Patologie 1-07 8.1.2007 13:00 Str. 21
proLékaře.cz | 27.10.2026

Severity of Opiate Intoxication to Gender and Age

Shigeev S.

Department of Forensic Medicine Faculty of Medicine People's Friendship University of Russia

Summary

The paper presents the toxicological characteristics of 198 cases of acute parenteral heroin intoxication in the whole range of concentrations of their metabolites, which are encountered in practice. An attempt was made to estimate the risk of death within possible blood morphine concentrations in acute heroin intoxication, by taking into account gender- and age-related differences. The median lethal morphine concentration (LD_{50}) has been found to greatly differ in males (0.78 µg/ml) and females (0.98 µg/ml) and in those aged under (0.39 µg/ml) and above (1.50 µg/ml) 25 years. At the age under 25 years, most victims show nearly the same response in the narrow range of concentrations (LD_{50} = 0.39 µg/ml; LD_{100} = 1.57 µg/ml); in persons above 25 years of age, there are great individual differences in their sensitivity to the concentration of a toxic substance (LD_{50} = 1.50 µg/ml; LD_{100} = 3.90 µg/ml).
Key words: morphine – morphine concentration – opiate intoxication – toxicity criteria

Souhrn

Závažnost intoxikace opiáty v závislosti na věku a pohlaví

V práci jsou uvedeny toxikologické charakteristiky 198 případů akutní parenterální intoxikace heroinem a úplný seznam koncentrací jejich metabolitů, které se používají v praxi. Byl učiněn pokus stanovit riziko úmrtí při určitých koncentracích morfinu v krvi u akutní intoxikace heroinem v závislosti na věku a pohlaví. Bylo zjištěno, že střední smrtná koncentrace morfinu (LD50) se významně liší u mužů (0,78 µg/ml) a u žen (0,98 µg/ml) a u osob mladších (0,39 µg/ml) a starších (1,50 µg/ml) 25 let. Při věku nižším než 25 let, většina obětí vykazuje téměř totožné reakce v úzkém rozmezí koncentrací (LD50 = 0,39 µg/ml; LD100 = 1,57 µg/ml). U osob starších než 25 let jsou velké individuální rozdíly v jejich citlivosti na koncentraci toxické látky (LD50 = 1,50 µg/ml; LD100 = 3,90 µg/ml).

Klíčová slova: morfin – koncentrace morfinu – intoxikace opiáty – hranice toxicity

Soud Lék., 52, 2007, No. 1, p. 21–24

Introduction

In the past two decades, the spread of narcotic drug abuse has increased to the extent that addiction has now attained epidemic proportions in many countries and cities. The most commonly used narcotics are opiates and their semisynthetic analogues with actions similar to those of opiates – opioids [4, 7], the more frequently abused one being heroin [3, 5]. Women and children are also involved in the usage of narcotic and psychoactive agents.

It is known that in relation to gender and age, the body's functional status can enhance, reduce, or pervert tolerance of a toxic substance. This statement is supported by forensic medical and clinical practices, laboratory studies showing that the same toxic agent can cause individually varying reactions, all other things being equal, since the body's resistance to poison depends not only on its quantity (dose) and quality, but also on different characteristics of the body's status. The relationship of the body's resistance to poisons to gender and sex is very important in terms of the biological characteristics of the body and the toxic effects of xenobiotics.

Materials and Methods

Case records of 198 inpatients treated in the intensive care units of Moscow city hospitals for acute parenteral opiate intoxication were studied. Their mean age was 24.5 years (16-56 years); most of them were males (83.8%; 166/198). There were 35 (17.7%) females. By taking into account

Patologie 1-07 8.1.2007 13:00 Str. 22
proLékaře.cz | 27.10.2026

the high ability of heroin to cause physical dependence that develops within on an average of 1.5-3 months of its intravenous injection, it can be stated that most of the examinees were chronic drug addicts. According to age, all the victims were divided into 2 groups: those under 25 years of age (n = 117) and those above 25 years (n = 81) in an effort to identify persons with a high or low tolerance of opiates.

