

## Hormonal levels in male heroin addicts and methadone detoxification

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*Heroin addicts which we studied were associated with low plasma testosterone (T), luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL) and cortisol but only the T was significantly ( $P < 0.05$ ) lower than in a control group. During low dosage methadone detoxification over 7 days, the hormonal levels were increased from pretreatment levels but the T was still significantly ( $P < 0.05$ ) lower than in normal male controls. At the end of 14 days methadone treatment, we found that the T, LH and FSH levels were significantly ( $P < 0.05$ ) higher than in the control group. Moreover, there was a 48% HIV seropositive rate among the heroin addicted group.*

**Key words :** Heroin, Addict, T, LH, FSH, PRL, Cortisol, HIV.

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ผู้ติดเชื้อเอดส์ชนิดเอโรอินพบว่ามีระดับฮอร์โมนเทสโทสเตอโรน (T), ลูทีไนซิงฮอร์โมน (LH), ฟอลลิเคิลสติมูเลตติ้งฮอร์โมน (FSH), โพรแลคติน (PRL) และคอร์ติซอล (Cortisol) ในพลาสมาลดลง แต่ T จะมีระดับลดลงอย่างมีนัยสำคัญ ( $P < 0.05$ ) เมื่อเปรียบเทียบกับกลุ่มควบคุมระหว่างการบำบัดรักษาด้วยเมธาโดนเป็นเวลา 7 วัน พบว่าระดับฮอร์โมนต่างๆ จะเพิ่มขึ้นจากเดิม แต่ T ยังคงมีระดับต่ำกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ ( $P < 0.05$ ) เมื่อสิ้นสุดการบำบัดรักษาด้วยเมธาโดน 14 วัน พบว่าระดับฮอร์โมน T, LH, FSH จะสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ( $P < 0.05$ ) และนอกจากนี้ยังพบว่าในกลุ่มที่ใช้ยาเสพติดจะมีผลเลือด HIV เป็นบวกถึง 48 เปอร์เซ็นต์

Narcotics abuse is a very important problem throughout the world. Heroin, which is synthesized from morphine, is the most commonly used drug in Thailand. Its use is very widespread in adolescents and the number of new addicts increases by 2000 every month.<sup>(1)</sup> One idea to assist addicts withdrawal from heroin is by substituting another substance. Methadone, which acts more slowly than heroin but is still addictive, is one of the most substitution treatments used in Thailand. The effects of heroin and methadone preferred have been reported to cause subtle derangements of hypothalamic-pituitary function.<sup>(2,3)</sup> There is also a relationship between the effects on the central nervous system and the reproductive system. Previous reports<sup>(4-8)</sup> have shown differences in the effects of opiates on hormones, and these differences were probably related to different doses, regimens of narcotics, and acute or chronic administration of the narcotics. Animal and human studies have show that effects of morphine, methadone and heroin are closely related to sex steroid levels in plasma, but this remain to be resolved. There fore, the objective of this study was to evaluate the hormonal levels of testosterone (T), luteinzing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL) and cortisol in heroin addicts before and during a 14 day methadone detoxification treatment. The result of this studies will show the effect of heroin to hormones before and during methadone treatment. The knowledge of this basic result may be explained about relation of hormones to sexual physiology and glucose tolerance in heroin addicts.

## Materials and methods

Fifty heroin addicts were admitted to Thanyarak Hospital during the period December 1993 - February 1994. All male subjects were age range 15-45 years old and evidence of taking intravenous drugs at least 1 year before admission. The subjects were interviewed and blood samples were collected before and on 7 and 14 day of methadone treatments. If the subjects could not collect blood samples complete 3 times, they should be excluded from this studies. Urine samples were collected before and after every 3 days until day 14 of treatment.

Fifty normal male controls were recluded healthy males, not use all of narcotics and age range 15 - 45 years old. The subjects were interviewed, blood and urine samples were collected only one time.

