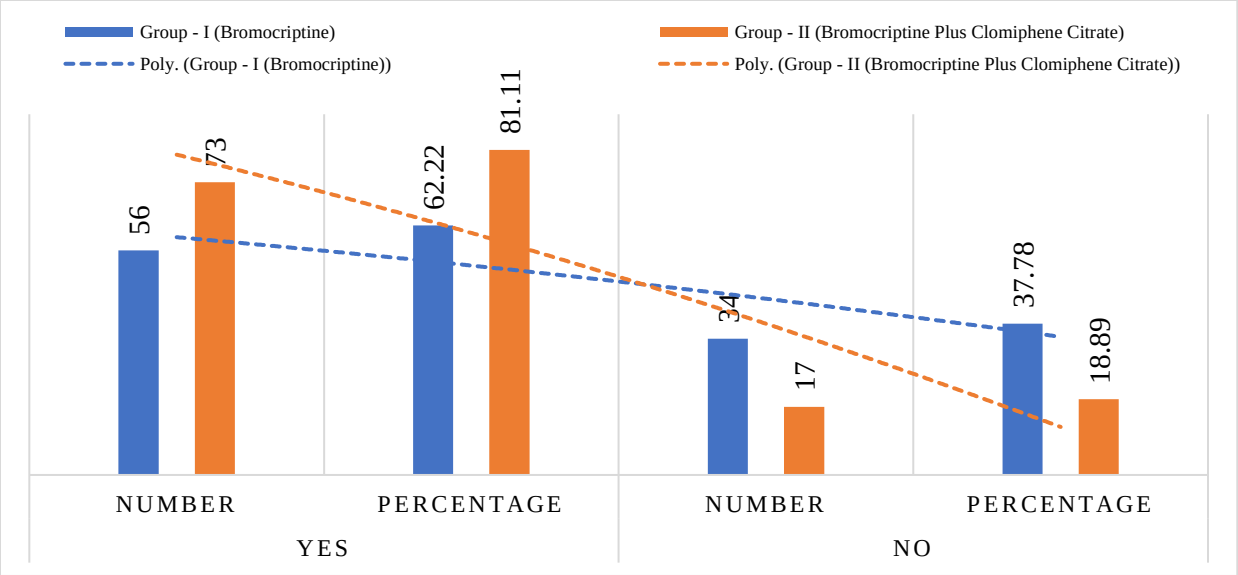
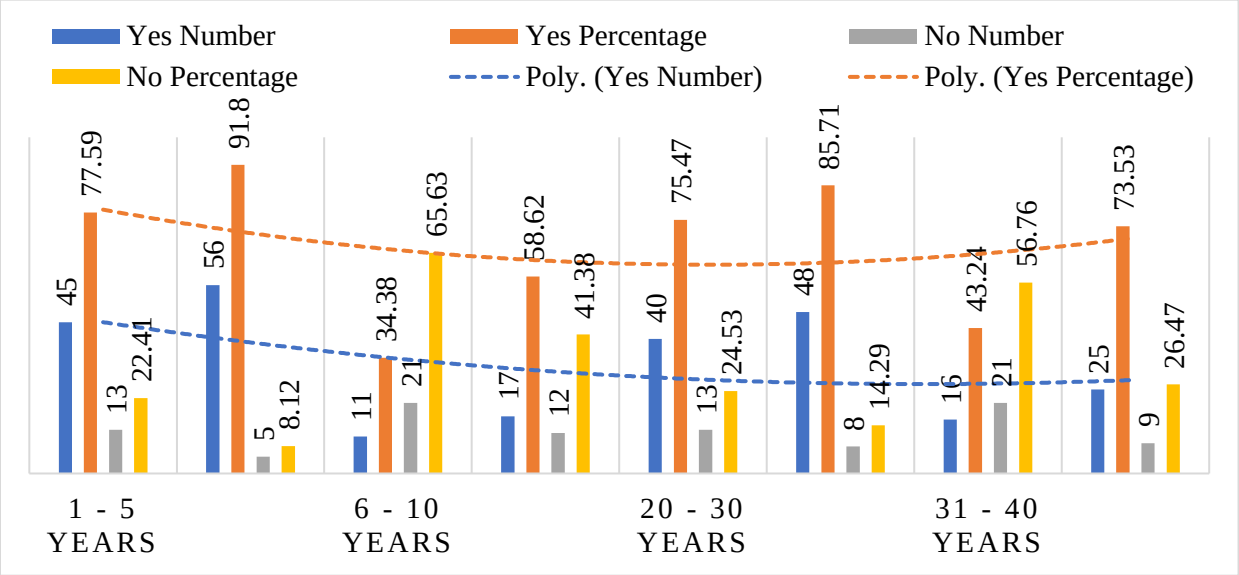
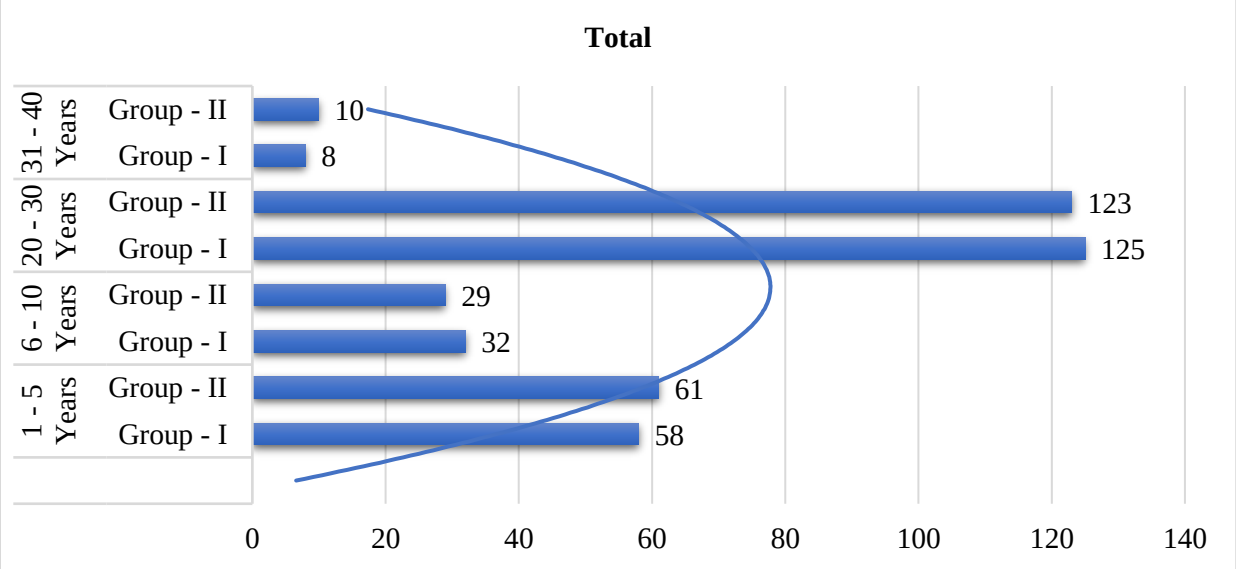