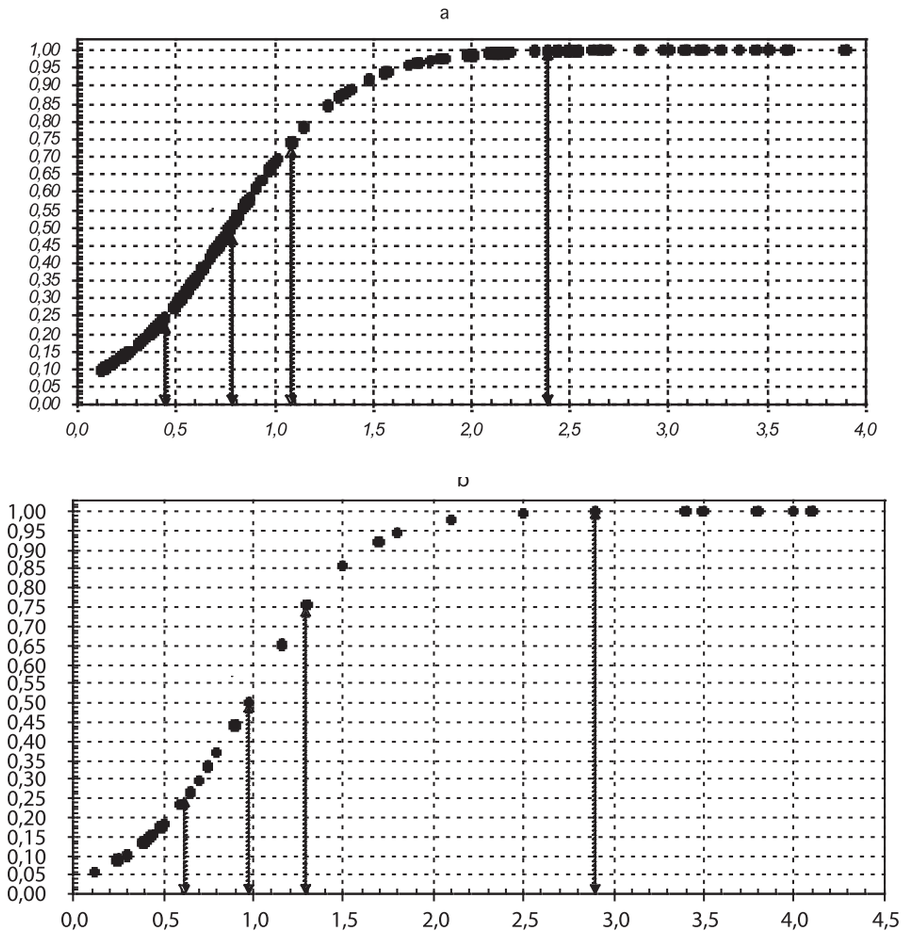


Fig. 1. Death probability (as ordinate in terms of conventional units) against blood morphine concentration (as abscissa, μg/ml): a – males (n = 163); b – females (n = 35).

While examining the clinical material, the chief condition was the accuracy of a final condition, which was based on the chromatographic mass-spectrometric determination (LC/MS method, a GCMS-Qp5050 device (Japan)) of the type and blood concentration of a narcotic agent and its metabolites. Morphine was detected in the blood of all victims (100%); the urine contained the major marker and metabolite of heroin – 6-0-monoacetylmorphine.

On describing the central distribution trends, the median (Me), maximum (max), and minimum (min) values were estimated, by presenting the results as Me (min-max). By determining the correlation between the parameters, the Spearman rank correlation coefficient (r_s) was employed. The correlation coefficient ≥ 0.3 (95% CI) was considered significant. The criteria for quantitative toxicity, which are lethal doses (LD_{25}, LD_{50}, LD_{75}, and LD_{100}, were determined by the least squares estimator using the probit analysis. In our case, we used a logit-regression belonging to the nonlinear estimation methods when a response was taken as only two values (0 – "alive" or 1 – "dead"). In our study, the method was based on the assumption that there was a functional relationship between the dependent (the occurrence of death) variable and the independent one (the concentration of metabolites), which we attempted to establish. The findings were used to estimate death probability in a varying range of concentrations. During pharmacological and toxicological studies, a reasonable estimate of the activity of an agent is known to be achieved in some cases when a response to this substance in its alternative form is taken into account. The alternative reaction is the reaction that occurs or does not occur and that may be surely identified by an investigator, in our case, this is "alive" or

Patologie 1-07 8.1.2007 13:00 Str. 23
proLékaře.cz | 27.10.2026

"dead", that is to say "all-or-non reaction" in the foreign literature. The alternative form of taking into account the effects may provide a more accurate characterization of the activity of a test toxic substance.

Results

Blood toxicological studies of inpatients (n = 198) for acute poisoning detected morphine (1.5 μg/ml (0.1-4.1 μg/ml)) in all cases (100%). Forensic chemical studies of blood, urine, and viscera from those who had died from intoxication (n = 55) within the first 48 hours after admission revealed morphine only in urine (4.4 μg/ml (0.06-12.0 μg/ml)) just in 58.2% of cases (32/55); in other cases (41.8% of the 55 victims), toxicologically important substances were not revealed in all study media.

