Effect of Heroin Abuse on Pituitary-Gonadal Axis in Male Subjects

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In this work, the effect of chronic heroin abuse on the pituitary-gonadal axis was investigated. The study comprised 17 patients and 13 control subjects. 47% of the patients reported symptoms of sexual dysfunction. Hormonal assays demonstrated a significant reduction in serum testosterone and serum FSH in the patients group. It was suggested that opiates exert a direct inhibitory effect on the secretory function of the testes and an indirect inhibitory effect on spermatogenesis through inhibition of FSH. Further research is needed to verify this hypothesis.

(Egypt.J. Psychiat.,1993,16:91-97).

Introduction

Many opiate abusers report sexual dysfunction in the form of decreased libido and / or failure of erection. This effect may be due to the psychological condition during opiate abuse or it may be due to an endocrinological disturbance caused by the chronic consumpion of opiates.

Many research reports support the last possibility. Rasmussen (1991) found that naloxone (an opiate antagonist) caused an increased gonadotrophin releasing hormone after ovariectomy in rats. Naloxone was also found to increase serum luteinizing hormone (LH) and serum cortisol in healthy women (Baranovska, 1990). Briski and Sylvester (1991) found that endogenous opioid peptides are involved in stress-induced prolactin release in aging rats. A comparable conclusion was reached by Tejwani et al. (1991) in a separate report. Dermorphine (an opiate-like heptapeptide) was found to decrease plasma LH in a group of fertile women (Petraglia et al., 1985).

The authors hypothesized that chronic opiate abuse had an effect on the pituitary-gonadal axis in human male subjects mainly through inhibition of LH and consequently suppression of testosterone secretion.

Subjects and Method

Male chronic heroin abusers (more than six months duration) in the age range of 20 - 50 years were included in the study. The patients were selected from Al-Salama Hospital in Jeddah, Kingdom of Saudi Arabia. They were all admitted to the inpatient section for treatment of heroin abuse. For each patient, the following was done:

(1) Personal history.

(2) Full psychiatric history concentrating on duration of heroin abuse, concomittant abuse of other drugs, previous attempts at treatment from heroin abuse.

(3) Sexual history concentrating on history of decreased libido and / or decreased erection.

(4) Medical history concentrating on history of chronic hepatic, renal and en-

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docrinological conditions; and history of medical treatment during the previous six months.

(5) Full medical examination.

(6) ECG, liver function tests, serum BUN, and serum creatinine.

(7) Urine opiates, urine tetrahydrocannabinol, serum benzodiazepines, serum cocaine and serum amphetamine.

(8) Serum prolactin, serum follicle stimulating hormone (FSH), serum luteinizing hormone (LH) and serum testosterone. These were performed by Automated Enzyme Linked Immuno-Absorbant Assay (ELISA) Technique, using ES 600 Boehringer Mannheim.

Blood and urine samples were drawn before any withdrawal symptom appeared and before any drug was given to the patient.

Exclusion criteria were history of attempted treatment of heroin abuse or interrupted course of heroin abuse within the previous six months, history or evidence of abuse of other drugs during that same period (except cannabis), history or evidence of medical disease or medical treatment during the same period, unclear or conflicting history concerning the pattern of heroin abuse, and finally failure to draw the blood or urine samples as specified before.

The patient sample was a consecutive one.

Control subjects were healthy male volunteers aging from 20 to 50 years, with no history or evidence of medical treatment or medical illness and no history or evidence of substance abuse within the previous six months. They were workers in the same hospital. They were subjected to clinical examination and laboratory investigation similar to the study group.

Statistical Analysis

As appropriate, the following statistical tests were used: Fisher's Exact Probability Test (Surwillo, 1980), Student t Test for difference between independent sample means (Surwillo, 1980), t Test for difference between independent sample proportions (Koenker, 1976), and Contingency Coefficient C (Surwillo, 1980).

