بسم الله الرحمن الرحيم

﴿ قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا
عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ ﴾

صدق الله العظيم

سورة البقرة (أية٣٢)

ADDICTIVE DRUGS ABUSE AND EFFICIENCY OF LOCAL ANAESTHESIA

THESIS
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by

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LIST OF ABBREVIATIONS

AAA	acute alveolar abscess
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine transaminase
ANOVA	Analysis of variance
AO	alveolar osteitis
APRs	acute phase reactants
APA	acute periodontal abscess
AST	Aspartate transaminase
BUN	Blood Urea Nitrogen
C3	complement 3
CBC	Complete blood count
CRP	C-reactive protein
CNS	central nervous system
DA	Drug addicts
EEG	Electroenchephalogram
ELISA	Enzyme Linked Immunosorbent Assay
ESR	erythrocyte sedimentation rate
GHB	gamma hydroxybutate
GVHD	graft versus host disease
HCl	Hydrochloric
HCV	Hepatitis C virus
IgE	immunoglobulin E
i.m	intramuscular
kDa	Kilo Dalton
LASER	light amplification by stimulated emission of radiation
LA	Local anesthesia
LBP	low back pain
LSD	D-Lysergic acid diethylamide
MDMA	methylene -Dioxy-meth-ampheramine
mg/L	Milligram per litre
NMR	Nuclear magnetic resonance
NS	Non significant
OIH	opioid-induced hyperalgesia
PCP	Phencyclidine
RA	rheumatoid arthritis
RBC	Red blood cells
SLE	systemic lupus erythematosus
THC	Tetrahydrocannabinol
TMJ	Temporomandibular joint
U/L	Unit per litre
US	ultrasound
USP	United States Pharmacopeia
VAS	Visual Analogue Scale
WBC	White blood cells

Introduction and review of literature

INTRODUCTION AND REVIEW OF LITERATURE

It is paramount to understand what is meant by dependence, addiction and abuse. Drug abuse, is a term used to identify the interplay between a drug and a subject beyond the correct use of a drug to treat and cure a disease under medical prescription [(1)].

A definition of substance abuse is the misuse of a psychoactive drug to the detriment of the individual but which fails to meet the criteria for dependence. Criteria for dependence include: compulsion, tolerance to the drug where greater doses are required to produce an effect, withdrawal symptoms and multiple unsuccessful attempts to desist from, or at least control, substance use. Dependence has been shown to have a neurochemical basis and is widely considered as a disease process [(2)].

Addiction is a vague term relating to abuse, although still used, should be replaced with dependence. It is the compulsive need for and use of a habit forming substance (as heroin, nicotine, or alcohol) characterized by tolerance and by well defined physiological symptoms upon withdrawal [(3)].

Drug addiction is characterized by compulsive drug taking that persists despite escalating costs and adverse consequences. Over the past 20 years, sensitization of the appetitive effects of drugs has emerged as a possible mechanism underlying enhanced drug use [(4)].

Drug addiction has become one of the most serious problems in the world. It has been estimated that genetic factors contribute to 40%–60% of the vulnerability to drug addiction, and environmental factors provide the remainder. Over the past three decades, a number of technologies have been used to generate such candidate genes or vulnerable chromosome regions [(5)].

Abuse and addiction are behavioral syndromes that exist along a continuum from minimal use to abuse to addictive use, while tolerance and physical dependence are biological phenomena that can be defined precisely in the laboratory and diagnosed accurately in the clinic [(6)].

Concerning the etiology of drug addiction, dependency may be viewed as a subset of brain and behavior disorders, which include all psychiatric diagnoses. Current recognition of addiction, acceptance of it as a medical disorder by the public, and treatment options for it roughly mirror conditions for schizophrenia, bipolar disorder, and major depressive disorders [(7)].

Similarly, as for each of these disorders, major questions are raised concerning the etiology of addiction, including the relative roles of genetic and environmental factors, neurochemical and neuroanatomic changes, and the course of the illness [(7)].

Drug dependence is a state, that may be either physical or psychologic, or both, that occurs as a consequence of the interaction between a drug and a patient. It is characterized by a compulsion to take the drug to obtain its effects or to prevent the abstinence syndrome [(8)].

