

Comparison Between the Effect of Clomid and Pregnyl on Sperm Concentration, Percentage of Sperm Progressive and Percentage of Normal Sperm Morphology.

Thu-Alfeqar R. Tweij

Department of Basic Science, College of Dentistry, University of Kufa, Al Najaf Al-Ashraf, Iraq

Abstract

The most common abnormal parameters that view in seminal fluid analysis in infertile men are low sperm concentration, decrease in percentage of sperm progressive and decrease in percentage of normal sperm morphology, which constitute more than 80 % of the causes of male infertility, and due to presence of variation between several drugs that use to treat the infertility, the current study worked comparison between clomid and pregnyl to differentiate what is the best to use it where can be treat more than cause of these reasons. **Methods:** Fifty patients they divided into two groups, each group composed of 25 patients. From all patients in the two groups takes two samples of seminal fluid one before treatment and the other after three months of treatment to measure the sperm concentration, percentage of sperm progressive and percentage of normal sperm morphology. **Results:** The first group of the patients treated by clomid they showed significant improvement in sperm concentration ($P = 0.000$), percentage of sperm progressive ($P = 0.012$) and percentage of normal sperm morphology ($P = 0.036$). While the patients in the second group who treated by pregnyl they showed significant enhancing in sperm concentration only ($P = 0.002$).

Keywords: Spermatogenesis, Sperm count, Sperm progressive, Sperm morphology, Clomid, Pregnyl

Introduction

Male infertility define inability of the male to produce women pregnancy during the first year of marriage. There are many factors responsible on the infertility which divided to male factors and female factors. Male factors form about (30-40)% of infertility{1}. The most important male factors are low spermatozoa count (Oligozoospermia), abnormal sperm morphology (teratozoospermia) and poor sperm motility (asthenozoospermia){2,3}.

Low sperm count may be occur due to many causes that lead to defect in spermatogenesis such as hormonal deficiency, genetic abnormalities, smoking, exposure to high heat for prolonged periods, impotence and other factors{4}. Also use of certain drugs such as cimetidine and spironolactone are interfere with the synthesis of sexual hormones and their effects. Cimetidine which is H_2 blockers used in the treatment of stomach or duodenal ulcer and usually used for long period (usually six month and more), this drug is enzyme inhibitor that decrease steroid synthesis that is to say it will decrease sexual hormones synthesis which are important in stimulation and maintains of spermatogenesis, example of these enzymes are follicle-stimulating hormone, luteinizing hormone and testosterone. While spironolactone block androgen receptors and has additional effect which is reducing 17α hydroxylase/C17-20 lyase activity, leading to reduced testosterone biosynthesis{5}.

The belief now the shape of sperm is considered one of the essential fertile tools. The sperm morphology give perception to sperm cell development in the testis during spermatogenesis that is to say the men with abnormal sperm mean have defect in cell maturation (problem in spermatogenesis) which may lead to failure of the sperm to penetrate the eggs and fertilize{6}. The sperm consist of head and neck and midpiece and tail. The head which take oval shape has acrosomal region which form about (40-70)% of it and contains the genetic material of the father in its nucleus. In the midpiece there are the mitochondria which produce the energy to sperm movement. While the tail is important to push the head, toward the egg {7,8}. The abnormalities in the sperm, may be occur due to many factors, like chemical exposure, disease, congenital birth defects, and lifestyle habits. In several situations, the reasons of abnormalities are unknown.

Sperm progressive motility, should be considered one of the important factors that affect on the fertilization because it is essential for the sperm to pass through the cumulus cell, corona radiata, and finally the zona pellucida and then occur fertilization{9}. The most important situations that associated with decrease in sperm

progression are increase mitochondrial abnormalities{10} and structural deformities in the flagella{11}. The pathological reasons for this problem is related to rise in oxidative factors in the seminal plasma{12}, progression in the age {13}, and electromagnetic radiation {14}.

In the current study we will take two of the most frequent drugs that used in treatment of infertility and show their effect on sperm count, sperm progressive, and sperm morphology, which are clomid (Clomiphene citrate) and pregnyl (Human chorionic gonadotropin (hCG)).