Results

35 male heroin abusers were recruited to the study, 18 patients were excluded due to one of the mentioned reasons. Of the 17 patients who stayed in the study, 7 had a positive result for tetrahydrocannabinol in urine (+ve C subgroup) and 10 patients were negative (-ve C subgroup). The duration of heroin abuse in the study sample was 1.87 ± 0.9 years. The control group contained 13 healthy male subjects after the exclusion of one person for history of using antidepressant drugs within the previous six months.

Table (1) shows the age distribution and mean age among the total patient group, + ve C and - ve C subgroups, and the control group. No statistically significant difference was found between the total patient group and the control group, and between the + ve C and - ve C patient subgroups.

As shown in table (2), the total patient group comprised statistically significant less married subjects than the control group ($p = 0.02$). The +ve C subgroup did not differ from the - ve C subgroup in this matter ($p = 0.356$). p was calculated by the Fisher's exact probability test (Surwillo, 1980).

As shown in table (3), control subjects did not report any sexual dysfunction compared to 52.9% in the total patient group. The difference was statistically significant ($t = \pm 3.045$, $df = 28$, $p < 0.01$). The + ve C and - ve C subgroups did not differ in this concern.

Although table (4) shows a relative increase in serum prolactin in the patient group compared to controls, yet this increase did not reach statistical significance ($t = \pm 0.4353$, $df = 28$, $p > 0.10$). Similarly, the apparent increase in serum prolactin among the + ve C subgroup compared to the - ve C subgroup did not attain statistical significance ($t = \pm 0.5221$, $df = 15$, $p > 0.10$).

All subjects in the patient group and in the control group had within normal levels of serum FSH (0.8 - 9.0 U/L). Yet the mean level among the control group was 7.5 (± 2.05) U / L compared to 2.66 (± 1.11) U / L in the total patient group (see table 5). The difference was statistically significant ($t = \pm 2.0804$, $df = 28$, $p<0.05$). The mean levels for the + ve C and -ve C subgroups were 2.97 ± 1.32 and 2.45 ± 0.95 U / L respectively. There was no statistically significant difference between the two subgroups ($t = \pm 0.3197$, $df = 15$, $p > 0.10$).

Concerning serum LH, all individuals in the patient group and in the control group had within normal serum levels (0.5 - 10 U / L). There was apparent increase in the mean level in the patient group compared to the control group (respectively, 3.99 ± 1.83 U / L and 1.20 ± 0.52 U / L); yet the difference did not reach statistical significance ($t = \pm 1.4666$, $df = 28$, $p > 0.10$). The mean serum level among the + ve C and - ve C subgroups was 4.96 (± 1.86) U / L and 3.32 (± 1.55) U / L respectively. The difference was not statistically significant (table 6).

As shown in table (7), no statistically significant difference was found between the total patient group and control group regarding mean serum testosterone levels ($t = \pm 0.4849$, $df = 28$, $p > 0.10$). Similarly, the + ve C group did not differ from the - ve C group ($t = \pm 0.7646$, $df = 15$, $p > 0.10$).

Interestingly, more patients had below normal serum testosterone levels than control subjects (47% and 7.7% respectively). The difference reached statistical significance ($t = \pm 2.7706$, $df = 28$, $p < 0.01$). The + ve C group did not differ statistically from the - ve C group in this regard ($t = \pm 1.3617$, $df = 15$, $p > 0.10$).

To investigate the correlation between the report of sexual dysfunction and a below normal serum testosterone level among the patient group, the contingency coefficient C (Surwillo, 1980) was calculated between the the two variables. It was found to be 0.125 ($p>0.10$) which is a negligible correlation.

Table 1
Age Distribution and Mean Age Among Different Patients Groups and Control Group

	Patients Groups			
Age Groups	Total	+ ve C	- ve C	Control Group
20 - 30	9	2	7	.
31 - 40	6	4	2	12
41 - 50	2	1	1	1
No.	17	7	10	13
Mean	29.88	31.14	29.0	35.54
S.D.	± 6.25	± 6.54	± 6.24	± 2.79

Table 2
Distribution of Marital Status among Different Patient Groups and Control Subjects

Marital Status	Patients Groups			Control Group
	Total	+ ve C	- ve C	
Married	11	5	6	13
Single	6	2	4	-
No	17	7	10	13

Table 3
Distribution of Sexual Dysfunction Symptoms among Different Patient Groups and Control Subjects.

