Prevention and Treatment of HIV Addicted Patients: a Biopsychosocial Approach


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ABSTRACT

Injecting drug use is the main route of HIV transmission in many parts of Indonesia. Efforts to prevent HIV-transmission through injecting drug use mostly focus on subjects who actively inject. In scientific publications, the term 'injecting drug users' tends to be used without a clear definition and without specifying the pattern of drug use as current or former drug use, frequency, duration, type of injected drug(s) or context (e.g. imprisonment). Actually, injecting drug users (IDUs) have different drug use patterns, risk behavior, somatic co-morbidity, psychiatric co-morbidity, and psychosocial problems. In fact, these patients are suffering from addiction as a chronic brain disease in co-occurrence with somatic and psychiatric disorder and many social problems. Failing in addressing the problems comprehensively will lead to the failure of drug treatment. This is why addiction can be best studied and treated from a biopsychosocial perspective. Accordingly, treatment goals can be differentiated in crisis intervention, cure or recovery (detoxification, relapse prevention), and care or partial remission (stabilization and harm reduction). In summary, injecting drug use in Indonesia is not a single entity and patient oriented prevention and care for IDUs, especially focusing on their addiction, should be addressed to prevent the transmission of HIV/AIDS.

Key words: HIV patients, addicted patients, drug user, biopsychosocial approach.

INTRODUCTION

The prevalence of HIV/AIDS has greatly increased in recent years in Indonesia.1,2 The number of infected cases increases because of the transmission of these viruses through injecting risk behaviour, sexual risk behaviour, and other risk behaviour, but injecting drug use is mostly underlying this trend.3 Compared to other countries, Indonesia has the highest HIV-prevalence rates among IDUs, ranging from 43–56% in official reports.4 A recent survey in Bandung showed that 75% of 210 IDUs recruited through respondent-driven sampling were reported to be HIV-tested, and 63% of them to be HIV-positive (Iskandar, unpublished report). Injecting drug use is mostly a result of drug addiction, and we can, therefore, conclude that drug addiction and injecting drug use are the main factors driving HIV-infection in Indonesia.

Generally, the concept of injecting drug use is overly simplified, with little attention on the underlying problem of drug addiction. Too often, service providers and policy makers propagate needle exchange programs and/or pharmacotherapy as the ‘one fits all’ harm reduction without having properly characterized all problems of the addicted patient(s). In order to reduce the spread of HIV, a state of the art of addiction has to be applied on the development of treatment programs.

Until recently, the most common view was that drug addicts were weak or bad people, unwilling to control their behavior and gratifications.5,6 However, it has been shown that addiction is a chronic brain disease.5,7 In one important study of more than 3,000 twin pairs, Tsuang and colleagues reported that both environmental and...
genetic factors influenced abuse and dependence for several types of drugs, with genetic factors accounting for over 50% of the variance for opiate abuse or dependence. A family study found that the adjusted odds ratio for having the same drug disorder in adult first-degree relatives was over 7 for cocaine and over 10 for opioids, again indicating an involvement of genetic factors.

This change in paradigm has serious consequences for the way professionals should look at addicted patients and their disease. In this article we first give an overview of the current insights in the psychopathology and the consequences for their diagnosis. Then we will address the etiology, including genetics, drug induced changes in the brain, and environmental factors. The drug addiction and associated risk behavior are often accompanied by somatic, psychiatric and social problems, which will also be discussed. Finally, we will discuss the consequences regarding addiction as a complex biopsychosocial phenomenon for prevention and treatment.

PSYCHOPATHOLOGY AND DIAGNOSIS

At cellular level, all drugs of abuse share a common characteristic which underlies their abuse potential: initial use in the mode and pattern of abuse leads to rapid increase or decrease of receptor and/or transporter function, neurotransmitter/neuropeptide activity, and secondary messenger signaling. Changes in the gene expression of target proteins follow frequent, repeated exposure. Cessation of drug use leads to similarly profound changes. Thus, recurrent “on-off” use of short-acting drugs produces long-term, perhaps profound changes. The phosphorylation of receptors by GPCR kinases (GRKs) leads to the recruitment of arrestins. Interaction of arrestins with GPCRs results in an uncoupling of G-protein signaling from receptors (receptor desensitization) and a recruitment of the endocytic machinery leads to receptor internalization. However, morphine induces only weak or partial desensitization and little to no endocytosis. This will lead to tolerance and dependence that occur with chronic morphine treatment.

