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Scientific review

ADVERSE EFFECTS OF SUBSTANCE ABUSE OVERDOSE AND POISONING

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Abstract: The symptoms and signs of substance abuse overdose and poisoning by some chemicals (cannabinoids, amphetamine, cocaine, and opioids) and drugs (anabolic steroids) are described in this paper, ingested for the purpose of achieving mood alteration or better sports results. Hashish and marijuana can cause toxic psychosis, along with confusion, disorientation, hallucinations, tension or depression and panic and fear attacks, as well as somatic disturbances, a shortness of breath, heart palpitations, dry mouth, conjunctiva hyperemia and an unsteady gait. Cocaine and amphetamine overdose have a toxic effect on all organs, especially the brain and the heart. The first to be manifested is agitation and mydriasis, and later on, hypertension, tachycardia, chest pain like angina pectoris, dilated pupils and hyperthermia. Convulsions are possible as well. Opioid overdose or poisoning (heroin and morphine-like substances) displays three typical signs: a) from disorientation to drowsiness and coma; b) irregular breathing, and c) constricted pupils. The poisoning is often accompanied by hypotension, bradycardia, hypothermia and a lack of urination due to bladder atony. Regarding sports stimulants, the greatest adverse effects on human health are caused by anabolic steroids. Their abuse leads to various sexual disorders, and with adolescents a stunted growth of the long bones.
Acute poisoning caused by substance and psychotropic substance abuse is a crisis situation. The standard principles and methods that are accepted in emergency medicine, with some specificities for acute poisoning, are applied in the diagnosis and treatment. Treatment with psychologists and psychiatrists is necessary.

Keywords: *medicaments, substance abuse, overdose, acute poisoning, treatment*

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INTRODUCTION

Some drugs and chemicals are used for mood alteration or to achieve better results in sports and business life. Due to these substances being used in a manner that is not socially acceptable, they are called 'resources abuse.' In sports, some of these funds are called doping agents because they are 'able to artificially increase the working capacity, which is contrary to sports ethics, as well as the physical and mental integrity of athletes.' Their use may eventually lead to physical and/or psychological dependence, sometimes accompanied by incidents: various involuntary actions, and overdose or acute poisoning, which can cause serious medical and social problems. Particularly dangerous is acute poisoning presented by a severe clinical picture, followed by complex treatment, complications, permanent sequelae and mortality (True et al., 2005). The last twenty years has seen a gradual increase of the number of those with substance misuse.

Substances that can cause mental and physical dependence or can be used for mood alteration are cannabinoids, cocaine, amphetamine and its derivatives, opioids and substances used in order to achieve better results in sports competitions (Pumareiga et al., 2014).

Marihuana and hashish (cannabinoids)

Marijuana and hashish, known under the name as cannabinoids, have been used for mood alteration for centuries. In some countries their use is legalized, and they are consumed by smoking, chewing and ingesting. Overdose mortality is rare, but there are significant toxic effects in acute and chronic use.

Marijuana and hashish are obtained from the plant called Indian hemp (Cannabis indica), but in Serbia, there is one of its varieties, called hemp or Cannabis sativa. The plant contains about 400 compounds, of which sixty belong to the psychoactive cannabinoid group. In the pharmacological and toxicological sense, the most significant is tetrahydrocannabinol (THC). Marijuana contains 1-5%, hashish in the form of resin 5-15%, and in the form of oil up to 30-60% tetrahydrocannabinol.

When smoking marijuana, the effects of THC manifest themselves after 2-3 minutes, reaching a maximum after 10-20 minutes and lasting 90 to 120 minutes. If ingested, the effect occurs after 30-60 minutes, reaching a maximum after 2-3 hours and lasting 3-5 hours. The half-life of THC is 28-56 hours and it is eliminated in the feces and urine.

The adverse effects and signs of poisoning occur after the first use or in the case of excessive use. It is most commonly manifested as acute toxic psychosis with confusion, disorientation, hallucinations, extreme tension

or depression and panic and fear (Benowitz, 2012). This is accompanied by the following somatic disorders: rapid breathing, palpitations, chest pain, dry mouth, eye irritation, conjunctival hyperemia, dipoplia, photophobia, blepharospasm, and disturbances of the vision and an unstable gait. The ECG registers sinus tachycardia, and interference repolarization is possible. The effect never last more than 24 hours.