Sexual Symptoms	Patients Groups						Control Group	
	Total		+ ve C		-+ ve C			
	No	%	No	%	No	%	No	%
Decreased Libido	6	35.5	1	14.3	5	50.0	-	-
Impotence	5	29.4	1	14.3	4	40.0	-	-
No Symptoms	9	52.9	5	71.4	4	40.0	13	100
N	17		7		10		13	

Table 4
Distribution of Serum Prolactin Level among the Patient Groups and the Control Subjects (Normal range 0 - 25 ng / ml)

	Patients Groups						Control Group	
	Total		+ ve C		-+ ve C			
	No	%	No	%	No	%	No	%
Within normal	14	82.4	5	71.4	9	90.0	13	100
Above normal	3	17.6	2	28.6	1	10.0	-	-
Total	17		7		10		13	
Mean ± S.D.	15.39 ± 13.21		21.21 ± 16.75		11.32 ± 8.85		9.19 ± 5.33	

Table 5
Distribution of Serum FSH among Patient Groups and Control Subjects (Normal range 0.8 - 9.0 U/L)

	Patient Groups						Control Group	
	Total		+ ve C		- ve C			
	No	%	No	%	No	%	No	%
Below normal	-	-	-	-	-	-	-	-
Within normal	17	100	7	100	10	100	13	100
Mean ± S.D.	2.66 ±1.11		2.97±1.32		2.45 ± 0.95		7.50 ± 2.05	

Table 6
Distribution of Serum LH Level among Patient Groups and Control Group (Normal Range 0.5 - 10.0 U /L).

	Patient Groups						Control Group	
	Total		+ ve C		- ve C			
	No	%	No	%	No	%	No	%
Below normal	-	-	-	-	-	-	-	-
Within normal	17	100	7	100	10	100	13	100
Mean±S.D.	3.99±1.83		4.96±1.86		3.32±1.55		1.20± 0.52	

Table 7
Distribution of Serum Testosterone Level among the Patient Groups and Control Subjects. (Normal Range 9 - 38 nmol /L)

	Patient Groups						Control Group	
	Total		+ ve C		- ve C			
	No	%	No	%	No	%	No	%
Below normal	8	47.0	2	28.	6	60.0	1	7.7
Within normal	9	53.0	5	6	4	40.0	12	92.3
Total.	17		7	71.	10		13	
Mean ± S.D.	11.36±8.03		16.13±9.12	4	8.03±5.39		16.36±6.47	

Discussion

To our knowledge, this is the first study that investigates the effect of chronic opiate abuse on the pituitary-gonadal axis by a method that tries to eliminate the effect of psychotropic drugs on prolactin and consequently on testosterone.

In our study, more heroin abusers tended to be not married than control subjects. This may reflect a tendency toward less social and psychological adaptation. As expected, the report of sexual dysfunction was more common among heroin abusers. The additional consumption of cannabis by the abusers did not influence this finding.

The report of sexual difficulty did not correlate with decrease in serum testosterone. This may be due to the fact that the sexual symptoms were due to the psychological effect of heroin abuse as well. This opinion agrees with that of Abel (1984) who hypothesized that opiates substitute sexual satisfaction and have an indirect effect through impairment of health and a direct effect on the physiological and brain mechanisms that control sexual functions.

As for the effect of heroin on the pituitary-gonadal axis, this study demonstrated a decrease in the serum level of FSH. The value of this finding should be confirmed by performing spermatogenic count in heroin abusers in correlation with their serum FSH in further research.

Serum prolactin level was not affected by chronic heroin abuse. This was a sign for the success of our method in eliminating the effect of stress of withdrawal of opiates and of psychotropic drugs on serum prolactin. Both would have caused a false elevation of prolactin.