Table – II: Age-Wise Comparison of Treatment Success

Treatment Success		Yes		No		Total	P-Value
		Number	Percentage	Number	Percentage		
1 – 5 Years	Group – I	45	77.59	13	22.41	58	0.0405
	Group – II	56	91.8	5	8.12	61	
6 – 10 Years	Group – I	11	34.38	21	65.63	32	0.0746
	Group – II	17	58.62	12	41.38	29	
20 – 30 Years	Group – I	40	75.47	13	24.53	125	0.2263
	Group – II	48	85.71	8	14.29	123	
31 – 40 Years	Group – I	16	43.24	21	56.76	8	0.0157
	Group – II	25	73.53	9	26.47	10	





DISCUSSION:

The objective of this research was to compare the success rate of treatment between bromocriptine plus clomiphene citrate and bromocriptine among patients of hyperprolactinemic infertility. In the age bracket of 20 years to 40 years the mean age was (29.68 ± 5.45) years. Patients were divided into two groups respectively Group A & B with respective mean age of (28.47 ± 3.22) years and (27.58 ± 4.52) years. According to Motazedian S, the reported mean age was 28 years [9]. Another author also reported a mean age of 29 years [10]. Both the reported mean age values are similar to the outcomes of our research.

We reported a mean infertility duration of (5.69 ± 3.47) years which is more than as reported in the past studies [11 – 12]. This late presentation may be related to lack of awareness and culture of consultation with Hakeem. Group – A received (1.25 mg) dose of bromocriptine with a snack before going to bed and gradually increased the dose from (1.25 – 2.5) mg twice a day with food intake for a period of three to four weeks; the treatment was maintained for a period of six months. Pregnancy waited for one year after the initiation of treatment. Group – B received bromocriptine with the same amount of dose and treatment approach as used in Group – A. We also compared the success rate between both groups. The

success rate in Group – A was reported in 56 patients (62.22%); whereas, Group – B presented a success rate among 73 patients (81.11%). Study Group – B presented a significantly higher success rate of treatment than the patients of Group – A (P-Value 0.0078).

Mahmood S compared single bromocriptine versus bromocriptine plus clomiphene citrate for the management of hyperprolactinemic infertility and found that alone bromocriptine is less efficient than bromocriptine combined with clomiphene citrate [13]. The efficacy of bromocriptine was 65%; whereas, the efficacy of bromocriptine plus clomiphene citrate was 75%. These outcomes are also comparable to the outcomes as reported in this particular research. Tripathy reported a success rate of 75.8% for clomiphene with bromocriptine which is also similar to our reported outcomes [14]. Anate M found bromocriptine plus clomiphene citrate more effective in order to achieve pregnancy [15]. Sabuncu and Webster also reported similar bromocriptine efficacy respectively 59% & 58% as compared to our reported efficacy of (62.22%) [16, 17]. A little lower efficacy rate (56%) was reported by Motazedian S and Mahmood IH than our reported efficacy [18, 19].

CONCLUSION:

Study outcomes speak for the efficacy of bromocriptine plus clomiphene citrate in comparison to sole bromocriptine as a treatment approach to manage hyperprolactinemic infertility. Therefore, the use of bromocriptine plus clomiphene citrate as a treatment option is suggested over the use of bromocriptine alone for the achievement of the majority of pregnancies among women with the hyperprolactinemic infertile profile.

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