

## DETERMINATION OF TOXIC SUBSTANCES IN SWEAT SECRET OF SEVERE FORMS OF POISONING - TOXIC COMA. CLINICAL MEANING.

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### SUMMARY:

The aim is to investigation of toxic substances in sweat secret, blood and urine of patients with toxic coma. Study includes 4 patients in toxic coma, caused by: amitriptyline, diazepam, carbamazepine, amitriptyline and clomipramine. The concentration of the drugs substances is determined in sweat samples, collected after stimulation of eccrine sweat glands, using the pilocarpin ionophoresis - a modified method by Gibson and Cooc (1959), and in blood and urine, taken at the same time with the first sweat sample. The analytical procedure includes a separation of the drugs from the sample with organic solvent, concentrating the extract, followed by analysis of the extract with GC 5890-series II, equipped with MSD-5971 and LC 1090-series II, Hewlett Packard. We have proved that in all sweat samples drugs exist (amitriptyline, diazepam, carbamazepine, amitriptyline and clomipramine). The drug concentration in sweat, compared to blood and urine, is less in all samples..

**Key words:** amitriptyline, diazepam, carbamazepine, amitriptyline and clomipramine; sweat glands; toxic coma

### INTRODUCTION:

The determination of toxic substances in sweat secret is not a commonly used method. It is an alternative of the analytical methods using blood, urine, hair, nails, stomach secret to prove xenobiotics. Our knowledge about the information that this method may give us is exceptionally small. Very few laboratories in the world have been using it because of its labor-consumption and lack of information. In the clinical practice this method was used by sweat extract analysis of drug abusers for proving drug presence, long time after taking off cocaine (1). The sweat glands excrete many drugs and toxic substances: it is proved for barbiturates (9), broom and Jodi (6, 10), selen, talium, arsen (7) cocaine (1), alcohol, acetone, phenol, chalogenic carbohydrates (7). It is accepted that drug sweat excretion has small pathogenic meaning for forming excreting dermatoses - bromoderma and jododerma (6). According to Al. Monov (10) the process of sweat elimination (drug and toxic excretion) has formed skin topical damages. The aim

of study is to determination of toxic substances in sweat secret of patients with severe form of poisoning- toxic coma. Clinical meaning.

### MATERIAL AND METHODS:

The analysis includes 4 patients (P) in toxic coma after poisoning with amitriptylin (P 1), amitriptylin and clomipramin (P 2), diazepam (P 3), carbamazepin (P 4). Samples of sweat are taken at the 12-th, 16-th, 18-th, 24-th hour after swallowing the drug, caused the poisoning. Samples of sweat are taken from non-affected skin in forearm area. Simultaneously with the first sweat sample is taken blood serum and urine. Pilocarpin ionophoresis for sweat stimulation: This is Gibson and Cooc (1959) modified method (5). After washing and drying the inside and outside area at the right forearm, a tampon is put with 0.2% pilocarpin (inside) and 0.6% NaH<sub>2</sub>CO<sub>3</sub> (outside). The anode is connected with the pilocarpin's tampon and the cathode is connected with sodium bicarbonate tampon. Sweat secret is stimulated with 5 mA electricity for 15 minutes. After the stimulation the electrodes must be removed, the inside and outside area of forearm - washed and dried. Preliminary the filter paper (5891, Schleicher&Schnell, Germany) is weighted. The filter paper is placed in sweat's area and covered with parafilm. After 30 minutes the filter paper is removed. It is soaked up with sweat and again is weighted for measuring sweat quantity. Then the filter paper is cut in 2 mm stripes, which are left incubating for 24 hours in room temperature with 2 ml. Ethyl acetate. Hromato-massspectrometric analysis and fluid-fluid chromatographia have been used for detection of toxic substances.

### RESULTS AND DISCUSSION:

For patient 1 presence of Amitriptylin is proved in sweat, blood and urine. For patient 2 presence of Amitriptylin and Clomipramine (Anafranyl) is proved in sweat, blood and urine. For patient 3 presence of Diazepam in blood and urine is proved quantitatively, while in sweat - qualitatively. For patient 4 presence of Carbamazepin is proved in sweat, blood and urine (tabl.1) .