The toxic effects of opiates on males and females were evaluated in all age groups, by using the calculated death risk-blood morphine concentration ratios presented as plots (Fig. 1 and 2).

The mean blood morphine levels were 0.8 μg/ml (0.1-3.9 μg/ml) in males (n = 163) and 0.8 μg/ml (0.1-4.1 μg/ml) in females (n = 35). The results suggest that the probability of fatal opiate poisoning is less in females than in males (Fig. 1). In males and females, the scatter of the most commonly used concentrations is nearly the same, the change in the probability of death due to opiates, which is associated with the altered concentration of their metabolites (the curve slope), suggests that most victims will respond nearly equally in the narrow range of their concentrations (up to 2.0 μg/ml); however, the risk of severe complications and death is much higher in males (the plot curve is shifted to the left). The critical blood morphine concentration (LD_{50}) is 0.98 μg/ml in females and about 1.2 times less (0.78 μg/ml) in males. In the range of high con-

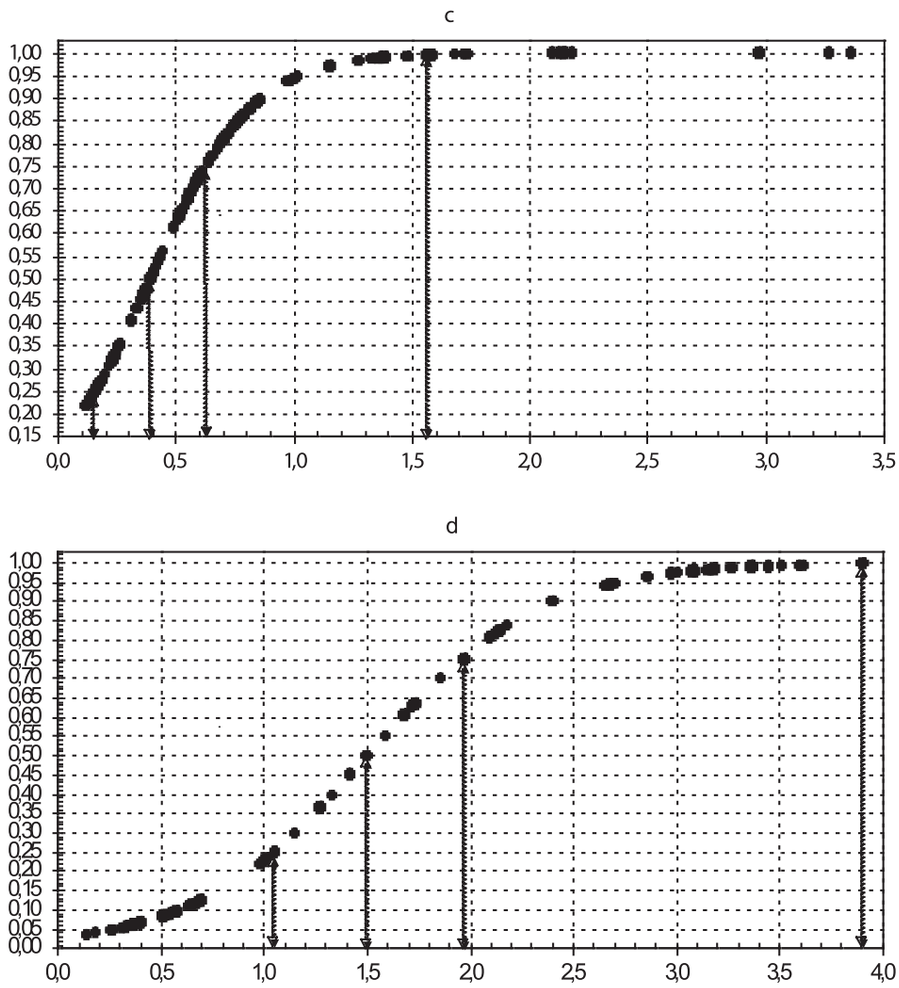


Fig. 2. Death probability (as ordinate in terms of conventional units) against blood morphine concentrations (as abscissa, μg/ml): c – in those under 25 years of age (a low tolerance) (n = 117); d – in those above 25 years (a high tolerance) (n = 81).

Patologie 1-07 8.1.2007 13:00 Str. 24
proLékaře.cz | 27.10.2026

centrations, the female body shows a high resistance to opiates, as exposure to chemical increases, gender-related differences in survival rates gradually become equal.