In central nerve system, MOR has a widespread distribution with particularly high levels in the striatal patches (striatum), thalamus, nucleus tractus solitarius, and spinal cord. The ability of MOR ligands to modulate presynaptic norepinephrine and dopamine release and may be critical in behavioral arousal and reward systems. The change in reward system function is regarded as the final common pathway to addiction. The change in the function of the frontal cortex makes a decrease of response inhibition and an increase in the salience of psychoactive substances. As a consequence, the imbalance between an impulsive part of the brain and the more reflective part is created which is mirrored in a behavioral imbalance between approach and avoidance of psychoactive substances. Before this imbalance results in inappropriate decision-making followed by the approach of a drug, the addicted patient is overwhelmed by ‘craving’, a strong longing for the drug. Although craving is regarded also as a central concept in addiction, it is hard to define because the gap between subjective experience and objective measurement of the phenomenon. Finally, the psychopathology of addiction is under influence of underlying vulnerability of the stress system in the hypothalamic pituitary adrenal axis.

According to DSM-IV, the most widely used manual for the classification of psychiatric disorders, a diagnosis of substance dependence is met if three or more of the following occur in a 12-month period: 1) tolerance, defined by the need for increased amount of substance to achieve the desired effect or diminished effect with continued use of the same amount of the substance; 2) development of a characteristic withdrawal syndrome when the substance is stopped or the use of the substance to prevent the onset of withdrawal; 3) increased or prolonged use; 4) a desire or unsuccessful attempts to cut down or control use; 5) significant time spent in activities related to drug procurement, use, and recovery; 6) important social, occupational, or recreational activities are sacrificed because of substance use; and 7) ongoing use despite the knowledge of...
ongoing physical or psychological harm related to substance use. However, most research on which the DSM-IV criteria are based is from the late 80’s and early 90’s of the last century. New insights are missing in the DSM-IV or are not linked to the criteria yet.

**GENETIC FACTORS**

It has been estimated that genetic contribution to addiction is 30-60% and opioid system has the biggest role in it. One of the genes in opioid system that has received a lot of attention in addiction studies is OPRM1 gene encoding MOR. MOR mediates positive reinforcement following direct (morphine) or indirect (alcohol, cannabinoids, nicotine) activation. (Figure 1)

![Figure 1. Relationship between Mu opioid receptor and addiction](image)

Mu opioid receptors [12] are largely distributed along reward circuits where they mediate the reinforcing activities of morphine and several non-opioid drugs. The non-opioid drugs act at their own receptors (GABA and NMDA receptors for alcohol, CB1 receptor for THC and nicotinic acetylcholine receptor for nicotine) and are likely to induce the release of endogenous opioid peptides that, in turn, activate mu receptors. Mu receptors, therefore, represent a convergent molecular gate in the initiation of addictive behaviors. Inadequate mu receptor activation might be one of the mechanisms underlying deregulation of reward pathways, which characterizes the addicted state [63].

The most frequent Single Nucleotide Polymorphism in MOR was A118G. The variant binds beta-endorphin with greater affinity, and activates K+ channels to a greater extent than the prototype receptor. It has also been reported that the A118G allele expresses approximately one-half the OPRM1 mRNA and about one-tenth the mu-opioid receptor protein. Therefore, subjects with the A118G allele would probably have greater response of the variant receptor but also have reduced receptor expression.

Another example of the genetic contribution is the inherited presence of an aldehyde dehydrogenase genotype (associated with alcohol metabolism) causes an involuntary skin “flushing” response to alcohol. Those whose initial, involuntary physiologic responses to alcohol are extremely gratifying will be more likely to use the drug again than those whose initial reaction is neutral or negative. Individuals who are homozygous for the aldehyde dehydrogenase allele (approximately 35% of the Chinese population, and 20% of Jewish males in Israel) have an especially unpleasant initial reaction to alcohol, and virtually no alcoholics have this genotype.

**DRUG INDUCED CHANGES IN BRAIN FUNCTION**

Anatomically, the brain circuitry involved in most of the actions of addictive drugs is the ventral tegmental area connecting the limbic cortex through the midbrain to the nucleus accumbens. Neurochemically, alcohol, opiates, cocaine, and nicotine have significant effects on the dopamine system, although through different mechanisms. Cocaine increases synaptic dopamine by blocking reuptake into presynaptic neurons; amphetamine produces increased presynaptic release of dopamine, whereas opiates and alcohol inhibit dopamine neurons producing increased firing rates. Opiates and alcohol also have direct effects on the endogenous opioid and possibly the γ-aminobutyric acid systems.