Chronic toxicity is manifested by discrete symptoms and signs: red eyes, a cough, decreased motivation for learning and work performance, lower memory and the loss of a sense of fine motor skills. With long-standing users, chronic bronchitis and a reduced pulmonary function are common, and some users develop endocrine disorders: the level of testosterone is reduced as well as spermatogenesis (formation of spermatozoa) in men, while women have disrupted menstrual cycles and ovulation. There is no clear evidence that all this affects reproduction or the possibility of conception. Pregnant women should abstain from cannabinoids, as they cause fetus weight and growth loss, but can also cause some damage on the cellular level. Children whose mothers used hashish or marijuana during pregnancy have a higher risk of nonlymphoblastic leukemia.

A toxicological-chemical analysis can detect metabolites of THC in the plasma, urine and stool seven days after taking cannabinoids.

The treatment of acute toxicity in these patients lasts approximately 24 hours and consists in the application of a sedative of the benzodiazepine type and rehydration therapy.

Cocaine

Cocaine is a sympathomimetic which very strongly stimulates the brain and acts as a local anesthetic. It is consumed by sniffing, ingestion, smoking and intravenous application. After smoking, snorting and intravenous consumption, the effects occur immediately, and after ingestion the effect occurs after 30 minutes. The half-life is 30 to 90 minutes.

In acute poisoning, overdose and in the case of chronic use, there is toxicity in all organs, especially the brain and heart (Benowitz, 2012). First, there is tension, agitation and mydriasis, and later hypertension, tachycardia and hyperthermia. Convulsions are also possible. As a result of hyperthermia and increased physical activity because of psychomotor restlessness, there is muscle damage and rhabdomyolysis, although most usually there are no subjective complaints in the locomotor system.

'Body packers' is a standardized concept for people who ingest wrapped packets of illicit drugs such as cocaine, heroin, amphetamines, etc. to transport them by internal concealment (Ellenhorn, 1997). Unless the packets of drugs in the stomach are ruptured, then cocaine transporting most

often do not lead to accidents. However, if there is a leakage and rupture of the packets, then there are drug-induced toxic effects and severe poisoning and such patients require intensive care, often ending fatally.

In chronic use, cocaine accelerates atherosclerosis, left ventricular hypertrophy and heart thrombus formation in blood vessels. This creates conditions for the formation of myocardial ischemia and myocardial infarction, but other organs as well: the kidneys, eyes, bowel and lungs and therefore, there are frequent complications of said organs. There is a serious suspicion that a young and previously healthy person is taking cocaine if it is determined that there is simultaneous damage to multiple organs.

As for treatment, it is most important to control and maintain vital functions. Psychomotor restlessness, convulsions, hypertension and tachycardia are alleviated by using benzodiazepine sedatives. In acute myocardial infarction or pulmonary edema, the standard therapy for the treatment of these patients is applied. Hyperthermia is treated with external cooling.

Amphetamines

Two groups of amphetamines are significant from a toxicological aspect:

a) The derivates of amphetamines, which include methamphetamine, phentermine, phenmetrazine, fenfluramine, methylphenidate, phenylpropanolamine and ephedrine, and
b) Hallucinogenic amphetamines, which include methylenedioxyamphetamine (MDA), methylenedioxymethamphetamine (MDMA or ecstasy), methyl diethanolamine (MDEA), mescaline and 4-methyl-2-5-dimetoxyamphetamine.

Amphetamines (such are MDMA, MDEA, and mescaline) in high doses lead to a release of serotonin, which in turn causes hallucinations. Amphetamines are consumed by ingestion, inhalation, smoking or intravenously. The effect lasts 12 to 24 hours.

The main toxic effects of amphetamines affect the cardiovascular and central nervous system, similar to cocaine. The dominant signs are elevated blood pressure, an increased heart rate, dilated pupils, convulsions, and a high fever (Albertson, 2012).

The signs which indicate a long-term use of amphetamines are persistent sneezing and nasal mucosa hyperemia while snorting; in the case of intravenous injection, there are visible needle traces and a painful redness in the elbow crease; tics and other involuntary movements.

The withdrawal syndrome in amphetamine addicts is manifested as psychological tension, stomach cramps, headache, drowsiness and depression.

