The effect of hormonal male contraception on sperm count

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Abstract:
Background: The hormonal method of contraception is one way of contraception that has been investigated for several years following the observations that spermatogenesis depends on stimulation by gonadotrophins, Follicle Stimulating Hormone and Luteinizing Hormone.

Objectives: To test the effect of combination of medroxyprogesterone acetate and testosterone enanthate on sperm count, body weight and sexual libido.

Subjects & Methods: 60 adult fertile male were included in this project and divided randomly according to random clinical trial (Triple blind technique) into two groups experimental and control groups, the experimental group include 30 adult fertile male with average age of 33.5 years, they received intramuscular injection of 150 mg of Medroxyprogesterone acetate every three months and intramuscular injection 250 mg of Testosterone enanthate (which is a physiological dose) every two weeks for 2 years, while the control group included also 30 adult fertile male with average age of 34.3 years, they were given normal saline injection . Seminal fluid analyses were done for each group every three months. The body weights of the experimental group were recorded before the treatment and then every 6 months during this project.

Results: The volunteers during the time of the project were in good general health, normal appetite, normal sexual drive (there was no loss of libido), all the volunteers of the experimental group were rendered into azospermic and oligospermic state from the first seminal fluid analysis, no one of their wives developed pregnancy. This study also revealed that there were no significant changes in the body weight of the experimental group before and during the treatment.

Conclusions: Medroxyprogesterone acetate and testosterone enanthate is an effective hormonal male contraception that makes all the experimental volunteers azospermic and oligospermic, and safe from the apparent side effects.

Key words: Male contraception, Medroxyprogesterone acetate, Fertility control

Introduction
The general goal of hormonal male contraception is to suppress sperm production in the testes. As in female oral contraception, the principle of hormonal suppression of spermatogenesis is based on influencing the endocrine feedback mechanism between hypothalamus, pituitary, and testes. Women have physiologically infertile periods and contraceptive methods are designed to eliminate cyclically occurring fertile peaks. Men, however, produce sperm and are fertile continuously. A safe, reversible, and acceptable contraceptive method interrupting this state must achieve either azoospermia or severe oligospermia with dysfunction of any remaining sperm. To reach this goal, the pituitary gonadotrophins Luteinizing hormone (LH) and follicle stimulating hormone (FSH) must be completely suppressed, because residual FSH and intratesticular testosterone activity would suffice to maintain spermatogenesis.

However, testosterone must be available in sufficient amount outside the testes to maintain the many other functions dependant on that hormone, e.g., erythropoiesis, protein, mineral and bone metabolism as well as libido and potency, cognitive functions, and male personality [3].

Bruce & James (1998) [3] suggested that the formulations of hormonal male contraception must:
1-Suppress both FSH and LH (Depletion of intratesticular testosterone).
2-Replace of peripheral testosterone
Testosterone alone can accomplish the goals of hormonal male contraception; but nevertheless, some men remain fertile [4]. Compounds such as Gonadotrophins Releasing Hormone analogue (GnRH) or progestin synergistically suppresses pituitary gonadotrophins secretion or it may directly blocks sperm production so it has been combined with testosterone to optimize the contraceptive efficacy [5,6].

Subjects & Methods
1. The groups:
Sixty adult fertile male were included in this research. A triple blind technique of random clinical trial was applied, those fertile male were divided randomly into two groups, experimental and control groups. The experimental group were
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included 30 adult fertile male with average age of 33.5 years which received intramuscular injection of 150 mg of medroxyprogesterone acetate every 3 months and intramuscular injection of 250 mg of testosterone enanthate every 2 weeks for 2 years and control group which include 30 adult fertile male with average age of 34.3 years old which receive intramuscular injections of normal saline, the treatment of these two groups was according to triple blind method.

2. The Hormones:
The following hormones were used in the experimental group during the treatment:
A- Medroxyprogesterone acetate (MPA) which is synthetic progesterone structurally related to progesterone given by intramuscular injection in a dose of 150 mg every three months as a long acting contraceptive. MPA is slowly released after injection resulting in low but persisting levels. [7]
B- Testosterone enantheate 250 mg/ml, oily solution, the dose of was used in the experiment was 250mg every two weeks to keep the volunteers within the physiological level of testosterone and to maintain the peripheral testosterone.

3- Seminal fluid analysis:
Seminal fluid analysis was done for each group every 3 months during this project for 2 years to compare the readings between the control and experimental groups.

4- Body weight:
The body weights were recorded in the experimental group before the treatment and then every 6 months to see if there are any changes in the body weight.

Statistical study:
The data that were obtained in the present study were analyzed with a Microsoft office excel 2007. The significance of difference between the two groups were assessed by student’s test t-test [8], the (p) value <0.05 was considered to be significant, and <0.001 was considered to be highly significant.

Results
During the study which last about 2 years, all the volunteers were in good, normal health, good appetite, their sexual fantasy were normal (there was no loss of libido). Some of the volunteers complained from pain and irritation at the site of injection of Testosterone enanthate but these complaints were stopped while repeating the injections.

Table 1 illustrates the body weight of the experimental volunteers before and during the experiment (every 6 months) it appears so clear that there was no significant difference in the body weight (fig 1).

