RAPID OPIOIDS DETOXIFICATION UNDER GENERAL ANESTHESIA

Essay

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SUMMARY

Addiction is a chronically relapsing disorder characterized by compulsion to seek and take drug(s) regardless of the adverse consequences that may ensue

An opioid is any natural or synthetic compound, which has morphine-like properties

Opioid receptors are a group of G protein-coupled receptors with opioids as ligands. The endogenous opioids are dynorphins, enkephalins, endorphins, endomorphins and nociceptin.Opiate receptors are distributed widely in the brain, and are found in the spinal cord and digestive tract

OPIOID AGONISTS

The most widely used opioid analgesics are the pure agonists, and all of these are relatively selective for μ opioid receptors.

OPIOID ANTAGONISTS

Acts as competitive antagonist at all opioid receptors, but it has greatest affinity for μ receptors. Small doses of

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List of Abbreviations

HIV	Human immunodeficiency virus
SSTRs	Somatostatin receptors
AS	complementary Deoxyribonucleic acid
ORL	Nociceptin receptor
IUPHAR	International Union of Basic and Clinical Pharmacology
MOP	μ mu receptor
DOP	δ delta receptor
KOP	κ kappa receptor
NOP	Nociceptin receptor
CNS	Central nervous system
N/OFQ	Nociceptin/orphanin FQ
σ	Sigmma receptor
ζ	Zeta receptorl
OGFr	Opioid growth factor receptor
POMC	Proopiomelanocortin
ACTH	Adrenocorticotropic hormone
MSH	Melanocyte-stimulating hormone
RVLM	Rostral ventrolateral medulla
EEG	Electroencephalogram
CTZ	Chemoreceptor trigger zone

GABA	γ-aminobutyric acid
SA	Sinoatrial
AV	Atrioventricular
OBD	Opioid bowel dysfunction
NF κ	Nuclear factor kappa B
NMDA	N-methyl-D-aspartate
M6G	Morphine 6-glucuronide
CYP2D6	Cytochrome P450 2D6
MNTX	N-methylnaltrexone
FDA	Food and Drug Administration
CD4	cluster of differentiation 4
HCV	hepatitis C virus
ASA	American Society of Anesthesiologists
VIP	vasoactive intestinal polypeptide
BIS	bispectral index
SOWS	subjective opioid withdrawal scale
ROD	Rapid Opioids Detoxification
ASAM	The American Society of Addiction Medicine
IDP	Inpatient detoxification program

INTRODUCTION

Heroin dependence remains a significant public health problem .

Throughout the 20th century, many methods of opioid detoxification, including, artificial hibernation, and electroconvulsive therapy, have been proposed ***(Office of National Drug Control Policy, 2004).***

These approaches at that times produced greater morbidity and mortality than untreated withdrawal; however, despite improvements in recent decades, medically supervised heroin withdrawal remains interrupted by patient discomfort and high dropout rates so many patients either avoid treatment or leave it prematurely ***(Amato et al., 2004)***.

Conventional detoxification methods include, tapering doses of a substitute agonist drug, the use of μ-opioid receptor antagonists, and the use of clonidine which has been used alone and in combination with antagonists to reduce withdrawal symptoms ; These techniques, requiring 3–21 days, are associated with the onset of the withdrawal syndrome described previously and may necessitate admission for inpatient monitoring. Consequently, significant initial dropout rates are seen, ranging from 30–91%. ***(Mattick and Hall 1996).***

A different approach to detoxification from opioids emerged: the administration of a high-dose m-receptor antagonist during general anesthesia. Well-designed protocols accelerate detoxification and attenuate withdrawal symptoms. The procedure should result in 100% detoxification rates, should be safe, and should be accomplished in 4–6 h ***(Carroll, et al., 1997).***

Opioid addiction therapy includes successful detoxification, rehabilitation, and sometimes methadone maintenance. However, the patient may have physical, mental, and emotional pain while trying to achieve abstinence, so a detoxification technique that incorporates general anesthesia uses a high-dose opioid antagonist which will compress detoxification to within 6 h and avoiding the withdrawal manifestation. ***(O'Connor et al., 1997).***

Rehabilitation of people addicted to opioids can only begin after an initial period of abstinence; this period is variable and is associated with an extremely unpleasant "withdrawal" syndrome ***(O'Connor et al., 1997)***.

The character and severity of symptoms such as sweating, shivering, nausea, vomiting, diarrhea, abdominal cramping, anxiety, and muscle pain are major deterrents to patients wanting or needing to undergo detoxification***(Bickel et al.,1997).***

AIM OF THE WORK

The aim of the work is to show a promising treatment strategy in opioids detoxification with naltrexone under general anesthesia followed by long-term naltrexone therapy, It provides extra time for additional treatment to maintain abstinence from opioids, It may also prove less expensive, per success, than traditional methadone treatment.

