PHENOBARBITAL MONITORING IN BLOOD, URINE AND SWEAT AND IMPORTANCE OF SWEAT EXCRETION IN TOXIC COMA PATIENTS

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ABSTRACT

The examination of sweat excretion for the presence of drugs is a promising clinical method. A monitoring of phenobarbital in the blood, urine and sweat in a 22-year old patient in a toxic coma was carried out. Blood and urine samples were taken on the 13th, 26th, 40th, 46th and 58th hour and on the 8th day after the intoxication. Sweat samples were taken on the 11th, 12th and 13th hour after the poisoning. The highest plasma phenobarbital concentration (of 31,82 mg/ml) was registered on the 13th hour. There was a considerable renal excretion (of 49,24 mg/ml). The large volume of phenobarbital distribution became evident on the 46th and 58th hour. After the second day the phenobarbital level in the blood and urine considerably decreased. The sweat phenobarbital excretion was significant on the 13th hour and corresponded to the peak plasma concentration of the drug. Therefore, this excretion after acute intoxication possesses an information and evidence value. Its expert assessment with the cases with drug poisoning in the forensic medical practice could be recommended.

Keywords: phenobarbital intoxication, sweat excretion, plasma concentration, urinary excretion

INTRODUCTION

Recently, the intoxications with benzodiazepines, sedative and hypnotic drugs from other classes, and antidepressants prevail in Bulgaria. Nevertheless, barbiturates certainly causing a severe or even fatal poisoning still occupy a dominant position according to their incidence rate.

Although there is plenty of publications in the literature available the extraordinarily unsatisfactory number of communications dealing with the chemical and toxicological monitoring control of the biological fluids in the patients with barbiturate coma and during the poisoning itself should be mentioned (7,18).

The examination of sweat excretion for the presence of drugs is not a common clinical method. It is known that the drugs enter the sweat glands from the surrounding blood vessels through a simple diffusion as this transport is possible for the free fraction only (10,11,16). There exists very scanty data about the elimination of xenobiotics with the sweat in acute poisonings. Detection of cocaine in the sweat excretion in drug-dependent patients after exposure cessation has been reported (1). The opportunity for toxic

substance removal in this way as well as its clinical importance remains, however, insufficiently clarified yet.

The purposes of the present work are to perform a monitoring of the phenobarbital concentrations in the blood, urine and sweat, to examine its excretion in the sweat and to prove its diagnostic importance with a toxic coma patient.

MATERIAL AND METHODS

The case of a 22-year old patient (patient's record No 799/05.XI.2002) in a toxic coma after the intake of 4,0 g of phenobarbital was presented. Poison depuration was accomplished by means of gastric washing-up, a 48-hour moderate to forced diuresis, and administration of nootropic drugs, vitamins of B group, and symptomatic agents as well. Stomach lavage fluids, blood and urine samples were examined at patient's admission to the Clinic of Toxicology, on the 5th hour after the poisoning. The monitoring of blood and urine for the presence of phenobarbital was carried out on the 13th and 26th hour as well as on day 2 (on the 40th and 46th hour), on day 3 (on the 58th hour), and on day 8 from the onset of the intoxication.

Taking the sweat samples was performed on the 11th, 12th and 13th hour after the poisoning when the patient was already in a comatous state. The sweat glands were stimulated with electric current of 4 mA for 15 min after pilocarpine application. The liberated sweat was collected

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on a preliminarily weighed filter paper consequently incubated with ethyl acetate for 24 hours after a modified method of Gibson and Cooke (4).

The identification and quantitative determination of the phenobarbital in the materials under examination were done by the liquid chromatographic method by using a Hewlett Packard apparatus of Series II 1090 provided with DAD.

RESULTS

The data from the analysis of the samples from the lavage fluids, blood and urine taken from the patient at hospitalization, 5 hours after the poisoning (under the conditions of superficial coma) as well as on the 13th and 26th hour after the poisoning (in a comatous state) are presented on Table 1. The amount of phenobarbital in the blood and urine has been followed-up after patient's liberation from the coma, i. e., on the 40th, 46th and 58th hour (in a state of toxic encephalopathy), and on day 8 when no clinical effects of phenobarbital action could be detected any more.

