

Pituitary-Gonadal Axis Hormone and Semen Analysis in Narcotic Dependency

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Article information	Abstract
<p>Article history: Received: 2 Nov 2011 Accepted: 12 Jan 2012 Available online: 5 Nov 2012 ZJRMS 2013; 15(4):53-55</p> <p>Keywords: Addiction Sex Hormones Semen Analysis</p> <p>*Corresponding author at: Department of Physiology, School of Medicine, Lorestan University of Medical Sciences, Khoramabad, Iran. E-mail: asaee_ra@yahoo.com</p>	<p>Background: Drug abuse is associated with numerous complications including hormonal disorders of hypothalamic-pituitary-gonadal axis and spermatogenic disorders. We have compared the hormone concentration of pituitary-gonadal axis and the semen analysis in opioid-dependent and non-opioid-dependent men.</p> <p>Materials and Methods: In this case-control study, serum concentration of pituitary-gonadal axis hormones and semen analysis in 48 opioid-dependent men as eligible to participate in the study were compared with those in 12 non-dependent men.</p> <p>Results: Free testosterone concentration in all test groups was significantly less than that in control group. Furthermore, the concentration of Dihydrotestosterone (DHT) and Dehydroepiandrosterone Sulfate (DHEAS) in all test groups except those addicted to heroin was less than in those in control group. Concentrations of LH, FSH, prolactin, SHBG, progesterone and estradiol, normal and abnormal sperm count in test groups were significantly different from control group. However, in all test groups, sperm motility rate was less than control group. No significant relationship was found between the concentration of sex hormones and the status of sperms motility.</p> <p>Conclusion: Chronic use of opioids will affect testosterone hormone and sperm, and it will cause hypogonadism and impairment of sperm motility.</p> <p>Copyright © 2013 Zahedan University of Medical Sciences. All rights reserved.</p>

Introduction

Drug abuse is fundamental problems of the modern society. World Health Organization (WHO) estimates 200 million illegal drug users around the world [1]. Common drugs abused in Khorramabad, Lorestan consist of opium, heroin, norgesic and crack. The opium, derived from poppies, containing morphine as one of the main alkaloids of it [2]. The heroin is diacetylmorphine. Norgesic and crack are both new drugs recently abused by the addicts of the society. Known ingredients of the norgesic present in Iran are including buprenorphine and corticosteroid. Crack includes cocaine, ammonium chloride, salt and a small amount of water [3].

Drug abuse is associated with numerous complications including hormonal disorders of hypothalamic-pituitary-gonadal axis. However, different effects have been reported about various drugs. For example, use of marijuana decreases the concentration of gonadotropins [4] and use of cocaine increases it [1]; or about methadone, some studies have shown a reduction in level of testosterone hormone and gonadotropins [5] and some other investigations have reported a normal level of such elements [6]. On the other hand, Wisniewski et al. have reported that frequent use of cocaine and heroin will decrease the concentration of free testosterone; however, the concentration of gonadotropins will not change as compared to that in control group [7].

Additionally, the studies indicate that drug abuse is relevant to abnormal spermatogenesis in men [8], but

different mechanisms suggested for the effects of opioids on the spermatogenesis.

Therefore, considering to controversy in researches and with regard to few studies conducted in Iran, and no investigation have been carried out on the effects of norgesic and crack, in this study we compared serum concentration of pituitary gonadal axis hormones and the semen analysis in opium, heroin, norgesic and crack dependent men, with each other and with non dependent men.

Materials and Methods

In this case-control study, after approval from the Ethics Committee of the Lorestan university of medical sciences, 48 addicted men who had referred to psychiatric hospital of Khorramabad city for addiction treatment, participated in the study. group1: Opium-addicted men, group 2: Heroin-addicted men, group 3: Norgesic addicted men and group 4: Crack-addicted men; the addiction severity of them was measured as high by psychiatrist, based on the adjusted questionnaire of addiction severity index (ASI). The patients were in a range of 20-45 years old and body mass index (BMI) of 20-25. Group 5 included volunteer non-addicted men in the same age and BMI range.