All of blood samples were analyzed for T, LH, FSH, PRL and cortisol hormones by radio - immunoassay (RIA) of WHO and urine samples were examined of morpine by RIA kit of ROCHE. If urine sample found positive in normal male control, the subject would be excluded from the studies. Blood HIV testing was detected HIV antibodies in blood of heroin addicts before treatment and blood of normal male controls by enzyme-immuno assay (EIA) of ORGANON TEKNIK (NETHERLAND).

## Results

1. The generel characteristics of the intravenous heroin addicts are shown in Table I. The age-range of the subjects was 19-42 years ( $\bar{x}$ =30.82  $\pm$  5.67 years). Most of them were single, lived in Bangkok, had primary-secondary

single, lived in Bangkok, had primary-secondary education and incomes of 3000-5999 baht per month. The characteristics of normal male controls were 20-42 years old ( $\bar{x} = 28.74 \pm$

6.50 years). Most of them, had marital status single; lived in Bangkok; education at high school and income between 3000-5999 baht per

**Table 1.** Characteristics of Heroin addict and control groups.

Information	heroins (n=50) controls (n=50)			
	n	%	n	%
1. Age (years)				
15-24	9	18.0	15	30.0
25-34	25	50.0	24	48.0
>34	16	32.0	11	22.0
$\bar{x} \pm SD$	30.8 $\pm$ 5.7		29.0 $\pm$ 6.5	
2. Local province				
Bangkok	26	52.0	49	98.0
Ayuthaya	5	10.0	-	-
Pratumthani	2	4.0	-	-
Nonthaburi	3	6.0	1	2.0
Samutprakarn	4	8.0	-	-
Others	10	20.0	-	-
3. Marital status				
Single	36	72.0	26	52.0
Married	12	24.0	24	48.0
Separated	2	4.0	-	-
4. Education level				
Primary school	20	40.0	14	28.0
Secondary school	18	36.0	9	18.0
High school	11	22.0	27	54.0
Unknown	1	2.0	-	-
5. Occupation				
Employee	32	64.0	3	6.0
Commerce	6	12.0	-	-
Government employee	-	-	26	52.0
Farmer	5	10.0	-	-
Student	-	-	19	38.0
Unemployed	7	14.0	2	4.0
6. Income per month				
No income	7	14.0	21	42.0
<3000	5	10.0	-	-
3000-5999	27	54.0	22	44.0
>6000	11	22.0	7	14.0
7. HIV testing				
Positive	24	48.0	-	-
Negative	26	52.0	50	100

2. The characteristics of using drug in heroin group found that the first time of consumed drug was between 15-25 years old which the causes of initial consumption mostly was curiosity. They almost used drug 1-5 years by consumption 0.376-0.500 gram per day. They expended about 200 baht per day, and 44% of the subjects had never had previous drug treatments. However, they did want to give up drug in our program.

3. The hormone levels of the subjects are shown in Table 2. The data for our heroin addict group shows that before the treatment the T, LH, FSH, PRL, and cortisol levels were lower than in the normal males (control group). The T level was significantly different ( $P < 0.05$ ). During the 7 day of methadone treatments, all hormones levels increased, especially the T and PRL levels ( $P < 0.05$ ) over the normal group. After the end of the 14-day methadone treatment, most of hormone levels were increased. Moreover the T, LH, and FSH levels were significantly increased ( $P < 0.05$ ) from the normal group, but the PRL and cortisol levels were not different from the normal group.

**Table 2.** Characteristics of drug used in heroin addict group.

Information	Number Percentage	
	(n)	(%)
1. Age when first used drug (years)		
15-19	14	28.0
20-24	14	28.0
>24	22	44.0

2. Duration of drug used (years)		
1-5	27	54.0
6-10	14	28.0
>10	9	18.0
3. Quantity drug used per day (gram)		
0.083-0.166	4	8.0
0.167-0.375	12	24.0
0.376-0.500	21	42.0
0.501-1.000	13	26.0
4. Daily expenditure on drug (baht)		
≤ 200	30	60.0
201-400	15	30.0
401-600	5	10.0
5. Causes of initial drug		
persuasion	7	14.0
curiosity	37	74.0
having problem	4	8.0
feling enjoyment	2	4.0
6. Number of detoxification		
Never	22	44.0
1-3	17	34.0
4-9	7	14.0
>9	4	8.0
7. Reasons for treatment		
to quit	37	74.0
no money to buy drug	6	12.0
worsen health	1	2.0
for his family	3	6.0
for his work	2	4.0
fear of being arrested	1	2.0

