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SHORT COMMUNICATION

EFFECT OF CLOMIPHENE CITRATE ON SPERM DENSITY IN MALE PARTNERS OF INFERTILE COUPLES

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Abstract : Infertility is on the rise in today's world. A subnormal sperm count is frequently encountered in infertile couples (1).

Clomiphene citrate, l-[p-(β-diethyl aminoethoxy) phenyl]-1,2-diphenyl chloroethylene, is an orally active nonsteroidal agent distantly related to diethylstilbestrol. It is thought to stimulate pituitary gonadotropin release by excluding estradiol from hypothalamic receptor sites (2–4). This interaction neutralizes the normal negative feedback control of estrogen and results in enhanced secretion of LH-RH, FSH-RH and gonadotropins. Testosterone is produced by the Leydig cells in response to LH secretion. The concentration of testosterone in the tubular environment is believed to maintain the gametogenic function of the testis. Clomiphene citrate in the dose of 25 mg daily for 25 days with five days rest was administered to 25 extreme oligozoospermic men (group I) and 40 moderate oligozoospermic men (group II) the cycle being continued for three months (7).

Repeat semen analysis was done at the end of three months and all the routine seminal parameters were reevaluated. The data thus obtained was analyzed using Student's paired't' test. The mean sperm count in Group I increased from 3.84 ± 0.32 to 8.2 ± 1.58 ($P<0.05$) and in Group II from 13.05 ± 0.48 to 24.55 ± 1.73 ($P<0.001$). The mean motile sperm count in Group I increased from 1.74 ± 0.25 to 3.92 ± 0.83 ($P<0.05$) and in Group II from 8.27 ± 0.40 to 10.05 ± 0.56 ($P<0.01$).

Thus clomiphene citrate exerts its effect on spermatogenesis by raising the endogenous serum FSH, LH and testosterone levels to initiate and maintain gametogenesis (10). Researchers opined that this increase in endogenous gonadotrophins manifests itself in improving the sperm count, sperm motility and to certain extent morphology of the sperms, when there is no end-organ pathology.

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INTRODUCTION

Infertility is on the rise in today's world due to a multitude of factors like stress, cut throat competition, pollution, damage due to free radicals, smoking and rich diet. Male partners are responsible for 30% and also contribute to a further 20% (1).

A subnormal sperm count is frequently encountered in infertile males. The research in the field of reproductive biology tries to bring a ray of hope in the lives of those demoralized due to the stigma of infertility.

Clomiphene citrate, 1-[p-(β-diethyl aminoethoxy) phenyl]-1,2-diphenyl chloro-ethylene, is an orally active nonsteroidal agent distantly related to diethylstilbestrol. It is thought to stimulate pituitary gonadotropin release by excluding estradiol from hypothalamic receptor sites (2–4). This interaction neutralizes the normal negative feedback control of estrogen and results in enhanced secretion of LH-RH, FSH-RH and gonadotropins. Testosterone is produced by the Leydig cells in response to LH secretion. The concentration of testosterone in the tubular environment is believed to maintain the gametogenic function of the testis (5). This study evaluated the efficacy of clomiphene citrate on the conventional seminal parameters in infertile men.

MATERIALS AND METHODS

The study has been carried out in the semen analysis laboratory attached to the Department of Physiology, Govt. Medical College Nagpur. The cases included in this study were the patients referred from the departments of Sex and Marriage Counseling, Obstetrics and Gynecology, Surgery and Medicine of this Institute.

An exhaustive history was taken regarding age, occupation, previous illness and personal habits. A thorough physical examination was conducted.

The selection of the subjects was based on detailed history and the initial report of routine seminal analysis done according to WHO criteria (6). Sperm count was done using Neubaur's chamber. Sperm motility & grade of motility were noted.

Men whose initial semen analysis report showed severe (<10 million/ml), moderate oligozoospermia (10–19 million/ml) and normozoospermia (20–39 million/ml) were included in this study. Clomiphene citrate in the dose of 25 mg daily for 25 days with five days rest was administered to 25 extreme oligozoospermic men (group I) and 40 moderate oligozoospermic men (group II) the cycle being continued for three months (7),

Repeat semen analysis was done at the end of three months and all the routine seminal parameters were reevaluated. The data thus obtained was analyzed using Student's paired 't' test.

RESULTS AND DISCUSSION

Impaired spermatogenesis could be a result of subnormal testosterone levels in the testicular environment. Clomiphene citrate binds competitively to the estrogen receptors in the hypothalamus. This

TABLE I: Mean values ± S.E. of sperm count before and after treatment with clomiphene citrate in different groups are depicted in Table I.

S.N.	Groups	Mean sperm count in million/ ml±S.E.		Paired 't' test	Significance
		Before treatment	After treatment	't' value	
1.	Severe oligozoospermia	3.84±0.32	8.20±1.58	2.0638	P<0.05
2.	Moderate oligozoospermia	13.05±0.48	24.55±1.73	2.022	P<0.001

TABLE II: Mean motile sperm count in different groups before and after treatment with clomiphene citrate.

S.N.	Groups	Mean motile sperm count in million/ ml±S.E.		Paired 't' test	Significance
		Before treatment	After treatment	't' value	
1.	Severe oligozoospermia	1.74±0.25	3.92±0.83	2.0638	P<0.05
2.	Moderate oligozoospermia	8.27±0.40	10.05±0.56	2.022	P<0.01

interaction neutralizes the normal negative feedback control of estrogen on anterior hypothalamus and hypophyses so as to result in an enhanced excretion of leutinizing hormone-releasing hormone (LH-RH) and follicle stimulating hormone-releasing hormone (FSH-RH). This action is brought about by binding or occupying the steroid binding receptors in the hypothalamus and hypophyses thereby inducing the release of hypophyseal gonadotrophin-releasing hormone. When male hypofertility is secondary to either hypothalamic or pituitary dysfunction and not to end-organ pathology, enhanced gonadotrophin release should initiate a positive therapeutic change (2–4).

The Leydig cells in response to LH produce testosterone. The concentration of testosterone in the tubular environment is believed to maintain the gametogenic function of testes (5).

Clomiphene citrate stimulates adrenal androgen biosynthesis selectively (8). In turn, these steroids may be converted to testosterone thereby enhancing its intratesticular levels. Clomiphene citrate also increases seminal transferrin levels (8) as well as stimulates the sertoli cells (8), which help in the better supply of iron to the developing germ cells resulting in better production of spermatocytes (9).

Thus clomiphene citrate exerts its effect on the initiation and maintenance of spermatogenesis by raising the endogenous serum FSH, LH and testosterone levels (10). It appears that this increase in endogenous gonadotrophins manifests itself in improving the sperm count, sperm motility and to certain extent morphology of the sperms, when there is no end-organ pathology.

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