The addicts had used one type of drug for at least 6 months. The patients were assured of their information

confidentiality and they gave written consent for participation in this research. To check physical and mental health condition of the patients, they examined by a physician and a psychiatrist. The exclusion criteria which determined by interview and examination, consisted of having a history of liver, kidney and thyroid diseases, diabetes, hypertension, cancer, daily alcohol consumption, Wilson's disease, AIDS, hepatitis A, B, C, hemochromatosis, major mental illnesses and the use of some drugs like spironolactone, cimetidine and propranolol within 10 days before the sampling. Afterwards, to confirm physical health, a series of screening tests were done including the concentration of BUN, CBC, FBS, K⁺, Na⁺, U/A, LFT, TSH, T3, T4, creatinine, AIDS and hepatitis B and C.

After physical and mental health were confirmed, some tests performed including serum concentration of LH, FSH, free testosterone, total testosterone, DHT, DHEAS, prolactin, sex hormone binding globulin (SHBG), progesterone, estradiol and semen analysis. All specimens were collected within 8.00-10.00 AM. Serum samples were kept at temperature of -20°C before measurement.

To compare data of different groups, one-way Analysis of Variance (ANOVA) and Game's Havel methods were utilized. Spearman method was used to examine the relationship between different data. Data were expressed as standard error of the \pm mean and $p < 0.05$ was considered as significant.

Results

Among 73 patients, 13 cases were eliminated with hepatitis B, C and AIDS. The results of this examination showed that the concentration of free testosterone in the all test groups is significantly less than that in control group. Meanwhile, the concentration of DHT and DHEAS in all test groups, except heroin addicted group, was less than control group. Indeed, the reduction level of DHT concentration is greatly less than free testosterone

concentration. The concentration of LH, FSH, prolactin, SHBG, progesterone and estradiol in all test groups was not significantly different from control group (Table 1).

There are no significant differences in normal and abnormal sperm count in the test groups compare to control group; however, the sperm motility rate in all test groups was less than control group (Table 2). No significant relationship was found between sex hormones concentration and the status of sperms motility. Also there was no significant relationship between sex hormones concentration and the percentage of motile sperms with the duration of addiction.

Discussion

The results of the present study showed that free testosterone concentration in all test groups were significantly less than control group and there were no significant differences between the test groups. Furthermore, DHT and DHEAS concentrations in all test groups was less than control group except heroin addicted group. However, the reduction level of DHT concentration was much less than free testosterone that might be due to an increase in enzymatic activity of 5 α -reductase.

The reduction of DHEAS concentration might be due to a decrease in the enzymatic activity of adrenal gland in synthesizing DHEAS. Fazelpour et al. reported a drastic reduction in the level of plasma testosterone hormone of rats which were addicted to heroin [9]. Some other studies suggest that the reduction in plasma levels of testosterone is resulting from the inhibitory effect of opioids on the pituitary gonadotropins; however, at the present study, there was no significant difference between the gonadotropins concentration in any group, that is consistent with the studies conducted by Wisnivski et al. about the unchanged gonadotropins and decreased concentration of free testosterone in the people addicted to cocaine and heroin [7].

Table 1 . Concentration of Hypothalamic-Gonadal Axis Hormones in Different Groups

	Opium	Heroin	Norgestic	Crack	Non addict
Total testosterone(ng/ml)	5.68 \pm 3.21	5.93 \pm 2.42	5.01 \pm 4.27	3.98 \pm 2.29	5.32 \pm 1.36
Free testosterone (pg/ml)	1.81 \pm 2.09 ^a	0.6 \pm 0.76 ^b	0.32 \pm 0.37 ^c	0.2 \pm 0.12 ^d	10 \pm 6.5
Dihydrotestosterone (pg/ml)	435.75 \pm 70 ^a	638 \pm 308.31	357.71 \pm 97 ^c	451.1 \pm 163 ^d	676.8 \pm 105.16
Dehydroepiandrosterone Sulfate (pg/ml)	0.92 \pm 0.65 ^a	1.61 \pm 0.97	1.03 \pm 0.64 ^c	0.97 \pm 0.66 ^d	2.02 \pm 0.88
LH (IU/ml)	5.95 \pm 2.82	5.53 \pm 1.83	4.48 \pm 3.02	4.75 \pm 3.1	3.85 \pm 1.68
FSH (IU/ml)	4.2 \pm 3.52	4.25 \pm 3.22	3.39 \pm 2.32	3.69 \pm 3.7	3.39 \pm 2.3
SHBG (nmol/ml)	56.5 \pm 23.007	63.75 \pm 20.96	55.28 \pm 17.49	58.8 \pm 24.53	56.5 \pm 16.26
Progesterone (ng/ml)	0.4 \pm 0.29	0.58 \pm .25	0.48 \pm 0.26	0.6 \pm 0.3	0.47 \pm 0.2
Estradiol (pg/ml)	19.17 \pm 12.38	21.55 \pm 9.11	22.34 \pm 13.08	27.04 \pm 13.39	25.17 \pm 8.9
Prolactin (mIU/ml)	197 \pm 145	72.1 \pm 47.44	94.48 \pm 100	372 \pm 491	179 \pm 141