Table 1

Samples/Phenobarbital concentration	Time of examination after poisoning						
	5 th hour	13 th hour	26 th hour	40 th hour	46 th hour	58 th hour	8 th day
Blood serum (µg/ml)	28,80	31,82	15	21	3,90	18,48	7,72
Urine (µg/ml)	11,40	19,30	48	49,24	2,27	18,07	17,78

In the lavage fluids taken on the 5th hour after the poisoning there were no phenobarbital traces at all.

Table 2 demonstrates the amount of sweat in the single samples. On the 13th hour after the poisoning the sweat phenobarbital concentration is highest and corresponds to its peak plasma concentration (of 31,82 µg/ml) and the comatous state of the patient.

Table 2

Sweat samples	Time of examination after poisoning		
	11 th hour	12 th hour	13 th hour
Sweat amount (g)	0,3137	0,6322	0,3711
Phenobarbital amount (µg/ml)	5,68	5,59	11,72

DISCUSSION

It has been established that at patient's admission to the Clinic of Toxicology in a state of superficial coma there is no toxic substance in the washing-up fluids. It is well known that phenobarbital is characterized by a good re-

sorption in the gastrointestinal tract. In case of a toxic coma there is a longer period of retention lasting up to several days (12). In our case, because of the insufficient ionization of the drug (presenting as a weak acid) and its good lipid solubility, obviously, a rapid total resorption in the acid pH medium of the stomach has passed.

The peak plasma concentration of phenobarbital has been registered on the 13th hour. On the 40th hour the blood level remains comparatively high (of 21,00 µg/ml) and corresponds clinically to the soporous state of the patient. The parallel examination of the substance in the urine demonstrates a considerable renal excretion (of 49,24 µg/ml). The large volume of phenobarbital distribution becomes evident on the 46th and 58th hour. At the end of the second day when its sedimentation in the tissues sets in the phenobarbital level in the blood and urine considerably decreases. This reduction does not indicate the purification of the organism but displays only the redistribution of the drug from the central nervous system towards the peripheral tissues. This is one of the most significant peculiarities of barbiturate toxicokinetics (8,15,16). On the third day there is a sharp elevation of the phenobarbital concentration in the blood and urine as well (Fik's law of the balance of the poison in the extra- and intracellular environment). Clinically, the patient presents with manifestations of a toxic encephalopathy. The phenobarbital excretion continues until the 8th day from the onset of the intoxication without any apparent clinical effects. This phenomenon has been reported by other authors, too (7,17).

High-grade urinary excretion has been established at the end of the first and second day that corresponds to the detoxication treatment carried out, i. e., of forced diuresis.

The results from the examination demonstrate a significant phenobarbital excretion in the sweat samples analyzed. In the literature available data are paucity about the proof of phenobarbital in the sweat after acute poisoning (14). This does not allow the clearer definition of the clinical importance of this way of elimination of the toxic substances.

The amount of the excreted sweat differs in each case. In case of fever or warming this amount can increase by many times. In this way the sweat route of excretion enhances the opportunities for the purification of the organism. Markova (2004) suggest hypothesis, the elimination of the toxic substances through the sweat could, possibly, be involved in the pathogenesis of skin affections such as erythema, bullous dermatoses and necroses appearing early in the cases of toxic coma caused by barbiturates or other psychoactive drugs (6,13). Such a viewpoint is shared by some other investigators, too (2,3,5).

In the forensic medical literature a case of a young male has been reported where the cause for death has been established by using a toxicochemical analysis of his household linen capable of proving the presence of phenobarbital (Radoinova, 2002, personal communication). Initially, the falling of dust from the swallowed pills on the bed coverings has been considered, too.

Some investigations have shown that with the acute intoxications the drug having caused the poisoning can be proved

in the sweat of the comatous patients- amitriptyline, carbamazepine, diazepam, and leponex (9). These data allow us to accept that certain drugs fall through the sweat on clothes and coverings that could serve as material evidence in the medicolegal practice.

CONCLUSION

Drug toxicokinetics after over-dosage is characterized by a series of variances that define the specific course of the intoxication in any individual clinical case. Being familiar with them is an important precondition for the correct clinical management.

The sweat excretion of the phenobarbital and other drugs can be used not only for the reevaluation of the excretory depuration capacities of the organism but also for the explanation of the pathogenesis of skin lesions in toxic comatous states.

The established sweat excretion of the phenobarbital can possess an evidence value. An expert assessment of the cases with intoxications in the forensic medical practice is also possible when using the analysis of different tissues.

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