Clomid is the tread name of clomiphene. It is non-steroidal estrogen receptor modulator (estrogen receptor antagonist). This drug used in treatment of infertility in both male and female which competitively binds to estrogen receptors on the hypothalamus and pituitary gland, so interfering with estrogen's negative feedback, and therefore, may increase luteinizing hormone and follicle-stimulating hormone{15,16}. The result is stimulating cells of Leydig to yield testosterone and cells of Sertoli to promote testicular environment for spermatogenesis{17}. Lower than 5% of patients receive clomiphene may be complain from side effect which usually mild and these include weight gain, nausea, change in libido, gynecomastia, visual field changes, allergic dermatitis, dizziness and headache {18}.

Pregnyl market name for human chorionic gonadotropin which is a polypeptide hormone produced by the syncytiotrophoblast, part of the placenta, after implantation {19}. Is a heterodimeric composed of α and a β subunit. The α -subunit identical to that of luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone. The β subunit is unique for each of these hormones and responsible for their specific functions{20}. Higher than 75 percent of the human chorionic gonadotropin are metabolized in the liver; while the remainder is excreted by the kidney{19}. Human chorionic gonadotropin can be obtained from two ways, first one by extraction from urine of pregnant women. second, by recombinant DNA technology {21}.

Human chorionic gonadotropin act by stimulation sex steroid secretion by the testis through the activation of the LH/hCG receptor which is a type of G-protein-coupled receptor that is present in the Leydig cell membrane. In adult male, the activation of this receptor adenylyl cyclase system stimulate the synthesis and secretion of testosterone (T) and estradiol (E2). The final effect is stimulation and maintenance of spermatogenesis{22}. The side effects of human chorionic gonadotropin include headache, migraines, irritability, edema, depression, restlessness, fatigue, gynecomastia, precocious puberty, and renal impairment{23}.

Materials and Methods

2.1 Subjects:

Fifty men of 20-45 years old of admitted to fertility center in AL-Sader medical city were included for this study, where they are divided to two groups each group contain twenty five patients (N=25). Each participant provided seminal fluid sample before he take the drug and do analysis for this samples and measure the sperm concentration, percentage of sperm progressive and percentage of normal sperm shape by special technician. After which one of the groups (N=25) treated with clomiphene (clomid) and the other group (N=25) treated with human chorionic gonadotropin (pregnyl). After three months of treatment pulled other sample from each person of the two groups and then work analysis for these samples and measure the same parameters.

2.2 Semen analysis:

After continence period of 3 to 5 days the semen sample of each participant collect in a plastic container which should be sterile, wide-mouth and metal-free and via masturbation. After liquefaction usually within 20 to 40 minutes semen specimens are subject to analysis. Semen specimens processed by an expert technician depending to the fifth edition of WHO laboratory manual for the examination and processing of human semen{24}.

Results

The study and after the course of treatment which is 3 months appear patients in group one which treated by clomid are benefit more than other patients in second group.

As shown in the table-1 and figure-1 patients those taking clomid undergone good improvement in sperm concentration (P = 0.000) more than that associated by using pregnyl (P = 0.002).

Table-1: Effect of both Clomid and Pregnyl on sperm concentration.

Groups	Samples No.	Sperm concentration	Significant
		(million/ml) Mean ± S.E.M	
Clomid Before	25	9100000 ± 973721.38	0.000**
Clomid After	25	21880000 ± 3439510.62	
Pregnyl Before	25	5348000 ± 1079013.75	0.002*
Pregnyl After	25	10852000 ± 2267172.39	

(**):Highly significant difference.

(*):Significant difference.