Confusion exists because the correct use of prescribed medications for pain, anxiety, and even hypertension commonly produces tolerance and physical dependence. These are normal physiological adaptations to repeated use of drugs from many different categories [(9)].

Patients with pain are sometimes deprived of adequate opioid medication simply because they have shown evidence of tolerance and they exhibit withdrawal symptoms if the analgesic medication is abruptly stopped [(6)].

Psychic or psychogenic dependence has been traditionally recognized as another important feature of drug dependence. Psychic dependence may be accompanied by physical dependence. The Expert Committee on Addiction-producing Drugs of the World Health Organization has defined psychic dependence as a state of discomfort produced by withdrawal of a drug [(1)].

Physical dependence represents a physiologic and biochemical adaptation to the presence of an addicting drug so that the body is normal while drug concentrations are maintained. Removal of the drug unmasks an underlying pathophysiology. The "withdrawal syndrome" is often characterized by effects opposite to the acute pharmacologic actions of the drug itself. These disturbances are relieved dramatically by reestablishing an effective drug concentration[(1)].

Social dependence, besides physical and psychic dependence, is difficult to overcome when treating drug addiction. Social dependence may in fact be defined as an adaptation of the individual to his/her new condition. The psychologic dependence also may be halted by specific psychologic interventions. However, when the patient finally returns to normal life, he realizes that he no longer has any friends [(1)] .

Table (1) shows a comparison between substances of abuse while table (2) shows drugs of abuse by category [(8)]. It seems that cannabinoids are the most commonly used illicit drugs in the world [(10)].

Table (1): Comparison of Substances of Abuse

DRUG ABUSE	Tolerance	Withdrawal	Physical Addiction	Psychologic Addiction
Opioids	*High*	High	High	High
Sedative, hypnotic, Alcohol	Medium-high	Medium-high	High	Medium-high
Stimulants:				
Cocaine	Low	Low	Medium-low	Medium-high
Amphetamine	Medium-high	Low	Medium-low	Medium-high
Hallucinogens:				
LSD	Some	No	Low	Low
PCP	Low	No	Low	Low
Marijuana	Low	Low	Low	Low
Nicotine	Yes	Yes	yes	Yes

Requa-Clark B , 2000 [8]

Table (2): Drugs of abuse by category

DRUG GROUP	Most common example	Other example
Opioids	Heroin	Morphine Codeine Meperidine Hydromorphone
Stimulants	Cocaine Methamphetamine	Amphetamines Methylphenidate Nicotine
Depressants (sedative-hypnotics)	Ethanol Benzodiazepines Inhalants Nitrous oxide	Barbiturates Nonbarbiturate sedatives
Hallucinogens	D-Lysergic acid diethylamide (LSD)	Mescaline Phencyclidine (PCP)
Others	Marijuana	Caffeine

Requa-Clark B , 2000 [8]

Cocaine dependence is a chronically relapsing disorder leading to a variety of medical complications along with devastating psycho-social consequences. It remains a major public health problem bearing enormous societal costs and is currently afflicting over 1.5 million American citizens. Craving, is one of the most malignant and treatment resistant features of cocaine dependence [(11)].

A complex interface of major clinical and public health importance is observed if cocaine abuse precedes that of heroin or is concomitant. Heroin may hypothetically serve as a “mood balancer” which transiently dampens subthreshold excitatory states and mood swings. Craving for the suppressed hypomania could lead to cocaine abuse, which eventually unmasks a frank bipolar disorder in some cases leading to mixed state, severe mania, as well as psychosis beyond mania [(12)].

The doses of opioid analgesics required in some instances for adequate pain control can be identical to those taken by drug abusers. In addition, non-drug abusing populations can experience unpleasant effects from doses of opioid analgesics, highlighting the relevance of individual differences in the sensitivity to the reinforcing effects of these drugs. Frequency of use is also likely to influence the risk for abuse and addiction. This is not just related to the total dose administered, but also to the intervals between doses that can either facilitate or minimize the chances for the neuroadaptations that result in addiction [(13)].