The ventral tegmental area and the dopamine system have been associated with feelings of euphoria. Animals that receive mild electrical stimulation of the dopamine system contingent on a lever press will rapidly start to press that lever again and again, ignoring normal needs for water, food, or rest. As such, cocaine, opiates, and several other addictive drugs produce supernormal stimulation of this reward circuitry.

**SOCIAL CONTEXT**

External stressors are important environmental factors contributing to the development and relapse of addiction. Environmental factors include prenatal and perinatal events; events occurring in early childhood; and later events, such as peer pressure, drug related cues, conditioning, setting for drug self-exposure, and concomitant ongoing psychiatric disorders, such as depression or anxiety. For example, repeated pairing of a person (drug-using friend), place (bar, casino), thing (paycheck), or even an emotional state (anger, depression) with drug use can lead to rapid and entrenched learning or conditioning. Thus, in drug-dependent individuals who have been abstinent for long periods, an encounter with a person, place, or thing that previously was associated with their drug use, may produce a strong physiologic reaction, such as withdrawal-like symptoms, and a profound subjective
desire or craving for the drug. These responses can fuel the “loss of control” that is considered a hallmark of drug dependence.26

The etiological factors mentioned above influence both the initial and early perception of a self-administered drug and contribute to the progression from occasional to intermittent or regular use and addiction, or, alternatively, to early cessation of drug use.8,30,31 A variety of personality factors and traits may also contribute to initiation of drug abuse, including impulsivity and risk-taking, as well as intrinsic atypical stress responsiveness.8

**SOMATIC CO-MORBIDITY**

It has been estimated that HIV-seroprevalence is 52.4% among Indonesian IDUs.32 Because of addiction, drug users change their behavior, without regard to the potential or actual negative consequences.8 Because of this, transmission of HIV remains a major public health challenge in persons who use illicit psychoactive drugs in many countries.33 In Indonesia, the recent Integrated Biological-Behavioral Surveillance conducted among most-at-risk groups in 2007 showed that many IDUs in six cities had shared needles in the week prior to the interview, ranging from 9% in Semarang to 63% in Jakarta.34

Transmission of HIV and other viruses through sexual behavior may be equally important. Pisani et al. (2003) reported that in three big cities in Indonesia, over two thirds of IDUs were sexually active, 48% reported multiple partners, and 40% had bought sex from a female sex worker in the preceding 12 months. Consistent condom use was reported by 10%.35 The results from the Behavioral Surveillance Survey 2004-2005 showed that 96-99% of IDUs in several cities in Indonesia had multiple sex partners in the past year. Most of them knew that using condom can prevent HIV-transmission but only 25-38% used condoms in the last sexual contact with a sex worker, and only 10-29% of IDUs use condom consistently in the last year.36,37 This situation is not unique for Indonesia. In the Netherlands, which has a very effective harm reduction program, unprotected sex leads to continued HIV transmission among IDUs.38 Finally, former IDUs, compared with current IDUs, are more likely to have sexual contacts with people who do not use drugs39-42 may also bridge the HIV-epidemic among IDUs’ to the low prevalence non-drug-using general population.39,43

Besides the risk behavior, direct effect of opioid on the immune system may increase both the risk of HIV infection and disease progression.44,45 Opioid administration affects both innate and adaptative immunity, such as antibodies production, natural killer activity, cytotoxicity, cytokine production, chimiotaxism, and phagocytosis.44,45 Morphine is also known to activate the hypothalamic-pituitary-adrenal axis and release glucocorticoid, which is immunosuppressive.46 Besides, the ability of MOR activation to induce CCR5 expression suggesting MOR agonists, such as morphine, may promote susceptibility to HIV-1 infection and disease progression associated with this infection.47

Other medical conditions which are common among IDUs are viral hepatitis, liver disease, and bacterial infections like endocarditis, pneumonia and tuberculosis. Four factors contribute to drug users’ risk for medical conditions. First, illicit drugs may have direct toxicity. Second, certain risk behavior. Third, lower access to health service due to the stigmatization. Fourth, social-economic disadvantages lead to malnutrition. Another contributing factor is when drug users experience withdrawal symptom. IDUs in ARV treatment and experiencing withdrawal symptoms had a fivefold increased risk of death with respect to the others.48 Finally, disruption of daily routines by active drug use (impending self-care behavior such as medication adherence or appointment keeping), may adversely affect their health status.