<table>
<thead>
<tr>
<th>Time of Weight Measurement</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6 Months</td>
</tr>
<tr>
<td>Average Body Weight ± Standard Deviation (kg)</td>
<td>82.6±11.1</td>
<td>82.4±10.9</td>
</tr>
<tr>
<td>Statistical significance</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>
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Seminal fluid analysis were done every three months during the treatment, Table 2 revealed that there was highly significant reduction in the number of sperms in the experimental group when compared with those readings of control group (fig2). Hence treatment with Medroxyprogesterone acetate and testosterone enanthate rendered the treated volunteers into azoosperma and oligosperma, no one of the volunteer's wives developed pregnancy at the time of our project (they used pregnancy test to confirm or exclude pregnancy).

Table 2: Sperm count of experimental and control groups ±Standard deviation with statistical significant. *** Highly significant (P value <0.001)

<table>
<thead>
<tr>
<th>Time of test after starting treatment</th>
<th>Average Sperm Count ± Standard deviation(x10⁶/ml)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Experimental</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>3.1±2.7</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>3.5±3</td>
<td></td>
</tr>
<tr>
<td>9 months</td>
<td>3.2±2.8</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>3.3±3</td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>3.5±3</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>2.6±2.5</td>
<td></td>
</tr>
<tr>
<td>21 months</td>
<td>2.9±2.9</td>
<td></td>
</tr>
<tr>
<td>24 months</td>
<td>2.4±2.2</td>
<td></td>
</tr>
</tbody>
</table>
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Discussion

The hormonal male contraception is one way of contraception that has been investigated for several years and by several countries. In the past, studies which were investigating male contraception have involved high dose of male sex hormone testosterone, also these studies resulting in significant side effects [9]. The progesterone hormone is also the component of the female pills, and by a similar way to its effect in preventing ovulation in women, it stops the production of sperms [10].

As shown by table 1 and figure 1 there was no significant difference in the body weight before and during the experiment in the experimental volunteers this is due to the fact that as progesterone (MPA) suppresses Luteinizing hormone (LH) and subsequently testosterone produced within the body, so a small dose of testosterone is required to be given together with the progesterone, to replace this reduction and to return the testosterone level to within normal physiological level, the absence of testosterone is harmful since it is necessary to maintain normal male health as mentioned before, and to prevent the hypogonadism features such as weight gain [11].

All the experimental volunteers were rendered into azospermic and oligospermic state as illustrated by table 2 and figure 2, these changes are because the MPA is a long acting progesterone suppressing both FSH and LH, and each one has its specific and important action on spermatogenesis, in the normal male, FSH acts on Sertoli cells to facilitate sperm production and maturation, while its absence or blockade of the FSH receptor has deleterious effect on sperm count but mature sperms remain capable for fertilization [12]. LH stimulates the production of testosterone by Leydig’s cells and blockade of LH production shuts down the testicular secretion of testosterone and leads to cessation of sperm production [13].

In human and other mammalian species both FSH and LH are required for initiation of spermatogenesis during pubertal maturation, studies used GnRH antagonist [14] or hypophysectomized rat [15] suggested that FSH supports germ cell development up to round spermatid stage but in the absence of testosterone, the completion of the final stages of spermatogenesis was not achieved . FSH effects on spermatogenesis are primarily via Sertoli cell and spermatogonial proliferation and the stimulation of meiotic and post meiotic germ cell development in synergy with and dependant on testicular testosterone [16].

While the role of testosterone on seminiferous epithelium had been studied for several years, it had been observed that testosterone reverse the testicular regression which occurred after hypophysectomy but the testicular volume returns to only about 60%
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that of control group, testicular testosterone suppression make the conversion of step 7 to 8 spermatid proceed at only 15% of its normal efficacy. Treatment with LH antibody causes a rapid reduction and complete absence of round and elongated spermatids. The reduction in sperm count which shown in figure 2 and table 2 can be explained in that the hormonal perturbation as one type of testicular injuries results in germ cell apoptosis, this observation indicated that the seminiferous epithelium responds to most adverse environmental conditions by elimination of germ cells through programmed cell death, since the Sertoli cells are responsible for establishing the environment within the seminiferous epithelium, this implies that Sertoli cells have a way to initiate and control germ cell apoptosis, so hormonal deprivation by MPA is an example of the consequence on germ cells of removing the trophic factors that causes the Sertoli cells to be pro-survival, this is because that these cells contain androgen and FSH receptor, so they modulate the trophic input through the production of number of paracrine acting. So testosterone and FSH deprivation causes a decrease in Sertoli cell derived pro-survival factors.

References:
13-Jeya, M; Suresh, R; Krishnamurthy, HN&Moudgal, NR: Changes in testicular function following specific deprivation of Luteinizing Hormone in the adult male rat. J. of endocrinology Oct, 1995; Vol 147, No.1: 111-120.
14-Zhengwei, Y; Wreford, NG; Schlatt; Weinbauer, GF & McLachlan, RI: Gonadotrophins Releasing Hormone antagonist - induced gonadotrophins withdrawal acutely and specifically impair spermatogonial development in the adult macaque Macaca fascularis. J. Reprod. Fertil. , 1998; 112: 139-149.
17-MarshallGR; Wiking, ET; Plant, TM & Ludecke, DE: Stimulation of

18-O'Donnell, L; McLachlan, RI; Wreford, NG & Robertson, MD: Testosterone promotes the conversion of round spermatids between stages 7 and 8 of the rat spermatogenic cycle. *Endocrinology*, 1994; 135: 2608-2614.

