

The Effect of Recreational Drugs on Hormonal Parameters in Pakistani Infertile Males

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Abstract

Objective: To determine the effects of the different recreational drugs (cigarettes, dipping tobacco and marijuana) on the hormonal parameters of infertile Pakistani males.

Methodology: This case Control study was conducted at the Institute of Basic Medical Science, Khyber Medical University (IBMS-KMU), Peshawar, Bannu Medical College (BMC), Samad Clinical Laboratories, and Shah Noor Medical laboratories Bannu from 2016-2018. The study population consisted of 160 apparently healthy infertile adult males of Pashtoon ancestry which were divided in to four groups, consisting of (n = 40) subjects each. The serum was brought to room temperature and then left for 30 minutes. Hormonal profiles of LH, FSH and testosterone were measured by ELISA technique using commercially available kits.

Results: The level of FSH in the serum of controls, smokers, dipping tobacco users and marijuana users was 1.72 IU/L, 2.50 IU/L, 2.12 IU/L and 3.06 IU/L respectively. The results show an increase in the level of FSH in the recreational drugs users as compared to controls. The level of serum Luteinizing hormone among different groups was observed to be 2.44 IU/L, 1.91 IU/L, 2.11 IU/L and 2.04 IU/L for controls, smokers, dipping tobacco users and marijuana users respectively, showing a decrease in groups using recreational drugs as compared to controls. The decrease was more pronounced in smokers, followed by marijuana users and dipping tobacco users. Serum testosterone level in different groups of the study were 4.42 ng/ml, 3.81 ng/ml, 3.57 ng/ml and 3.59 ng/ml in controls, cigarette smokers, dipping tobacco users and marijuana users, respectively.

Conclusion: Our study showed that the users of recreational drugs affect the hormonal parameters, which in turn causes a decrease in sperm count, and active motility, thereby causing infertility.

Key words: Recreational drugs (Naswar, marijuana, & cigarette) seminal parameters.

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Introduction

In the preceding millennium, the world's population peaked at almost 6 billion people. As a result, the population explosion has a number of negative consequences, one of which is the masking impact on infertility rates. More than a third of all males in the globe use tobacco in some form, with 21.6 percent of men in the United States smoking cigarettes.¹ There is a clear association between smoking and a variety of negative health effects, including respiratory disorders, cardiovascular diseases, and cancers of the lungs, oesophagus, stomach, bladder, and other bodily organs.²

Use of recreational drugs like cigarettes, dipping tobacco

and marijuana is related to social factors especially the influence of parents and peers. Taste and smell also increase the inclination towards smoking. As cigarette smoking is suggested to be mood stabilizer, this may reinforce and maintain daily use among the young people.³ The decrease in male fertility is not conclusively demonstrated by available data, but its impact on various semen parameters is regarded as a risk factor for infertility.⁴

Dipping tobacco (Naswar) is a one of the type of smokeless tobacco (*Nicotiana tabacum*) which is typically produced and used in South East and Central Asia and, particularly in Pakistan. Serum nicotine and cotinine levels were found to be increased in rats when they were exposed to smoking. Both these adversely affected sperm fertilizing potential and

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spermatogenesis.⁵ The marijuana is used for thousands of years for medicinal and recreational purposes.⁶ Marijuana derived from female cannabis sativum plant, about 400 compounds in marijuana is derived, in which Delta-9-Tetrahydrocannabinol is the major psychoactive compound.⁷ The effects of marijuana in the human have been observed in relation to production and morphology of sperms. Oligospermia has been observed which is dose related.⁸

Various detrimental effects have been shown on various semen analysis parameters and forward progression rates. Ramlau-Hansen *et al* found that those who smoke cigarettes had lower volume of semen, a lower sperm count, and lower percentage of motile sperm compared to those who were not smoking. It was further suggested that the relationship between sperm concentration and cigarette smoking was dependent on the dose of smoking. Those who smoked more than 20 cigarettes per day had a 19% reduced sperm concentration as compared with non smokers. Thus, it was concluded that smoking in adults impaired the semen quality moderately.⁹ Kunzle *et al* demonstrated that cigarette smoking decreases total sperm count (17.5%), sperm density (15.3%) and total motile sperm (16.6%). Furthermore, ejaculate volume and morphology is decreased but not significantly.¹⁰

Saaramen *et al* noted that volume of semen per ejaculate was lower in smokers as compared With non-smokers. He also noted that the inhibition occur specifically in those who smoke more than 16 cigarettes per day.¹¹ In another study by Zhang *et al* it was found that decreased semen volume and sperm concentration occurred in smokers as compared to nonsmokers.¹² Keeping these in mind, the present study was designed to see the effect of recreational drugs on hormonal parameters in Pakistani infertile males.