**Tabl. 1.** Comparison of drug concentration in blood, urine and sweat secret.

Drug	Blood ( mg/ml )	Urine ( mg/ml )	Sweat ( mg/ml )
Amitriptylin (P□ 1)	0.42mg/ml	1.050mg/ml	0.200mg/ml
Amitriptylin(P□ 2)	1.5mg/ml	6.250mg/ml	0.078mg/ml
Clomipramine (P□ 2)	0.43mg/ml	0.970mg/ml	0.280mg/ml
Diazepam (P□ 3)	2.94mg/ml	0.174mg/ml	(+)
Carbamazepin (P□ 4)	12.35mg/ml	4.200mg/ml	3.267mg/ml

Our results demonstrate that in non-affected skin area sweat glands are functioning well. They excrete toxic substances (amitriptylin, clomipramin, diazepam, carbamazepin) in first sweat portion. Drugs get into gland's cells from surrounding blood vessels or from the interstitium by process of simple diffusion. Skin lesion complicates severe acute drug poisoning with approximately 5-6%. Their clinical manifestation are erythema spots in irregular form, vesicles and bullae, soft tissue infiltration and necrosis. They appear 12 hours after the drug swallowing and localize on different body parts, often, but not obligated to spots with trauma and pressure. U.W Laevell (8) proposes the hypothesis about possibility drugs to be excreted by the sweat glands following their necrosis (by toxic mechanism) and forming skin lesion and developing patient's hypertermia. G.W Beveridge (2), S. Mandy and A.B.Ackerman (9) decline this hypothesis, because they establish normal sweat glands in spots of non-affected skin and normal temperature by patient with skin lesions. Except from barbiturate intoxications, skin lesions can be developed from CO; glutethimid; benzodiazepines: tranxen, lorazepam, flunitrazepam; meprobamat; chlorprotixen; heroin, methadon; alcohols and organophosphate compaunds. The histological findings of erythema and bullae show intra- and subepidermal bullae, necrosis of skin appendix (sweat glands, hair follicles, fat glands). The pathogenesis of skin lesion in drug intoxication is still unclear. The regulation of sweat

secretion is accomplished by Autonomic Nerves System through spinal cords, hypothalamus and cerebral cortex. It is a proven fact, that by denervation through axon - reflex way without participation of the central regulating mechanism, sweat glands have being stimulated much more. We established this fact, because the sweat glands of patients with coma (when Central Nerves System is excluded) excrete significant quantities sweat, gradually decreasing after stimulating. Our findings of drugs in the early hours after the intoxication show us toxicokinetic behavior of drugs in acute intoxication. They have been distributed in peripheral tissue including skin. Is local affection of sweat glands possible through localized there drugs or other toxic substances (excreting mechanism)? Are skin lesions in drug induced coma an excreting dermatoses? We made analog with bromoderma, jododerma and other dermatoses, formed after sweat excretion (talium, arsenicum, selenium). Excreting mechanism is suggested about all this drugs, but not about Amitriptylin and Diasepam. We haven't found data about direct cytotoxic effects of these drugs. According to data oxidases with mixed function (OMF) present in skin cells epidermis, sweat glands and hair follicles (11,12,15 ). OMF participate in drug metabolism. P.Noonan and D. Paul show that skin oxidizes are 80-240 more active than hepatic oxidizes with mixed function(12,13). We propose a hypothesis about the possibility the local toxic skin effect to be caused by common cytotoxic mechanism trough forming free radicals in the metabolic process (3,4,11,15). According to Beveridge, late Mandy and Ackerman, the toxic mechanism theory is not acceptable because in non-affected skin area sweat glands are normal (2, 9). Our examination establishes good functioning of the sweat glands in normal skin area. Our clinical observation and other authors show that many factors may influence forming, localization and progress of skin damage. The pathogenesis is not cleared yet. We believe that our examinations will contribute to most fully and rightly understanding of skin lesion's forming mechanism in acute intoxication.

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