

## AN INVESTIGATION ON THE RELATIONSHIP BETWEEN THE COMATOSE STATE AND THE SERUM LEVELS OF THE TOXIC AGENTS IN PATIENTS WITH ACUTE EXOGENOUS INTOXICATIONS

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### SUMMARY:

The aim of investigation of the relationship between the exotoxic coma and the serum levels of the toxic substances in patients with acute intoxications. We defined cerebral toxic agents were in 44 of the comatose patients. The established concentrations of the toxic substances at the admittance in the blood serum of comatose patients have been classified as fatal, toxic or therapeutic. These results show that in cases of mixed intoxications the coma can be associated more often with toxic or even therapeutic levels of the substance. We discuss that the plasma levels of a substance can not serve as criteria of severity of an intoxication in all cases as they are formed by the complex toxicokinetic of every medicament.; We can not predict the outcome of an intoxication using only it;. The plasma level of a substance can not be a precise criterion for the therapeutical scheme-a full volume of detoxic depuration measures should be carried out / sometimes the low plasma levels of a toxic agent can give a misleading data about a light intoxication /. The plasma level by itself can not be a precise criterion when we take a decision to make an extracorporeal detoxification of the blood as we expect from this method to extract the medicaments from their tissue depot and to raise their serum concentrations after that.

**Key words:** plazma level, drugs, comma

### INTRODUCTION:

The discrepancy between toxic plazma level and the severity of toxic symptoms is unusual in toxicology, and the phenomenon has not yet been fully explained. Plasma concentration of drugs have been measured folloing overdoses, but they have been shown not always to be a useful guide for treatment or in predict outcome of poisoning. Plasma levels may correlate with a number of effects both at therautical and toxic concentration. The aim of investigation of the relationship between the exotoxic coma and the serum levels of the toxic substances in patients with acute intoxications.

### MATERIAL AND METHODS:

Investigation of 5381 patients with acute exogenous intoxications treated in Naval hospital –Varna during the period 1995-2005, including 297 patients with exotoxic coma. The stage of the coma has been defined according to the four-degree scale.

The following cerebral toxic agents were defined in 44 of the comatose patients: barbiturates, glutetimid, Tardyl, benzodiazepines, neuroleptics, organophosphate pesticides, anticonvulsants, antidepressants, Baclofen, Rimicid, ethanol, methanol. The identification and the quantitative analysis of the toxic agents in blood serum have been made by Gas Chromatography, Liquid Chromatography and Chromato-Massspectrometrical methods using apparatus of Hewlett Packard firm. The established concentrations of the toxic substances at the admittance in the blood serum of comatose patients have been classified as fatal, toxic or therapeutic. / Stead A., A. Moffat Bulletin of international association of forensic toxicologists, Human Toxicology 3, 1983, 437- 446 /(5).

### RESULTS AND DISCUSSION:

33 patients with mixed intoxications have been investigated. A fatal concentration of the toxic substances in blood serum has been established in 13 cases, toxic concentration- in 9 cases and therapeutic concentration- in 11 cases. In 11 comatose cases of mono intoxications we have verified the dose of the toxic substance. In 9 of these patients the concentration was fatal, in 1- toxic and in 1- therapeutic. These results show that in cases of mixed intoxications the coma can be associated more often with toxic or even therapeutic levels of the substance. We relate this data to the potentiating of the toxic effects in cases of taking the toxic substances together at the same time. In mono intoxications the correlation between the fatal concentration and the coma was clearly outlined. In cases of mono intoxications coma associated to toxic or therapeutic concentrations of one substance was observed

more rarely. It is well known that the plasma level can correlate with the number of the effects in therapeutic or toxic concentration (1,2,3). In cases of overdose sometimes severe toxic symptoms have been observed associated with relatively low, sometimes real therapeutic levels of the substance/ for instance tricyclic antidepressants, verapamil or glutethimid /. These differences are not due to methodological divergences. The discrepancy between the toxic plasma levels and the severity of the toxic symptoms is not usual in toxicology cases. The phenomenon has not been fully explained yet. It is considered that medicines that are weak bases with pK 9.3- 9.7 taken orally are quickly and fully absorbed in the gastrointestinal tract. After therapeutic oral doses the peak plasma level is reached within the period of 2 to 8 hours after the ingestion. In cases of overdose and strong anticholinergic effect the emptying of the stomach is slowed down and further absorption can be slowed down even to 15 hours. In contrast of this the beginning of the clinical toxicity in cases of overdose is early, quickly and severe symptoms appear in the first hour or first several hours. Many lethal cases are registered in the first hours after the appearance of the clinical symptoms. In addition all the medicines with high lipophilicity have a great volume of distribution mainly in the

fat tissue. Their plasma half life is different and is between 9 and 15 hours. We should expect that during the distribution and after that clinical toxicity symptoms will appear at the target sites of the initial medicaments and as well of their metabolites. With contemporary up-to date methods a volume of distribution is measured between 10 and 50 l per kilogram. Therefore the plasma level of these medicines should be extremely low or even negative (3,4).

#### CONCLUSIONS:

1. The plasma levels of a substance can not serve as criteria of severity of an intoxication in all cases as they are formed by the complex toxicokinetic of every medicament.
2. We can not predict the outcome of an intoxication using only it.
3. The plasma level of a substance can not be a precise criterion for the therapeutic scheme-a full volume of detoxic depuration measures should be carried out / sometimes the low plasma levels of a toxic agent can give a misleading data about a light intoxication /. The plasma level by itself can not be a precise criterion when we take a decision to make an extracorporeal detoxification of the blood as we expect from this method to extract the medicaments from their tissue depot and to raise their serum concentrations after that.

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