In our study, serum LH tended to in-

crease among heroin abusers. The increase did not reach statistical significance. This finding was contrary to what was hypothesized on the basis of previous reports in the literature. The discrepancy may have arisen from the fact that the work of Petraglia et al. (1985) and of Baranovska (1990) was performed on females. Could there be a sex difference in the effect of opiates on LH? In addition, could there be a difference between the short term and the chronic effect of opiates on LH? Both possibilities need further verification.

In this study, serum testosterone level fell below normal range in 47% of heroin abusers. This finding is difficult to explain in the absence of either hyperprolactinaemia or decreased LH. One should then speculate that opiates exert an inhibitory effect on secretion of testosterone by the testis. This opinion finds partial support from the fact that in our patients LH tended to be elevated denoting absence of the negative feedback mechanism testosterone usually exerts on the production of LH. This hypothesis needs verification by further research including testicular biopsy and histochemical studies on the secretory function of the testes in heroin abusers.

It is worth noting that two Egyptian studies were performed on heroin abusers and demonstrated a decrease in serum testosterone (Ali et al., 1987; Abdel Mohsen et al., Submitted for Publication). One major difference between the present study and those two studies was that they were both conducted on heroin abusers under medical treatment. They did not exclude the effect of withdrawal symptoms and of psychotropic drugs on the level of testosterone. In fact, the second study demonstrated an increase in serum prolactin in its sample. This was, in our opinion, due to methodological consideration rather than due to effect of heroin itself. The second difference was that none of those two studies explored the other two pituitary hormones affecting gonadal functions, namely, FSH and LH.

Finally, our study demonstrated that the additional consumption of cannabis in our sample did not have any effect on the obtained results.

Conclusion

This study demonstrated a definite increase in sexual dysfunction in heroin abusers. This was associated with a decrease in serum testosterone and serum FSH. A direct effect of opiates on the secretory function of the testes was speculated. Further research in the field using more investigation of testicular function was suggested.

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L'Effet de l'Abus de l'Héroine sur l'Axe Pituitaire-Gonadique chez les Sujets Mâles

Dans ce travail, l'effet de l'abus de l'héroine chronique sur l'axe pituitaire-gonadique a été investigué. L'étude a compris 17 malades et 13 sujets de contrôl. 47% des malades ont présenté des symptômes de dysfonctionnement sexuelle. Le titrage hormonal a demontré une réduction significative de sérum de testostérone et de sérum de l'hormone stimulant des follécules chez le groupe de malades.

Il était suggéré que les opiates exercent un effet inhibiteur sur la fonction sécréteure des testicules et un effet inhibiteur indirect sur le spermatogenèse à travers l'inhibition des follécules. En effet, on a besoin de plus de recherches pour vérifier cette hypothèse.

تأثير سوء إستخدام الهيروين على محور الغدة النخامية والغدد التناسلية فى الأشخاص الذكور

تمت دراسة تأثير سوء الاستخدام المزمن للهيروين على محور الغدة النخامية والغدد التناسلية فى الذكور، وقد اشتملت الدراسة على ١٧ مريضاً و١٣ شخصاً فى عينة ضابطة وقد أظهرت النتائج أن ٤٧٪ من المرضى أوردوا أعراضاً تتعلق باضطراب فى الوظائف الجنسية، أما قياسات الهرمونات فقد أظهرت انخفاضاً ذا دلالة فى مستوى هرمون التستوستيرون والهرمون المثير للبويصلات فى مجموعة المرضى، وقد تم استعراض النتائج فى المناقشة، ويقترح الباحثان أن الأفيونات لها تأثير مثبط مباشر على الوظائف الإفرازية للخصيتين، وتأثير مثبط غير مباشر على وظيفة تكوين الخلايا المنوية من خلال تثبيط الهرمون المثير للبويصلات، مما يتطلب مزيدا من البحث لتحقيق هذه الفرضية.