**PSYCHIATRIC CO-MORBIDITY**

Besides somatic problems, IDUs may also have more psychiatric disorders. A study among methadone patients in The Netherlands reported a concurrent prevalence of co-morbidity of psychiatric disorders of 59.3%.49 Preliminary data in Bandung showed that more than one-third of methadone maintenance treatment (MMT) patients may have some kind of psychiatric problem (Hidayat, unpublished data). Some studies showed that drug use disorders had strong associations with mood, anxiety, and personality disorders. Axis I and II comorbidity with drug use disorders has been associated with underachievement, decreased work productivity, poor health, neuropsychological impairment, human immunodeficiency virus infection, hepatitis, social dysfunction, violence, incarceration, poverty, homelessness, a lower probability of recovery, poor treatment outcome, and poor quality of life.5,8,11,26,50-52

These social consequences are important in shaping the generally held view that drug dependence is primarily a social problem that requires interdiction and law enforcement rather than a health problem that requires prevention and treatment.26 The high drop-out, non-compliance, and relapse rates during and after
There are 4 goals to be distinguished: the treatment should consider the complexity of IDU's like the other chronic diseases. The type and the goal of illnesses. That is why, drug dependence has to be treated adherence and relapse rates are similar across these hypertension, and asthma showed that medication dependence versus type 2 diabetes mellitus, patients only received detoxification. A review on drug with acute problems only, and as a result many addicted each kind of drug has its own characteristics, prevention of spread of viral blood borne infections among IDUs could benefit from tailoring interventions according to the type of drug used.

PREVENTION AND TREATMENT

For effective control of HIV in Indonesia, both prevention and treatment of addiction are important. Preventive programs to those with high susceptibility to addiction should be started at an early age by giving information, education, communication, and developing learned behavior techniques such as life skill training, cognitive behavioral therapy, etc. For those who have become addicted, optimal care should be delivered. Since each kind of drug has its own characteristics, prevention and relapse rates are similar across these illnesses. That is why, drug dependence has to be treated like the other chronic diseases. The type and the goal of the treatment should consider the complexity of IDU’s problem. There are 4 goals to be distinguished:

1. Palliation; Palliation is aimed to reduce symptoms and to relieve suffering from chronic dependent patients of whom no care or cure is feasible.
2. Care and stabilization, represented by maintenance treatment and based on harm-reduction. It is directed toward reducing illicit drug use, drug-related criminality and health problems, ultimately resulting in improved health and social functioning.
3. Cure, represented by abstinence-oriented treatment aimed at stable abstinence and ultimately resulting in recovery from addiction. This goal contains two treatment phases, namely detoxification and relapse prevention.
4. Crisis intervention. Crisis intervention is aimed at immediate survival and frequently necessary after a high overdose rate.

Therefore, the approach should be started by screening. Screening is performed to evaluate the possible presence of a particular problem. Further assessment is continued for those who have has problems. Assessment is used for defining the nature of that problem and developing specific treatment recommendations for addressing the problem. The assessment and diagnostic processes are important and should be as the basis for determining the treatment plan. The treatment plan should be made by integrating evidence, therapist knowledge and appraisal, and the patient preferences. (Table 1) All of these steps have to consider the drug use, somatic and psychiatric comorbidity of the patients. Treatment for somatic comorbidity is described for the Indonesian setting in two publications.

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<th>Table 1. Diagnostic and treatment process</th>
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<td><strong>Screening</strong></td>
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However, as in treatments for other chronic disorders, the major problems are medication adherence, early drop-out, and relapse among drug dependent patients. In fact, problems of poverty, lack of family support, and psychiatric co-morbidity were major and approximately equal predictors of noncompliance and relapse across all chronic illnesses. The best outcomes from treatments of drug dependence have been seen among patients in long-term methadone maintenance programs and among the many who have continued participating in support groups.

CONCLUSION

The biopsychosocial approach does not consider one intervention superior above other ones. On the contrary, a combination of biological, psychological, sociocultural...
interventions has to be implemented together according to the individual needs and problems of the patients. Failure in providing such a comprehensive treatment will worsen the overall condition of the patients. From a public health view, it will reduce the effectiveness of HIV/AIDS intervention programs.

REFERENCES