Sexual Dysfunction in Opiate Use Disorder in Male Egyptian Patients

Thesis

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Mostafa Ahmed ElSaid Abd El Qader

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List of Abbreviations

Abbr.	Title
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	**:** Dehydroepiand Rosterone sulfates
DHT	**:** 5 a –dihydrotestosterone
5-HT	**:** 5-hydroxytryptamine
DOR	**:** Δ-opioid receptors
ED	**:** Erectile dysfunction
EOPs	**:** Endogenous opioid peptides
FDA	**:** Food and drug administration
GABA	**:** Gama amino buteric 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

OUD **:** 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 neuro-transmitter 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).***