COMMENTARY

Opioid related disorders

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Abstract

In Sanskrit opium is known as ‘ahi phen’; in Northeast India it is referred to as ‘kani’. India, surrounded on both sides by the infamous routes of illicit transport, namely the *Golden Triangle* (Burma-Thailand-Laos) and the *Golden Crescent* (Iran-Afghanistan-Pakistan) has been particularly severely affected. More recently, a fourth receptor type, OFQ/N (ORL-1), has been accepted as part of an extended family of opioid receptors. About 90% with opioid dependence have additional psychiatric illness. The initial euphoria is followed by a period of sedation, known in street parlance as “nodding off.” Adverse effects include potential transmission of hepatitis and human immunodeficiency virus (HIV) through the use of contaminated needles. Physical dependence, as evidenced by tolerance or withdrawal, is a criterion that is neither necessary nor sufficient for the diagnosis of opioid dependence. Besides abstinence and harm minimisation, goals of the treatment include improving social and occupational functioning and improving quality of life.

Rahman MA. Opioid related disorders. Dysphrenia. 2013;4(1):78-81.

Keywords: Opium. India. Receptor. Comorbidity. Dependence. Counselling.

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Received on 26 January 2012. Accepted on 3 July 2012.

Introduction

The word opium is derived from the Greek word ‘opion’. In Sanskrit it is known as ‘ahi phen’, meaning snake venom; in Arabia it is known as ‘afyun’; in Chinese it is ‘yapin’; in Persian it is known as ‘afium’ ; in Northeast India it is referred to as ‘kani’. Opium is an extract of the exudates derived from seed pods of opium poppy, papever somniferum which belongs to family papaveraceae. Opium contains many alkaloids that are frequently used as analgesic, antitussive, antispasmodic in modern medicines. Poppy plant was cultivated in the ancient civilisations of Egypt, Mesopotamia and Persia. Archaeological evidence fossilised poppy seeds suggest that Neanderthal man may have used the opium poppy over thirty thousand years ago. First written reference to the poppy appears in Sumerian text dated around 4000 BC. The flowers was known as ‘hul gil’, plants of joy. Homer conveys its effect in the ‘Odyssey’. Galen listed its medical indication like chronic headache, vertigo, deafness, colicky pain, melancholy. In 1805 German chemist Friedrich Serterner isolated the pure active ingredient in the opium; he named this chemical ‘morphine’, after morpheus, the Greek God of dreams. In 1874 a German chemist invented ‘heroin’ by adding two acetyl groups to morphine.

Epidemiology

In the last few decades, use of opioids has increased markedly all over the world.[1] India, surrounded on both sides by the infamous routes of illicit transport, namely the *Golden Triangle* (Burma-Thailand-Laos) and the *Golden Crescent* (Iran-Afghanistan-Pakistan) has been particularly severely affected.[1] The National Household Survey of Drug Use in the country[2] found that the nationwide prevalence of opioid use is 0.7%. Among the opiate users, the largest proportion were opium users followed by heroin, cough syrup and other opiates and 22.3% of the abusers were dependent as per the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) criteria.[3] The European Monitoring Centre for Drugs and Drug Addiction reports that heroin use in the general population is less than one per cent.[4] In 2006 the National Survey on Drug Use and Health (NSDUH) reported the lifetime prevalence of heroin use among persons aged 12 years or older to be approximately 3.8 million people or 1.5 percent of the community dwelling population in the United States.[5]

Neuropharmacology

The primary effects of the opioids are mediated through the opioid receptors. The μ-opioid receptors are involved in the regulation and mediation of analgesia, respiratory depression, constipation and dependence; the kappa-opioid receptors, with analgesia, diuresis and sedation; the delta-opioid receptors, possibly with analgesia. More recently, a fourth receptor type, OFQ/N (ORL-1), has been accepted as part of an extended family of opioid receptors. The opioids also have significant effects on the dopaminergic, noradrenergic and cholinergic neurotransmitter systems. Short-term use of opioids apparently decreases the activity of the

noradrenergic neurons in the locus coeruleus. Long-term use activates a compensatory homeostatic mechanism within the neurons and opioid withdrawal results in rebound hyperactivity. Several types of data indicate that the addictive rewarding properties of opioids are mediated through activation of the ventral tegmental area dopaminergic neurons that project to the cerebral cortex and the limbic system. Results of at least one study using positron emission tomography (PET) have suggested that one effect of all opioids is decreased cerebral blood flow in selected brain regions in persons with opioid dependence.

Classification of opioids

Natural: Morphine, codeine.

Semisynthetic: Diacetylmorphine (heroin), ethylmorphine, pholcodeine.

Synthetic: Pethidine (meperidine), fentanyl, methadone, dextropropoxyphen, ethoheptazine.