Treatment is carried out after an assessment of the vital functions. Special attention is given to arterial blood pressure and the heart rate. Agitated patients should be sedated by intramuscular or intravenous benzodiazepine sedatives and hypnotics.

The cause of death in amphetamine overdose is cardiac arrhythmias, convulsions and hypertension with complications (myocardial infarction or bleeding in the brain).

Opioids

This is a group of alkaloids that has an effect similar to opiates or morphine. Today, they are in the form of natural, semi-synthetic, synthetic and mixed agonist/antagonist preparations. The term 'opiates' includes natural ingredients-agonists such as morphine and codeine and semi-synthetic opioids. Polysynthetic opioids are obtained by structural changes of morphine. The most famous are heroin, hydromorphone, oxymorphone and oxycodone. Synthetic opioids are obtained by artificial synthesis, such are meperidine, methadone, diphenoxylate, fentanyl and propoxyphene. Opioids which have properties of both agonists and opiate antagonists are buprenorphine, nalorphine and pentazocine.

Opioids are used in medicine as analgesics and anesthetics, but they have been used for mood alteration from ancient times. Therapeutic and toxic actions are exerted through specific places - opioid receptors, located in the brain.

Opioids are ingested into the organism by parental and peroral administration and by inhaling.

In poisoning or opioid overdose, there are three typical signs: a) from disorientation to drowsiness and coma; b) irregular breathing, and c) extreme myosis, or excessive constriction of the pupils, whose size is sometimes compared to a small point or a pinpoint. Due to insufficient breathing and poor perfusion of blood and oxygen tissue, the patient is often cyanotic ('blue as a plum'), which is a sign of a seriously impaired breathing function. This is a bad prognostic sign for the ultimate outcome or survival, and if tissue hypoxia, especially of the brain and the heart lasts long, then there are lasting consequences. Poisoning is often accompanied by hypotension, bradycardia, hypothermia, and inability to urinate due to urinary bladder atonia. In a small number of cases, lung damage progresses to non-cardiogenic pulmonary edema, or acute respiratory distress syndrome (ARDS), which, despite acute poisoning, endangers patient vitality and requires a highly effective treatment in the intensive care unit (Albertson, 2012).

A toxicological-chemical analysis of urine can be used to check for different opioids and their metabolites. The easiest ones to verify are heroin, morphine, codeine, or their metabolites, in the first 24 hours of poisoning.

Treatment should begin immediately. The vital signs should be checked, and if necessary, cardiopulmonary resuscitation performed. Particularly effective in treatment is the antidote naloxone (Narcan, Narcanti), which is a pharmacological antagonist for opiates. It displaces opioids from receptors in the brain that have bound and very quickly, within 30-60 seconds, they cancel the toxic effects.

Performance enhancing drugs

This group includes a number of natural and synthetic substances that are used as stimulants in sports in order to achieve better results. These are anabolic steroids, certain peptides and glycoprotein hormones which have the characteristics of stimulants, diuretics, marijuana, corticosteroids, beta adrenergic receptor stimulators, beta adrenergic receptor blockers and narcotics (Dikić, 2013).

From all the above, the substances which have the most adverse effects on human health are anabolic steroids. They are usually in the clinical practice administered as medicaments in the treatment of hypogonadism, anemia, and chronic endometriosis.

In sports, the most commonly used preparations are consumed orally and are mainly derived synthetically, such as methandrostenolone, oxandrolone, stanozolol, oxymetholone and methyltestosterone. Esters of nandrolone, testosterone and metenolone are used for intramuscular administration.

Anabolic steroids increase muscle mass and strength and are usually used by young men. According to research in the US and Canada, from a survey of a few thousand students, from 2.8% to 6.6% used anabolic steroids. Taking the recommended dose once should not be risky, but a multiple dose or long-term use of the recommended dose can seriously damage the health.

Clinical manifestations of long-term use or poisoning with anabolic steroids are effects on androgen receptors (male sex hormone) and estrogen (female sex hormone). In men, they lead to atrophy of the testicles, reduction in the number of sperm, enlargement of the prostate, and growth of the breasts. Women lose their menstrual period, suffer from hair loss, form male-type malformations, display clitoris increase, while the voice becomes deeper and more rough. With adolescents, the long bone growth ends before its time.

