HEROIN ADDICTION AND SEX HORMONES IN MALES

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ABSTRACT

To investigate the effects of illicit heroin abuse on the endocrine system a study was carried out in North West Frontier Province (NWFP) where heroin addiction is prevalent. Sixty-eight subjects were included in this study. Thirty-three were untreated heroin addicts visiting TM drug abuse treatment centres" in Peshawar and 35 age matched normal males. Urine samples of all addicts showed the presence of morphine. The serum concentrations of testosterone (T) in addicts was 228 ng/ml, leutinizing hormone (LH) 10.7 mlUfml and folical stimulating hormone (FSH) 4.9 mlU/ml whereas the corresponding values for control males were T 630 ng/ml, LH 14.3 mlU/ml and FSH mlU/ml, respectively. Heroin exerts a depletion effect on T and FSH levels in more or less all the groups studied irrespective of age, amount of heroin intake per day and period of contact with heroin. LH levels remain unaffected and are within clinically accepted normal range (JPMA42: 210,1992).

INTRODUCTION

Heroin is two to three times as potent analgesically as morphone. Soon after its synthesis and realization of its potency it was introduced as a non-addictive sedative to replace morphine. Heroin is now considered to be the most addictive of all known drugs. Its use, initially produces intense euphoric effects, but continuous use, inevitably leads to derangement of both mind and body, often culminating in violent termination of life[1]. Heroin has adverse effects on all major systems of the body[2,5] including impairment of sexual function. Acute doses of either heroin or morphine prevent ovulation in female rats4 and rabbits'. The Chronic doses of either heroin or morphine totally disrupts estrous cycle in rodents[6] and significantly lowers testosterone levels in rats[7]. Clinical manifestations such as decreased sexual desire and performance, menstrual irregularity and infertility among heroin abusers are attributed in part, to altered gonadal functions[8-11]. The aim of this study was to determine the possible endocrine changes by estimating the testosterone, leutinizing hormone and follical stimulating hormone in sera of heroin addicts.

PATIENTS AND METHODS

Experimental subjects

Sixty eight subjects were included in this study. Thirty three were untreated heroin addicts visiting drug abuse treatment centres of Khyber Teaching Hospital, Lady Reading Hospital and Green December Movement, Peshawar. They were actively taking heroin either by vapour inhalation (changing the dragon method) or by smoking in cigarettes. The remaining 35 males of the same age as addicts were studied as controls. A detailed history was taken from consenting individuals regarding their age, marital status, period of heroin abuse and quantity of heroin taken every day. Serum and urine samples were collected from these addicts prior to therapy.

Collection of biological samples

Midstream urine samples were collected in clean plastic bottles and 3 ml of blood was drawn between 0900 and 1300 hours from the ante-cubital vein and the serum was separated. All samples were stored at -20°C until analysed for hormones and morphine.

Detection of morphine in urine

Morphine was detected in urine samples by TLC method. Ten ml aliquotes of urine samples were acid hydrolysed by adding 1 ml of 6M HCl in a boiling water bath for one hour. After cooling the mixture 0.5 ml 70% K_2CO_3 was added and tubes shaken gently till effervescence stopped. 2 ml of alkaline buffer (pH 9.5) and 20 ml of extracting buffer was then added and after shaking the tubes for 5 minutes, the contents were centrifuged at 1000 rpm for 3 minutes. The upper adueous layer was discarded and the lower organic layer was washed twice with equal volumes of phosphate buffer (pH 10). The washings were discarded and the organic phase was filtered through What man No.1 filter paper and dried. The residue was redissolved in 50 ul of methanol. Ten ul was spotted on salica gel GF 254 (0.2 mm, 20 x 20 cm glass backed) TLC plates. Five ul of reference morphone was also spotted on the same plate along side. The plates were developed in ethyl acetage/methabol/ammonia (85:10:5 v/v/v) solvent system. The chromatograms were visualized under ultraviolet light and then sprayed with iodoplatinate spray reagent, which reacts with morphone to give a blue colour.

Estimation of hormones and morphine in serum

Testosterone (T), leutinizing hormone (LII), follical stimulatinghormone (ESH) and morphone (ME) were estimated by radioimmunoassay using commercially available radioimmunoassay kits supplied by Coat-A-Count, Diagnostic Products Corporation, USA. All determinations were made in duplicate on ALIKA ARC-300 Auto Well Gamma Counter over 1 minute. Statistical analysis was done using Students 't' test.

RESULTS

Serum concentrations of T, LII and FSH in normal subjects and heroin addicts are shown in Tables I and II.

TABLE I. Hormone concentrations in serum of normal males.

Age (Years)	No.	Testosterone (ng/100 ml)	Leutinizing hormone (mIU/ml)	Follical stimulating hormone (mIU/ml)
18-25 21.0±2.5	14	623.84±28.04	13.58±1.27	9.81±1.12
26-35 30.0±3.0	12	667.30±49.31	11.92±1.35	13.53±1.50
36-50 43.2±5.0	9	569.12±46.04	18.56±2.58	10.43±1.41
18-50	35	630.36±23.31	14.27±1.03	11.12±0.80
Normal values		360-990	upto 25	0-20

TABLE II. Heroin (morphine equivalent, ME) and hormone concentrations in serum of male heroin addicts

Age (Years)	No	Heroin (ME) (ng/ml)	Testosterone (ng/100 ml)	Leutinizing hormone (mIU/ml)	Follical stimulating hormone (mIU/ml)
18-25	11	46.42±11.59	228.20±36.91	10.69±1.82	4.97±2.52
26-35	14	42.84±7.01	444.01±62.43	16.17±2.57	5.02±2.20
36-50	8	20.56±4.35	433.85±80.55	14.43±2.85	5.70±1.84
18-50	33	37.87±5.17	376.30±37.59	14.56±1.56	5.17±1.30
Normal values		-	360-990	Upto 25	0-20

The results are the mean ± S.E.