Endogenous opioid: There are three different groups of endogenous opiod.

1. Endorphins are involved in neural transmission and pain suppression. They are released naturally in the body when a person is physically hurt.

2. Enkephalins are pentapeptide involved in regulating nociception in the body.

3. Dinorphins act through kappa receptors and regulate analgesia.

Opioid agonist and antagonist drugs

Mixed agonist and antagonist: Nalorphine, levallorphan, pentazocine, nalbuphine.

Partial agonist: Buprenorphine, butorphanol.

Pure antagonist: Naloxone, naltrexon.

Comorbidity

About 90% with opioid dependence have additional psychiatric illness: major depressive disorder, alcohol use disorders, antisocial personality disorder, anxiety disorders, about 15 percent attempt to commit suicide at least once.

Aetiology

Psychosocial factor: The incidence of opioid dependence is greater in low socioeconomic classes than in higher socioeconomic classes. Social factors associated with urban poverty probably contribute to opioid dependence. About 50 percent of urban heroin users are children of single parents or divorced parents and are from families in which at least one other member has a substance-related disorder. Behavioural problems in school or other signs of conduct disorder are at high risk for opioid dependence.

Biological and genetic factor: Individuals who abuse a substance from any category are more likely to abuse substances from other categories. Monozygotic twins are more likely than dizygotic twins to be concordant for opioid dependence. A person with an opioid-related disorder may have had genetically determined hypoactivity of the opiate system. May also be associated with abnormal functioning in either the dopaminergic or the noradrenergic neurotransmitter system.

Psychodynamic theory: In psychoanalytic literature, has been described in terms of libidinal fixation, with regression to pregenital, oral, levels of psychosexual development. Serious ego pathology, often thought to be associated with substance abuse. Problems of the relation between the ego and affects emerge as a key area of difficulty. Produces a positive experience after first use – acts as a positive reinforcer for substance seeking behaviour.

Clinical features

Opioids are subjectively addictive because of the euphoric high (the rush) that users experience, especially those who take the substances intravenously (IV). The associated symptoms include a feeling of warmth, heaviness of the extremities, dry mouth, itchy face (especially the nose), and facial flushing. The initial euphoria is followed by a period of sedation, known in street parlance as “nodding off.” Opioid use can induce dysphoria, nausea, and vomiting in opioid naive persons. The physical effects include respiratory depression, pupillary constriction, smooth muscle contraction (including the ureters and the bile ducts), constipation, and changes in blood pressure, heart rate, and body temperature.[6]

As well as euphoria and analgesia, opioids produce respiratory depression, constipation, reduced appetite and low libido. Tolerance develops rapidly, leading to increasing dosage. When the drug is stopped, tolerance diminishes rapidly so that a dose taken after an interval of abstinence has greater effects than it would have had before the interval.[7]

Morphine and heroin withdrawal: The morphine and heroin withdrawal syndrome begins six to eight hours after the last dose. The withdrawal syndrome reaches its peak intensity during the second or third day. Subsides during the next seven to ten days, but some symptoms may persist for six months or longer.

Meperidine: The withdrawal syndrome from meperidine begins quickly, reaches a peak in eight to 12 hours, and ends in four to five days.

Methadone: Methadone withdrawal usually begins one to three days after the last dose and ends in ten to 14 days.

Adverse effects: Potential transmission of hepatitis and human immunodeficiency virus (HIV) through the use of contaminated needles. Anaphylactic shock, pulmonary oedema, and death if they do not receive prompt treatment. Idiosyncratic drug interaction between meperidine and monoamine oxidase inhibitors (MAOIs), which can produce gross autonomic instability, severe behavioural agitation, coma, seizures, and death.

Related to mode of self administration of drug – parenteral: Cellulitis, thrombophleblitis, endocarditis, septicaemia, pulmonary hypertension.

Smoking/chasing: Chronic bronchitis, respiratory infection.

Declining in living standards: Nutritional deficiency, vitamin deficiency, poor immune status, recurrent infection, pulmonary tuberculosis.

Miscellaneous: Drug overdose, accidental injury while intoxicated.

Opioid overdose: Death from an overdose of an opioid is usually attributable to respiratory arrest from the respiratory depressant effect of the drug. Marked unresponsiveness, coma, slow respiration, hypothermia, hypotension, and bradycardia. Clinical triad of coma, pinpoint pupils, and respiratory depression, clinicians should consider opioid overdose as a primary diagnosis.

