

Sexual Dysfunction in Opiate Use Disorder in Male Egyptian Patients

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

| <i>Abbr.</i> | <i>Title</i> |
|---------------|--|
| ABP | : Androgen-binding protein |
| ACTH | : Adrenocorticotropin hormone |
| APN | : Aminopeptidase N |
| ART | : Androgen Replacement Therapy |
| BMT | : Buprenorphine maintenance treatment |
| CRH | : Corticotropin-releasing hormone |
| CYP450 | : Cytochrome P450 |
| DE | : Delayed ejaculation |
| DHEAS | : Dehydroepiandrosterone sulfates |
| DHT | : 5 α -dihydrotestosterone |
| 5-HT | : 5-hydroxytryptamine |
| DOR | : Δ -opioid receptors |
| ED | : Erectile dysfunction |
| EOPs | : Endogenous opioid peptides |
| FDA | : Food and drug administration |
| GABA | : Gamma amino butyric acid |
| GnRH | : Gonadotrophin releasing hormone |
| HDL | : High-density lipoprotein |
| HPA | : The hypothalamo-pituitary-adrenal axis |
| IELT | : Intravaginal ejaculatory latency time |

| | |
|---------------|--|
| IMS | : Intercontinental Marketing Services |
| KOR | : κ -opioid receptors |
| LH | : Luteinizing hormone |
| LPH | : Lipotropin |
| M1/M3 | : muscarinic receptor |
| MMT | : Methadone maintenance treatment |
| MOR | : μ -opioid receptors |
| MSH | : Melanotropin stimulating hormone |
| NEP | : Endopeptidase neutral N |
| NMDA | : N-methyl-D-aspartate |
| NO | : Nitric oxide |
| NOS | : Nitric oxide synthase |
| NSAIDs | : Non -steroidal anti-inflammatory drugs |
| OE | : Opioid Endocrinopathy |
| OPIAD | : Opioid-induced androgen deficiency |
| ORL1 | : The orphanin 1 |
| OD | : Opiate use disorder |
| PDYN | : Pro-dynorphin |
| PE | : Premature ejaculation |
| PENK | : Pro-enkephalin |
| POMC | : Pro-opiomelanocortin |
| PRL | : Prolactin hormone |
| RE | : Retrograde ejaculation |

| | |
|--------------|---|
| ROS | : Reactive oxygen species |
| SD | : Sexual dysfunction |
| SD | : Standard deviation |
| SHBG | : Sex hormone-binding globulin |
| SNRIs | : Serotonin Noradrenaline reuptake inhibitors |
| SOD | : Superoxide dismutase |
| SPSS | : Statistical package for social science |
| SS | : Serotonin syndrome |
| SSRI | : Selective serotonin reuptake inhibitor |
| TCAs | : Tricyclic antidepressant |
| WHO | : World Health Organization |

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Introduction

Psychoactive substances (drugs) are substances that have the ability to change an individual's consciousness, mood or thinking process and are associated with dose tolerance and dependence. Despite the prohibitions, illicit use of psychoactive substances is fairly wide spread in many societies. Substance use and dependence cause a significant burden to individuals and societies throughout the world (*Jiann, 2008*).

Fertility is considered as a life conservative phenomenon. Changes in the sexual activity are commonly found in addicted subjects. The effects of drug abuse on sexual functions and sex hormones are one of the major scopes of investigations throughout the world (*Hejazian et al., 2007*).

Psychoactive substances are believed to be aphrodisiac; but in reality they have deleterious effects on all the aspects of sexual function. These substances may exert their inhibitory effect on erection through their effects on central neurotransmitter pathways (serotogenic, adrenergic or dopaminergic). Besides, some also may exhibit vasoconstricting properties (cocaine), impair endothelium function (nicotine) or suppress the release of luteinizing hormone from the pituitary, resulting in hypogonadism (morphine). Whether withdrawal from the substances could restore erectile function remains unknown (*Jiann, 2008*).

Evidence suggests that opioids – both endogenous and exogenous – can bind to opioid receptors primarily in the hypothalamus, but potentially also in the pituitary and the testes, to modulate gonadal function (*Drolet et al., 2001*). Decreased release, or interference with the normal pulsatility of release of GNRH at the level of the hypothalamus, has been documented, with consequent decreased release of LH and FSH from the pituitary. Direct effects of opioids on the testes, including decreased secretion of testosterone and testicular interstitial fluid, have been documented (*Katz, 2005*).

In addition, opioids decrease levels of the growth hormone, cortisol, and dehydroepiandrosterone sulfate (DHEAS). Opioids also blunt the cortisol response to corticotropin. While the clinical significance of decreased growth hormone and cortisol levels remain speculative, decreased gonadal and adrenal androgen production contribute to the now well-documented symptoms of opioid-induced endocrinopathy (*Colameco & Coren, 2009*).

In regular heroin users, decreased libido has been reported in the majority of addicts, erectile dysfunction in 39~48% and delayed ejaculation in over 50% of the addicts (*Jiann, 2008*). *Palha & Esteves (2002)* reported there was a significant decrease in weekly sexual intercourse and

masturbatory activity in 101 heroin male addicts compared with healthy controls.

One study showed that the serum free testosterone in opium addicts were decreased significantly compared to the controls. This reduction was directly proportional to the duration of opium usage. The LH and FSH level in opium addicts showed also significant reduction compared to the controls (*Hejazian et al., 2007*).

Previous studies (*Moshtaghi et al., 2005*) indicated that there is a positive co-relation between the dose of opium and the plasma prolactin level (as an inhibitor of GnRH) in opium dependents, thus the suppression of gonadotropine secretion by adenohypophysis may be due to suppression of GnRH release from the hypothalamus. However there are some reports suggesting the direct effects of opium on pituitary gonadotropine releasing cells via kappa and mu opioid receptors (*Hejazian et al., 2007*).

Whether erectile function could be restored needs further study. In one study measuring hormonal status one month after cessation of heroin use, testosterone levels returned to normal (*Katz, 2005*). Hypersexuality episodes may be observed in men experiencing opiate withdrawal, with spontaneous erections and nocturnal ejaculation (*Jiann, 2008*).