**Table 3.** Hormones level of control and heroin addicted groups.

Hormones	T (nmole/L)	LH (IU/L)	FSH (IU/L)	PRL (mU/L)	Cortisol (nmole/L)
Groups	X ± SD	X ± SD	X ± SD	X ± SD	X ± SD
Controls (n=50)	23.0 ± 7.2	7.1 ± 3.1	3.4 ± 2.4	315.5 ± 187.1	498.3 ± 245.8
Heroin addicts before treatment (n=50)	12.1* ± 6.6	5.7 ± 4.4	2.7 ± 1.9	226.7 ± 245.8	489.1 ± 245.8
Methadone treatment, 7 days (n=50)	18.9* ± 8.8	7.2 ± 4.3	3.2 ± 2.4	493.4* ± 286.3	502.7 ± 249.4
Methadone treatment, 14 days (n=50)	28.9* ± 7.8	10.8* ± 4.8	5.7* ± 2.8	317.8 ± 186.8	614.4 ± 274.3

\*Significant difference from control group  $p < 0.05$

4. In the pre-treatment urine morphine testing at 3 day intervals, there were 100% positive results while the urine morphine levels

decreased during the methadone treatment and showed negative results at the end of the treatment. (Table 4)

**Table 4.** Urine morphine examination in control and heroin addict groups which classify by quantity drug used per day.

Groups	P or N	Results of urine examination			
		Percentage (%)			
		Quantity of drug per day (gm)			
		0.083-0.166 (n=4)	0.167-0.375 (n=12)	0.376-0.500 (n=21)	0.501-1.000 (n=13)
Control group	N	-	-	-	-
Methadone treatment,3 days	P	100.0	100.0	100.0	100.0
Methadone treatment,6 days	P	50.0	58.3	71.4	61.5
	N	50.0	41.7	28.6	38.5
Methadone treatment,9 days	P	-	8.3	9.5	23.1
	N	100.0	91.7	90.5	76.9
Methadone treatment,12 days	P	-	-	-	7.7
	N	100.0	100.0	100.0	92.3
Methadone treatment,14 days	N	100.0	100.0	100.0	100.0

P = Positive result

N = Negative result

ment. (Table 4)

5. Blood samples of the heroin addict group showed 48% HIV seropositive while HIV was seronegative in the control group (Table 1).

## Discussion

1. The characteristics of the intravenous heroin addicts in this study showed that the age range of drug use was 19-42 years and this is an expanded trend from the 1983-1987 period which reported age ranges of 26-28 years old.<sup>(9)</sup> Most of those subjects were single, of low education and first used drugs from 15-25 years of age which supported the Trongswad et al report.<sup>(10)</sup> Even

though 64% of the addicts were employed and had incomes of 3000-5999 baht per month they expended about 200 baht/day for drugs. They are thus both economic and social problems for Thailand. Moreover, the social environment is a very important factor because most of drug dependence increased depending on curiosity (74.0%) and persuasion (14.0%).

2. The TLH, FSH, PRL and cortisol hormone levels were depressed by heroin, and this supports several previous reports,<sup>(11-16)</sup> but Cushman<sup>(6)</sup> reported that T levels were unchanged in addicts. In our study of heroin addicts, the T level was significantly ( $p < 0.05$ )

levels in normal men was extending from 15.8 to 30.2 nmole/l while in addicts before treatment was 5.5 to 18.7 nmol/l which was low T level in normal male controls, So it could be concluded that heroin was mostly effected sex steroid hormones in plasma which possible affected upon testicular function because both LH and FSH controlled function of leydig cells and synthesized of T. Buena et al.<sup>(17)</sup> reported that sexual function did not change when serum testosterone level were pharmacologically varied within the normal male range. Cicero et al<sup>(18)</sup> found that on all measures of secondary -sex-organs and testicular function, heroin addicts appeared to fall between the methadone and control subjects.