Materials and Methods

The study was conducted in Institute of Basic Medical Science, Khyber Medical University (IBMS-KMU) Peshawar, Bannu Medical College (BMC) Bannu, Samad Clinical laboratories and Shah Noor Medical laboratories Bannu from 2016-2018.

The study population consisted of 160 apparently healthy infertile adult males. The study subjects were mostly of Pashtoon ancestry. The participants were divided in to four groups: cigarettes smokers (n = 40), dipping tobacco users (n =40), marijuana users (n = 40) and 40 young healthy infertile controls. The following inclusion & exclusion were adopted.

Inclusion & Exclusion criteria; All the subjects who were infertile and using recreational drugs (Naswar, Cigarettes

and Marijuana) for a minimum five years' time were included. While, infertile males who were using multi drugs, chronic diseases such as diabetes, hypertension, nephrotic syndrome or arterial fibrillation, and non-willing persons were excluded from the study.

The serum was brought to room temperature and then left for 30 minutes. Hormonal profiles of LH, FSH and testosterone were measured by ELISA technique using commercially available kits.

Statistical analyses were carried out using SPSS 19. The normality of the data was tested using Kolmogorov-Smirnov and Shapiro-Wilk tests and histograms. Abnormalities in sperms variables were not normally distributed and were log transformed for analysis. Summary statistics were calculated and data were expressed as means \pm standard deviation. Age, height, weight, BMI, SBP, DBP, and semen analysis parameters were compared between groups by ANOVA. p-Value less than 0.05 was accepted as significant.

Results

In this study 160 infertile healthy subjects were recruited. The study participants were mostly of Pashtoon ancestry of Pakistani population. The infertile subjects were further divided in to four groups. Among them 40 were cigarette smokers, 40 were marijuana users, 40 were using dipping tobacco (naswar) and 40 were infertile males who were not using any recreational drugs (control). All the participants of the study had used these drugs for more than five years and they were still using the same drugs.

Table I summarizes the hormonal profile of the subjects. The level of FSH in the serum of controls, smokers, dipping tobacco users and marijuana users was 1.72 IU/L, 2.50 IU/L, 2.12 IU/L and 3.06 IU/L respectively. The results show an increase in the level of FSH in the recreational drugs users as compared to controls. The increase in FSH is significant in marijuana users followed by cigarette smokers and dipping tobacco users. The level of serum Luteinizing hormone among different groups was observed to be 2.44 IU/L, 1.91 IU/L, 2.11 IU/L and 2.04 IU/L for controls, smokers, dipping tobacco users and marijuana users respectively. The level of serum LH was found to be decreased in groups using recreational drugs as compared to controls. The decrease was more pronounced in smokers, followed by marijuana users and dipping tobacco users. Serum testosterone level in different groups of the study were 4.42 ng/ml, 3.81 ng/ml, 3.57 ng/ml and 3.59 ng/l in controls, cigarette smokers, dipping tobacco users and marijuana users respectively as shown in table I. The level of testosterone is decreased in the three groups using

Table I: Hormonal profile of the participants				
Parameters	Control	Smokers	Dippers	Marijuana
**FSH	1.72(1.32-2.22)	2.50(1.78-3.52)	2.12(1.67-2.69)	3.06(2.26-4.15)*
**LH	2.44(2.03-2.92)	1.91(1.48-2.47)	2.11(1.67-2.66)	2.04(1.3-2.54)
Testosterone	4.42 ± 1.77	3.81 ± 1.95	3.57 ± 1.99	3.59 ± 1.60

*P = < 0.05 for difference in controls and Marijuana.

recreational drugs as compared to controls. The decrease is more in dipping tobacco users followed by marijuana users and cigarette smokers.

The levels of serum testosterone and LH were reduced in drug users which were not significant while serum levels of FSH were increased in all types of drug users and the increase in marijuana users was significant (P=0.025).

Values are mean ± SD** log transformed for analysis; values are geometric mean (CI). All the data were normally distributed except for FSH and LH, which were not normal; and log transformed for analysis.

Discussion

Infertility is defined as the inability to get pregnancy within 12 months through regular unprotected sexual relations with the same opposite partner.¹³ Male fertility potentials are of great interest to various academicians & researchers. Male infertility is a clinical syndrome which is a collection of different conditions and exhibits a variety of etiologies and has varying prognosis.¹⁴ It is unreasonable that one should consider that tests will tell us about the fertility of a man.