Chapter 1
Pathophysiology of addiction

Drugs such as cannabis, opium, and cocaine have been cultivated and used medicinally as well as recreationally for centuries. Opium poppies are believed to have been first grown in the region near modern-day Iraq as early as 3400 B.C. Opium was used primarily as an analgesic and anesthetic, but medical use did not become widespread until the development of the hypodermic needle in the early 1800s ***(Musto et al., 2002).***

Historical analysis also indicates that marijuana was smoked recreationally and medically in ancient China as early as 2737 B.C. ***(Musto .;1999***)

In South America, societies have grown and consumed coca, the plant grown to create cocaine, for centuries. The most common mode of administration is to chew the leaves of the coca plant, or to mix the leaves into a tea. ***(Streatfeild.;2002***).

Morphine is believed to have been prescribed often in the nineteenth and early twentieth centuries mainly as a cough suppressant to ease the suffering of individuals with tuberculosis***. (Musto .;1999) ,***

Although no data are available to empirically estimate incidence and prevalence. During the Civil War, it is believed that more than 400,000 soldiers became dependent on morphine, as it was liberally prescribed for pain associated battle wounds. (***Musto .;1999)***.

More systematic surveys of United States drug use began in the 1960s. A series of national household surveys on drug use conducted by the National Institute on Drug Abuse and later by the Substance Abuse and Mental Health Services Administration showed that illicit drug use, especially marijuana, increased greatly after the late 1960s. Heroin use also increased in the late 1960s, when the profile of users changed from "bohemians" to inner-city, unemployed males. (***Johnston et al .;2003)***.

National Institute on Drug Abuse, since 1975 indicate that 50% of 12th-grade students have used an illicit drug,with a high of 66% in 1982, a low rate of 41% in 1992, and 51% in 2004. Since 1975, over 80% of students felt that marijuana was easily available, ranging from 82.7% in 1992 to 90.4% in 1998. The most commonly used illicit opioid is heroin, with over 2 million users in the US ***(SAMHSA, 2006***).

Prescription opioid analgesic abuse is the fastest growing form of drug abuse in the US.Abused prescription opioids include hydrocodone (Vicodin, Lortab), oxycodone

(Percocet, OxyContin), hydromorphone (Dilaudid), fentanyl (Duragesic, Fentora), and others.***(SAMHSA, 2006***).

ADDICTION: DEFINITIONS AND NEUROBIOLOGY

Drug addiction is a chronically relapsing disorder characterized by compulsion to seek and take drug(s) regardless of the adverse consequences that may ensue. (***American Psychiatric Association, 1994.)***

Addicts typically exhibit decreased motivation for natural rewards (e.g., food, water, sex) that normally drive behavior. The abrupt cessation of drug use leads to the emergence of both affective (e.g., dysphoria, anxiety, anhedonia, somatic) and somatic withdrawal signs ***(Everitt and Wolf, 2002)***

However, the application of a systems approach to the study of addiction has provided new insights as to the role of brain regions comprising the limbic cortical-striatopallidal circuit in mediating the dysregulation of behavior that characterizes addiction ***(Everitt and Wolf, 2002)***

Addiction is defined by loss of control over an abusable substance, including an inability to voluntarily self-regulate drug use, compulsive preoccupation with obtaining or using adrug, and continued use despite of adverse consequences**.** ***(American Psychiatric Association, 1994.)***

Addiction is a multifaceted medical illness that develops as a result of interactions between the availability, cost, and pharmacology of a drug of abuse, environmental and psychosocial factors (e.g., occupation, peer group), genetic predisposition, comorbid psychiatric disorders, and drug exposure. Addiction has a highly variable clinical course. Initial drug use is voluntary behavior, and most users do not develop drug-dependence. However, repetitive drug exposure in a susceptible individual appears to cause fundamental changes in central nervous system function that produce the disease. Experimental evidence suggests that genetic predisposition to addiction may be related to alterations in neurocircuitry that enhance sensitivity to the reinforcing effects of drugs of abuse, thus overwhelming cognitive control of behavior***.(Nestler .; 2001.)***

A patient may enter recovery with abstinence and treatment, but once present, addictive disease is regarded as permanent. However, addiction may be managed successfully as a chronic disease, and many patients respond positively to treatment with long periods of abstinence***.(McLellan et al.2000.***)

The neurobiology of addiction is summarized in three concepts that have immediate bearing on the anesthesiologist caring for the patient with addiction: uniform

drug reward and reinforcement, cross-addiction, and disease permanence.The mesocorticolimbic dopamine system is central to the pathophysiology of addiction***.(Gardner . 2005.)***

This neurocircuitry involves the ventral tegmental area of the midbrain where dopaminergic neurons originate and the basal forebrain, the nucleus accumbens, and the amygdala to which these neurons project. All drugs abused by humans have been shown in animals to interact with this system to produce reinforcement.Permanent alterations in reinforcement neurocircuitry also appear to persist despite long-term abstinence and support the clinical notion of addiction as a chronic, incurable disease***.(McLellan et al. 2000)***

Diagnostic and Statistical Manual of Mental Disorders-IV Criteria for Substance Abuse and Dependence

1) Substance abuse: A maladaptive pattern of substance use leading to clinical impairment or distress in those who never met criteria for dependence in the past, manifested within a 12-month period by one or more of the following characteristics:

- Recurrent use resulting in a failure to fulfill role obligations at work, school, or home.

-Recurrent use in physically hazardous situations, such as driving or operating machines.