3. After methadone detoxification for 7 days it was found that the LH, FSH and cortisol levels increased to normal mean levels but the T level was still significantly ( $P < 0.05$ ) lower while the PRL level was significantly higher than in the controls. From this result it could be suggested that the low doses of methadone detoxification did not strongly depress the LH, FSH and cortisol but could elevate the PRL level, and this is supported by the Lafisca et al<sup>(19)</sup> and Judd et al<sup>(20)</sup> reports. Meldelson, et al<sup>(21)</sup> reported that testosterone levels remained depressed during methadone withdrawal and cortisol levels did not significantly change during both heroin use and methadone withdrawal over a 7 day. Mendelson and Mello<sup>(22)</sup> reported that recovery of testosterone levels to normal occurred after about one month of heroin abstinence. So this study should be prolonged for one month to evaluate and confirm hormone levels reverse to normal levels or not.

4. At the end of our methadone treatment, T, LH, FSH levels were significantly ( $p < 0.05$ ) higher than in the controls while the PRL and Cortisol levels were in the normal range. The results of this study showed that heroin effects were not permanently. Because of all of hormones could be increased after treatment. Some studies<sup>(23,24)</sup> reported that 93% of heroin addicts and 65% of those taking methadone had abnormal semen and the most frequent abnormality was in motility(78%).

5. The urine testing for morphine in the pretreatment heroin addicts was 100% positive and 100% negative after 14 days (Table 4). This testing could be showed that result of morphine in urine corresponded to doses of using heroin so the testing use to check the relapse of heroin between detoxification because of increasing morphine concentration in urine sample. Morphine was excreted after use drug within 24 hour, so we could find morphine in urine 2-3 days post drug used but rate of excretion depend on metabolism of body, length of time after using, method of using and the dose of the drug used of addicts.<sup>(25)</sup>

6. Serum screening in heroin addicts found 48.0% HIV seropositives. and 100% HIV seronegative in control males. The hormonal levels in HIV seronegative and HIV seronegative in addicts were not significant difference in this studies. But Rabkin et al<sup>(26)</sup> found that low levels serum testosterone in HIV illness. Data of Sittitrai et al<sup>(27)</sup> reported that in late 1987 a dramatic rise in seroprevalence was observed in intravenous drug users (IVDUs) present for methadone treatment at Thanyarak Hospital



methadone treatment at Thanyarak Hospital (Thongcharoen)<sup>(28)</sup> and the infection rate grew from 1.16% in December to stabilize at about 30% in August of 1988 which was similar to Bangkok Metropolitan Administration (BMA) studies. After two years, the number of people who were HIV positive grew rapidly, but there was a shift in risk factors from IVDUs to heterosexual females. In 1988, 85.8% of known seropositives had been IVDUs, 4.2% homosexual or bisexual males and 1.8% heterosexual females. By 1990, HIV in IVDUs had dropped to 63.6% and homosexual or bisexual males to 0.7% while the heterosexual females had risen to 16.2%.<sup>(29)</sup> Mastro et al.<sup>(30)</sup> reported that 89% of opiate users in Bangkok inject drugs and about one third are infected with HIV. He believed that the number of HIV-infected injection drug users in Bangkok would increase dramatically, placing new demands on existing health care facilities. Gossop et al.<sup>(31)</sup> reported that one of the most conspicuous risks of HIV transmission among drug injectors involves sharing injecting equipment which has been contaminated by infected blood. About 24% of his sample reported having shared injecting equipment while in custody. There is good overall awareness of the risks of health problems associated with drug injecting. The epidemic spread of HIV infection among IVDUs appeared in the beginning of 1988 and spread more rapidly in Bangkok and urban areas of provincial cities than in the rural areas. Therefore, methadone detoxification and rehabilitation are very important to prevent and control HIV infection among IVDUs.

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