The body's sensitivity to toxic substances changes throughout life. This is due to the processes of tissue development, maturation, and differentiation, to age-related features of the morphology, physiology, and biochemistry of organs and systems. The pattern of tissue vascularization, the permeability of blood-tissue and other barriers, and the functions of the nervous, endocrine, and immune systems undergo great changes in different periods of the body's development and life. Our results suggest that the probability of fatal opiate poisoning is highest in persons aged under 25 years (Fig. 2). The mean blood morphine levels was 0.6 µg/ml (0.1-3.4 µg/ml) in victims aged less than 25 years (n = 117) and 1.15 µg/ml (0.1-3.9 µg/ml) in those aged above 25 years (n = 81).

When parenterally administered, opiates show different toxicities in persons aged under and over 25 years. The action of toxic concentrations of opiate metabolites depends on age: the older a victim (but as the case in point is chronic drug addicts, tolerance as well) is, the higher resistance to them is. For example, the morphine level of 0.5 µg/ml is still conventionally safe (much less than LD_{25}) for persons who are above 25 years old, but at the same time it approaches LD_{50} for those who are less than 25 years old, by corresponding to the critical level. In the age group under 25 years, the curve is noticeable shifted to the left. That is to say that the risk of death in persons aged less than 25 years is much higher in the narrow range of blood morphine concentrations (LD_{25} = 0.15 µg/ml, LD_{75} = 0.62 µg/ml, LD_{100} = 1.57 µg/ml) while in most cases in the age group above 25 years, the outcome of poisoning is uncertain (to the blood morphine level of 3.90 µg/ml (LD_{100}).

Discussion

Thus, the presented plots may be used to make an approximate estimate of the risk of death within all possible blood morphine concentrations, by taking into account gender, age, and opiate tolerance. The median lethal blood morphine dose (LD_{50}) significantly differs in males (0.78 µg/ml) and females (0.98 µg/ml) and in persons aged under and above 25 years (0.39 µg/ml and 1.50 µg/ml, respectively). Furthermore, the slope of the plots shows how great a change in the probability of death due to opiates will be with the changed concentration of their metabolites. The steep slope suggests that most victims will respond nearly equally in the narrow range of relatively low concentrations. This applies to victims of both sexes whose age is under 25 years (LD_{50} = 0.39 µg/ml; LD_{100} = 1.57 µg/ml). The flat slope indicates that there are great differences in the sensitivity to the concentration of a toxic substance in individual victims – these are persons aged above 25 years (LD_{50} = 1.50 µg/ml, LD_{100} = 3.90 µg/ml).

Conclusions

The foregoing suggests the necessity of having a critical appraisal of the positive results of a forensic chemical study as evidence for fatal opiate intoxication particularly due to the absence of unambiguous morphological equivalents of this pathology and to the ambiguity of toxicological parameters in acute and fatal poisonings [1, 2, 6].

References

1. **Baselt RC.** Disposition of Toxic Drugs and Chemicals in Man, 6th ed. Biomedical Publications, Foster City, CA; 2002.
2. **Druid H, Holmgren P.** A Compilation of Fatal and Control Concentrations of Drugs in Postmortem Femoral Blood. *J Forensic Science*. 1997;42: 79–87.
   Gerostamoulos J, Staikos V, Drummer OH. Heroin-related deaths in Victoria: a review of cases for 1997 and 1998. *Drug Alcohol Depend* 2001;61: 123–127.
3. **Hall WD, Degenhardt LJ, Lynskey MT.** Opioid overdose mortality in Australia, 1964-1997: birth-cohort trends. *Med J Aust* 1999;171:34-37.
4. **Oxman G, Kowalski S, Drapela L, Gray ES, Fafara S, Lyons H, et al.** Heroin overdose deaths-Multnomah County, Oregon, 1993-1999. *MMWR Morb Mortal Wkly Rep* 2000;49:633-636.
5. **Platt JJ.** *Heroin Addiction: Theory, Research, and Treatment, 2nd edition*, Robert E. Krieger Publishing Company, Malabar, Florida, USA; 1986.
6. **Solet D, Hagan H, Nakagawara J, Plough A, Ball J.** Unintentional opiate overdose deaths-King County, Washington, 1990-1999. *MMWR Morb Mortal Wkly Rep* 2000;49:636-640.

Dr. Sergey V. Shigeev, CSc.
Department of Forensic Medicine
Faculty of Medicine
People's Friendship University of Russia
21-67, Malysheva street, Moscow, Russia