The main symptoms of poisoning are arterial blood pressure jump, weakening of the contractile force of the heart, psychic alterations, liver damage, changes in the hormonal status, the occurrence of diabetes, the development of atherosclerosis and increase in cholesterol levels. Myocardial infarction in young athletes is most often the result of anabolic steroid abuse.

Psychologically, there are changeable moods, pronounced aggressiveness, depression and in some cases serious psychosis.

During physical exertion, injuries of the muscles and tendons are common, and sometimes ruptures occur as well. Less significant adverse effects of anabolic steroids are acne, hair loss, stretch marks on the skin of the trunk and extremities and increased secretion of the sebaceous glands. Due to water retention and salt increase, swelling occurs, especially of the shins and ankles. The level of immunoglobulin and the thyroid hormone is reduced.

How to suspect someone is using anabolic steroids? Men are well-developed, with pronounced acne on the face and the skin of the back, breast enhancement that is different from well-developed pectoral muscles and suspected of parental (intravenous or intramuscular) drug use. Women have deep voices, facial and back acne, increased body hair, a male type of baldness, and a face that resembles a male one (rougher lines and a visible growth of beard and mustache).

Urine testing by gas chromatography and mass spectrometry can be used to determine the testosterone and epitestosterone ratio. Epitestosterone is an inactive testosterone metabolite that is excreted in the testicles, but does not stimulate testosterone metabolism. The normal relationship between testosterone and epitestosterone in both men and women is 1:1. If this ratio is greater than 6:1, then this is a sign of androgenic steroid abuse.

Treatment of acute poisoning is performed in a hospital setting if there are severe manifestations and complications such as a heart attack, stroke or depression with suicidal ideas. These diseases are treated in the usual and standardized way, although in their pathogenesis there is chronic abuse of anabolic steroids. It is necessary to immediately stop the continued use of anabolic steroids, and include psychologists and psychiatrists in the process of treatment and withdrawal.

Simultaneous abuse of harmful substances and combined poisoning

With those who abuse drugs or take illicit stimulants, it should always be borne in mind that there is the possibility of simultaneous use of multiple substances or drugs (Todorović, 2006).

Polymedication poisoning occurs due to the simultaneous poisoning by different drugs, and the combined poisoning in the case of simultaneous overdose with two or more different harmful chemicals, of which one of the agents may be a drug. These poisonings have a particular clinical significance because they involve a simultaneously consumption of different chemical structures and action mechanisms which may be accompanied by synergistic or antagonistic action, addition or potentiating toxic effects, and this to a considerable degree can modify poisoning. This poisoning often has a worse

prognosis than acute poisoning individual agents. Particularly risky are concomitant drug poisoning of different groups of psychotropic drugs with abuse agents, such as heroin, cocaine, methamphetamine, marijuana and hashish (True et al., 2005).

The principles of diagnostics and treating substance abuse

A systematic and thorough approach to the patient is a prerequisite for a timely diagnosis. It includes the detailed history and heteroanamnesis, a clinical examination during which a neurological examination is carried out, toxicological-chemical analysis, biochemical parameters of the blood and urine, some target biochemical analyses, and optionally other additional diagnostics (native X ray of the abdomen, a chest and lungs X ray, endoscopic examinations) (Ellenhorn, 1997).

Since acute poisoning belongs to a specific group of crisis situations, it is necessary to control the vital functions of the patient upon first contact (a patent airway, quality and sufficiency of breathing, cardiac activity and a state of consciousness), and take the necessary measures.

In diagnostics and treatment, the standard principles and methods that are accepted in emergency medicine are implemented, with some specificity for acute poisoning (Bred et al., 2014).

All those assumed to be suffering from substance overdose and poisoning should be recommended further treatment by a psychiatrist (Chacravarthy et al., 2013). In the case of minors, the parents should be informed of everything. All cases of acute poisoning with substance abuse must be reported to the police. Particular attention should be paid if there is suspicion of attempted murder or suicide, in the case of minors or if the circumstances of poisoning are unclear.

CONCLUSION

Substance and psychoactive substance abuse is a serious medical and social problem due to frequency, creating mental and/or physical dependence, overdose or acute poisoning, complex and long treatment, but also, in severe cases a fatal outcome is possible. This applies particularly to minors and young adults. They are very important preventive medical and social dimensions, and with drug users or outpatients, hospital multidisciplinary treatment should be applied.

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