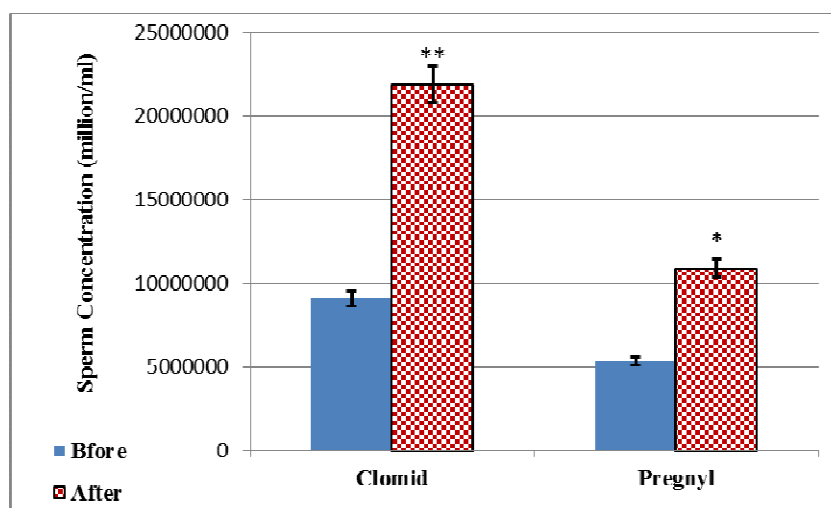


Figure-1: Enhancement effect of Clomid and Pregnyl on sperm concentration.

(**): Highly significant difference.

(*):Significant difference.

While in table-2 and figure-2 appear those treated by clomid obtained on significant enhancement ($P = 0.012$) in percentage of sperm progressive and those treated with pregnyl the enhancement is non-significant ($P = 0.330$).

Table-2: Significant effect of Clomid on percentage of sperm progressive versus non-significant effect by pregnyl.

Groups	Samples No.	Sperm Progressive %	Significant
		Mean \pm S.E.M	
Clomid Before	25	19.32 \pm 3.79	0.012*
Clomid After	25	27.32 \pm 5.27	
Pregnyl Before	25	6.40 \pm 2.07	0.330
Pregnyl After	25	8.76 \pm 2.74	

(*):Significant difference.

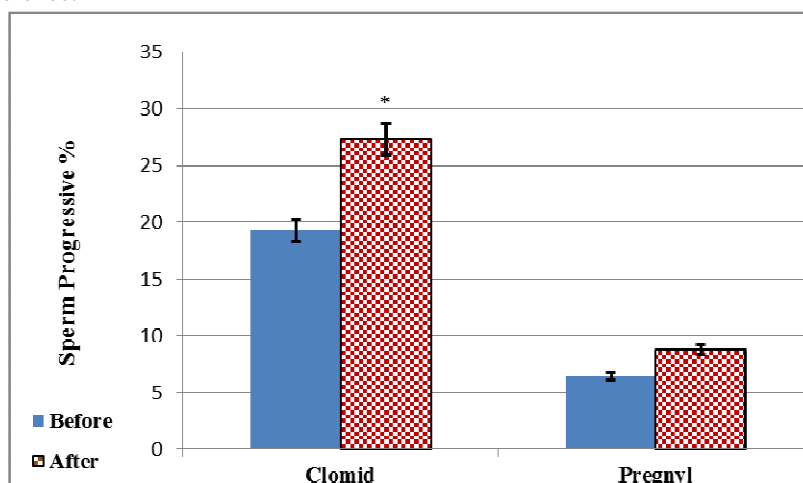


Figure-2: Differentiation between the effect of Clomid and Pregnyl on percentage of sperm progressive.

(*):Significant difference.

In table-3 and figure-3 showing the clomid has significant ($P = 0.036$) effect (increase) on percentage of normal sperm morphology while pregnyl lack this effect ($P = 0.696$).

Table-3: Comparison between the influence of Clomid and Pregnyl on the percentage of normal sperm morphology.

Groups	Samples No.	Normal Sperm Morphology %	Significant
		Mean \pm S.E.M	
Clomid Before	25	18.40 \pm 3.85	0.036*
Clomid After	25	27.16 \pm 4.75	
Pregnyl Before	25	18.32 \pm 4.78	0.696
Pregnyl After	25	20.00 \pm 5.29	

(*):Significant difference.