The main causative factors which are responsible for male infertility are testicular tissue absence, such as anorchism, bilateral castration, and Klinefelter's syndrome, in which production and function of sperm is impaired. Similarly, AZF gene deletion (Genetic risk of azoospermia factor) (y deletion), cryptorchidism, cancer of the testis, impaired transport of sperm, blockage of epididymus, failure of ejaculation, vasectomy, impotence and varicocele are also responsible for male infertility. Besides this, at age above 55 years, environmental agents like extremes of temperature, genitourinary infections, radiations, occupational hazards, nutritional deficiencies of trace elements, mainly zinc, selenium, vitamins, various recreational drugs like alcohol, tobacco abuse, and marijuana are reported to cause male infertility.¹⁵

It is quite refutable that cigarette smoking has detrimental effects on male reproduction, performance, and specifically on parameters of semen.¹³ There is a great and recent desire to better understand and treat male infertility, so it has become very important to reach the possible adverse effects of cigarette smoking on reproduction in males.¹⁴ Mutagen which are chemical agents, effects reproduction in males by

effecting directly on the testis and their ability of sperm production.^{16,17} The mechanism involved in these processes may be due to the hormonal control of sperm generation or they may directly affect sertolli and germ cells within the seminiferous tubules.^{18, 19} A number of studies have reported higher incidence of abnormal sperm cells, along with decreased motility and sperm count in male smokers.²⁰

In the present study we investigated the effects of cigarette smoking on the sex hormones of the infertile men who smoked for a long time. The cigarette smoke contains more than 4000 substances which are harmful. There has long been concern that smoking could have bad effects on male reproduction. First and foremost, cigarette smoking has adverse effects on semen quality including sperm count, semen volume, and motility of sperms along with morphology. Furthermore, disorders of reproductive hormones system defects in spermatogenesis, process of sperm maturation or defective spermatozoa function has been observed in smokers. Despite of the detrimental effects of smoking on male fertility, many of the smokers are fertile but they have a high risk of sub fertility or infertility.²¹

The level of LH was decreased in smokers than in controls and the decrease was dose related. The same was observed by Ochedalski et al²² who observed low level of LH and FSH in smokers than in nonsmokers whereas the level of testosterone did not differ. Ramlau-Hansen et al.²³ also observed a positive dose response relation between smoking and LH. However, Pasqualatto et al²⁴ evaluated the levels of hormones with no significant differences in levels of L H, FSH and testosterone.

The LH level in serum was decreased in marijuana users 2.04 IU/L than the non-users 2.44IU/L but it was not significant. In one of another study of 159 men attending infertility clinic also showed a positive correlation between percentage of motile sperms and marijuana use. Although biological mechanism by which marijuana affect semen quality and hormones levels are not yet fully known, however studies in vitro have shown that spermatozoa are hyper activated with low doses of marijuana while had inactivating effect in high doses.²⁵

In the present study it was noted that Marijuana has reduced both Testosterone and LH which has been found in other studies as well.^{26,27} Impaired sperm production, low testosterone secretion, low sperm motility have been seen in

animal with marijuana use.²⁸ About 65% decrease in testosterone has been observed in Rhesus monkey by marijuana.²⁹ In the present study the level of LH was decreased in marijuana users as compared to nonusers (Table I). The same were observed in other studies by Cone et al.³⁰ In the present study the level of FSH was increased in marijuana users as compared to non users. In another study by Cone et al.³⁰ the FSH level was not changed.

In the present study, we investigated the effects of 3 recreational drugs like cigarette smoking, naswar and marijuana on the semen quality and sex hormonal profiles of infertile men who had used these drugs for long time. Our study showed that the users of these recreational drugs affect hormonal profile, thus causing low testosterone, decreased LH and increased FSH levels to be observed, which in turn disturbs the seminal parameters. It was also observed that marijuana affected the semen parameters and sex hormones levels of infertile males more than the other drugs. As it is evident that the hypophysial hormones are well known to affect spermatogenesis and semen quality. When the balance between these hormones is disturbed, then spermatogenesis and hence semen quality is also affected. Although the present study was a preliminary pilot study with a limited number of patients, this study could have high implications for clinicians, andrologists and gynecologists dealing with such types of patients.

Conclusion

The levels of serum testosterone and LH were reduced in drug users which were not significant while serum levels of FSH were increased in all types of drug users and the increase in marijuana users was significant ($P=0.025$).

Disclosure: The paper is retracted from the M Phil thesis submitted in Khyber Medical University Peshawar in 2018

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