a= significant difference between groups 1 & 5

b= significant difference between groups 2 & 5

c= significant difference between groups 3 & 5

d= significant difference between groups 4 & 5

δ = significant difference between groups 2 & 3

Table 2. Semen Analysis in Different Groups

	Opium	Heroin	Norgestic	Crack	Non addict
pH	7.85 \pm 0.05	7.84 \pm 0.05	7.82 \pm 0.8	7.8 \pm 0.06	7.78 \pm 0.23
Sperm count	77.25 \pm 46.74	74.66 \pm 17	102 \pm 38	97 \pm 26	117 \pm 75.02
Abnormal sperms (%)	38.33 \pm 4.43	35 \pm 3.69	34.2 \pm 5.1	42.5 \pm 20.8	33 \pm 2.44
Motile sperms (%)	43.75 \pm 23.85 ^a	22 \pm 10.54 ^b	50 \pm 12.24 ^c	30 \pm 18.85 ^d	65 \pm 11.18
Non motile sperm (%)	56.25 \pm 23.8 ^a	12.08 \pm 4.5 ^b	50 \pm 12.24 ^c	70 \pm 18.85 ^d	35 \pm 11.18

a= significant difference between groups 1 & 5

b= significant difference between groups 2 & 5

c= significant difference between groups 3 & 5

d= significant difference between groups 4 & 5

δ = significant difference between groups 2 & 3

High levels of endorphins and enkephalins have been found in the semen which regulates steroidogenic activity of leydig cells through sertoli cells. On the other hand, external opioids stimulate beta-endorphin receptors directly and inhibit testicular function in rat [10]. Thus, the opioids might inhibit synthesis and secretion of testosterone by directly stimulating the beta-endorphin receptors existing in testes.

In this study, semen analysis showed that the percentage of motile sperms in test groups were significantly less than control group; however, no significant relationship was found between the sperm motility status and sex hormones concentration. On the other hand, considering the existence of μ receptors in human spermatozoa and the effects of μ receptors' agonists (such as morphine) on increment of percentage of non-motile sperms [11], opioids used in this study increased non motile sperm maybe through binding to spermatozoa μ receptors. These results are consistent with a reduction in sperm motility as the main sign of sperm pathology in heroin addicted men [12].

In the present study, there is no significant difference in prolactin concentration between all test groups and control group, while most of the previous studies have reported an increase in prolactin concentration by acute using heroin, buprenorphine and methadone [13]. However, some other studies have shown that opioids concentration doesn't change by long-term consumption of opioids [14]. Therefore, according to the duration of drug addiction in test groups, which was at least more

than one year, it may be argued that long-term consumption of drugs and tolerance is the reason of unchanged prolactin concentration in test groups. The latest finding in the present study is the lack of difference between current drugs in creating any disorder in pituitary gonadal axis and semen analysis that should be considered as a warning to the youths on the harmfulness of new drugs such as crack and norgesic which are deemed as low risk drugs to the public. However, in our study, it was not possible to control some factors affect on the level of pituitary gonadal axis hormones including stress, nutrition and the exact amount of narcotic used within a few recent days. Thus, it would be better to increase the samples in the future studies.

The results of this study showed that chronic use of opioids causes hypogonadism and disorder in sperm motility. So, in the narcotic addicts, reproduction status should be considered.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

No conflict.

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