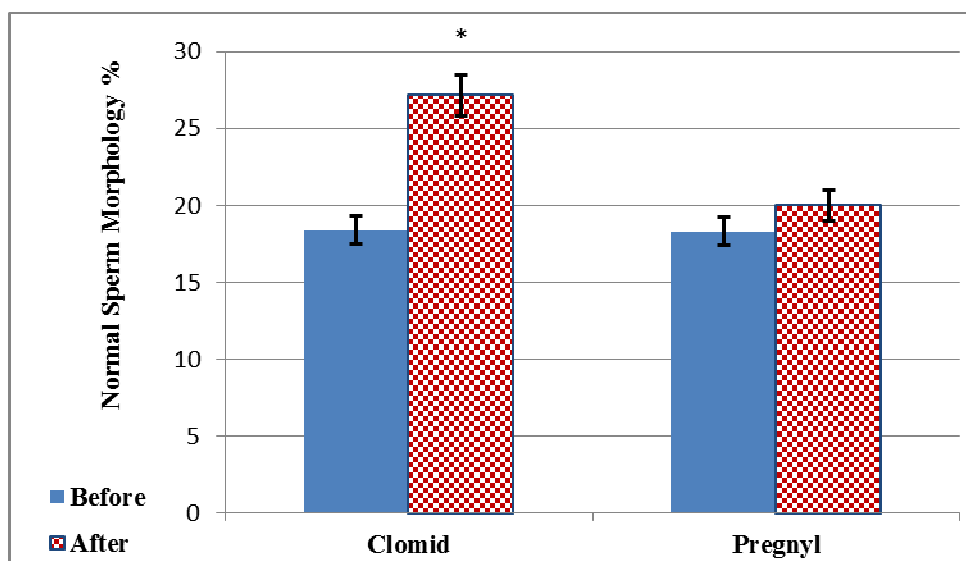


Figure-3: Good improvement of the percentage of normal sperm morphology via Clomid and negligible increment by Pregnyl.

(*):Significant difference.

Discussion

In the time in which we search about drug to treat specific disease clear to us there are many of drugs can be used to solve this problem. Previously we use one of this drugs and then check from this regimen to find out the range to take advantage. In the last years the selection of treatment to specific disease should be according to specific criteria such as who is it of the drugs more suitable, benefit and It can cure this disease by different ways that is to say the selected drug can be solves more than one problem which leads to this disease.

For example in treatment of hyperprolactinemia many of dopamine agonists drugs can be used such as cabergoline and bromocriptine in the USA and, additionally, quinagolide in the UK and other countries in Europa. But the long acting cabergoline appear to has advantages over than bromocriptine in terms of both efficacy and tolerability, and therefore it preferably to use in the treatment of hyperprolactinemia{25}.

For these reason now many of studies and research make comparison between two or more of drugs that used in the same purpose to evaluate these drugs and know what is has advantages more than the other which give priority to select it.

The current study show the clomid has multi-benefits in infertile men more than pregnyl because in addition to their high significant effect on sperm concentration (increase) by stimulation of spermatogenesis it also cause enhancement in percentage of both sperm progressive and normal sperm morphology, this means the clomid improves both the quantity and quality of sperm.

Clomiphene is a selective modulator of estrogen receptors because it a weak estrogen receptor antagonists so it will competes with estradiol on their receptors in hypothalamus, result in blocking the normal feedback mechanism of circulating estradiol which leads to prevention the estrogen from limiting of gonadotropin releasing hormone production. High level of gonadotropin releasing hormone will stimulate the pituitary gland to secrete more luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and then enhance production of testosterone by testes which stimulates excess production of sperm via spermatogenesis{26}.

Researchers opined the elevation in endogenous gonadotropins manifests itself in improving sperm motility, sperm concentration and to certain extent sperm morphology{27}.

In Moradi et al the results showed that clomiphene citrate had significant influence on sperm count, morphology, and motility ($P=0.01$), but non-significant effect on the semen volume ($P=0.57$){28}.

The study that performed via Rekha et al. reveal that there is significant improvement in sperm concentration, percentage of sperm morphology and sperm motility{29}.

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