Diagnosis and classification

The text revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[8] and ICD-10[3] definitions of opioid dependence are similar in that there is a high level of agreement between the two, and both have as their central feature an emphasis on the compulsive aspect of drug-using behaviour.[5] It is important to note that within both classification systems, physical dependence, as evidenced by tolerance or withdrawal, is a criterion that is neither necessary nor sufficient for the diagnosis of opioid dependence.[5]

Treatment and rehabilitation

The main goal of the treatment is total abstinence which remains difficult to achieve and alternate goals have to be pursued for some time. In this sub-group intervention is directed towards decreasing the harmful consequences of continued drug use. Such an effort is plausible and is called ‘harm minimisation’. Besides abstinence and harm minimisation, goals of the treatment include improving social and occupational functioning and improving quality of life.[9]

Overdose treatment: The first task in overdose treatment is to ensure an adequate airway. Tracheopharyngeal secretions should be aspirated; an airway may be inserted. Ventilated mechanically until naloxone, a specific opioid antagonist, can be given. Naloxone is administered IV at a slow rate initially about 0.8 mg per 70 kg of body weight. Signs of improvement (increased respiratory rate and pupillary dilation) should occur promptly. If no response to the initial dosage occurs, naloxone administration may be repeated after intervals of a few minutes.

Opioid agents for treating opioid withdrawal

Methadone: Methadone is a synthetic narcotic (an opioid) that substitutes for heroin and can be taken orally. Daily dosage of 20 to 80 mg suffices to stabilise a patient, although daily doses of up to 120 mg have been used.

Merits of substitution: Reduction in illicit drug consumption. Avoidance of medical complications of impurities in street preparations and complications of parenteral administration and overdose. Better nutritional and health status, with regular monitoring. Decrease in criminal behaviour. Improvement is social behaviour and psychological wellbeing. Increased productivity.

Buprenorphine: Daily dose of eight to ten mg appears to reduce heroin use. It attenuates or blocks the subjective effects of parenterally administered opioids such as heroin or morphine.

Levomethadyl (LAAM): LAAM is an opioid agonist that suppresses opioid withdrawal. It is no longer used, however, because some patients developed prolonged QT intervals associated with potentially fatal arrhythmias (torsades de pointes).

Pregnant women with opioid dependence

About three fourths of all infants born to addicted mothers experience the withdrawal syndrome. Can lead to miscarriage or foetal death. Low dose of methadone (ten to 40 mg daily) may be the least hazardous course to follow. At this dose, neonatal withdrawal is usually mild and can be managed with low doses of paregoric. Foetal acquired immunodeficiency syndrome (AIDS) transmission.

Role of psychosocial treatments for opioid dependence[5]

A key feature for all modalities of opioid dependence treatment is nonpharmacological services, including counselling. Counselling services occur in outpatient, inpatient, residential, day care and prison settings. Therapeutic approaches can vary widely, although in recent years manually driven forms of counselling have been developed (for example, for cognitive-behavioural and motivational enhancement forms of treatment).

Self-help and 12-step group therapy: Narcotics Anonymous (NA) is a self-help group of abstinent drug abusers modeled on the 12-step principles of Alcoholics Anonymous (AA). They provide an element of group support with a network of nonsubstance using peers who can help confront denial, intervene early when individuals report thinking and behaviours that may increase the risk of relapse, and provide a real world experience that is not always available in the professional treatment setting.

Family and network therapy: Family and network therapy can improve compliance with medication and can enhance outcomes in opioid addiction treatment. Network therapy can be employed easily in a office-based setting, so it is ideal for use in office-based buprenorphine or naltrexone treatment as well as methadone maintenance programmes. It aims to engage the patient's abstinent family and friends in counselling sessions along with the patient. The idea is to involve these supportive people in the patient's treatment such that they are knowledgeable about the treatment plan and can help promote and monitor treatment compliance.

Behavioural therapies: Nonpharmacological treatments can serve a useful and important function in the treatment of opioid dependence. For example, monitored urine collection and testing (or other biological assessments of body fluids for drug use) provides an objective index of treatment progress. Besides its usefulness in objectively assessing illicit drug use, drug testing can also serve a treatment purpose.

A second behavioural intervention that has received considerable attention and research is the use of voucher incentives. Again, a target goal is defined (e.g., a cocaine-negative urine sample), and achievement of the goal results in earning a monetary voucher. Typically, vouchers escalate in value as a longer duration of the target is achieved (e.g., more consequtive cocaine-negative urine samples). Patients do not receive cash payments but can use vouchers to purchase goods and services consistent with their treatment goals.

Therapeutic communities

Therapeutic communities are residences in which all members have a substance abuse problem. The goals are to abstinence from substances; to develop personal honesty, responsibility, and useful social skills; and to eliminate antisocial attitudes and criminal behaviour.

Education and needle exchange

Although the essential treatment of opioid use disorders is encouraging persons to abstain from opioids, education about the transmission of HIV must receive equal attention. Unsafe needle sharing is common when it is difficult to obtain enough clean needles and is also common in persons with legal difficulties, severe substance problems, and psychiatric symptoms.

Suggested reading

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