There was a significant (P <0.005)) decrease in levels in young (18-25 years) and mature (36-50 years> and FSII levels in only mature heroin addicts when compared with controls. Heroin had no effect on LII levels.

TABLE III. Heroin (morphine equivalent, ME) and hormone concentration as a function of quantity of heroin intake, in the serum of male heroin addicts.

Heroin intake (g/day)	No	Heroin (ME) (ng/ml)	Testosterone (ng/100 ml)	Leutinizing hormone (mIU/ml)	Follical stimulating hormone (mIU/ml)
0.5-1.5	13	34.89±7.81	361.00±51.16	10.69±2.22	4.75±1.85
2	15	32.04±6.93	421.80±62.84	16.62±2.47	2.70±1.00
3-4	5	55.40±15.73	275.26±88.86	11.25±2.31	10.45±5.13
0.5-4.0	33	37.87±5.17	376.30±37.59	14.56±1.56	5.17±1.30
Normal values		-	360-990	Upto 25	0-20

The results are the mean ± S.E.

Tables III and W show that the amount and duration of heroin intake had no effect on the hormone levels and the differences observed in three groups were statistically insignificant. All urine samples of heroin addicts were identified to contain morphine (expressed as morphine equivalent ME).

TABLE IV. Heroin (morphine equivalent, ME) and hormone concentrations, as a function of duration of heroin intake, in the serum of male heroin addicts.

Heroin intake (Years)	No.	Heroin (ME) (ng/ml)	Testosterone (ng/100 ml)	Leutinizing hormone (mIU/ml)	Follical stimulating lasting hormone (mIU/ml)
0-2	10	24.04±5.55	323.27±69.19	13.84±2.53	6.65±3.19
2-4	15	40.06±7.01	391.60±56.18	12.67±2.12	3.10±1.20
4-6	8	46.22±14.07	411.71±78.12	14.63±3.97	3.66±1.61
0-6	33	37.87±5.17	376.30±37.59	14.56±1.56	5.17±1.30
Normal values		-	360-990	Upto 25	0-20

The results are the mean ± S.E.

DISCUSSION

Heroin reduces sexual interest and potency, it may depress libido and increases the duration of the male erection resulting in delayed ejaculation12. Similar sexual disturbances were observed in heroin addicts in this study. Use of heroin and other norcotics decreases the sex hormone levels in humans as well as experimental animals and associated with this decrease is sexual dysfunction[13-18]. Serum and FSII levels were significantly lower in addicts in comparison to normal subjects whereas serum LII level did not change. These findings are similar to earlier reports[7,13,16,19,20]. The serum T levels are more or less equally affected regardless of age of the addicts, the amount of heroin intake per day and duration of addiction at least within the limits of our experiment. Although statistically there was no difference between T levels within the three groups, the T levels were lowest in short time addicts, a little higher in fair length of time addicts and highest in long time addicts indicating the metabolic adaptation that addicts' body is perhaps of addicts after prolonged use of heroin. The average value of young adults is almost half the average T values of mature adults and middle age adults, thus suggesting that the young addicts may be more prone to the adverse effects of heroin as compared to elder addicts. The serum FSH levels are also equally affected i.e., almost half of the average ESH values of controls, regardless of age of the addicts, amount of heroin intake and duration of addiction at least within the limit of our experiment. There is exception to the above stated fact that FSH levels are statistically not different in addicts taking excessive amount of heroin. The reason behind this fact may be firstly the small number of samples in the groups, secondly, although values of PSH are half of the normals but due to spread of data they are statistically non- significant In this study fill or rise in serum LH levels are found insignificant which are in accordance with the studies carried out by Cicero and his colleagues[21]. These workers had reported that LII levels do not necessarily correlate closely with plasma T levels in rats and had suggested that norcotics can directly influence the synthesis or secretion of T by the testes, independent of any direct effect on LH. The mechanism underlying drug induced suppression of plasma T levels remain a matter of conjecture. Among possibly sites of norcotic effects are, action at pituitary and/or hypothalamus, direct inhibition of gonadal steroidogenesis and change in peripheral steroid metabolism. Our results suggest a direct action of heroin on inhibition of steroidogenesis in adrenal and testicular tissues or changes in peripheral steroid metabolism. Serum T levels are depressed statistically when compared to the tontrols. Although in most of these groups T values remain within the clinically accepted normal range (360-990 ng/100 ml) but at lower level except in young adults, short time users and addicts taking relatively a small and excessive amount of heroin. In view of the decrease in serum T concentration found in many of the male heroin addicts in the present studies, it seems likely that the decrease in libido frequency observed in the addicts may be due at least partly to a decrease in serum T concentration.

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