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ACUTE INTOXICATIONS WITH NEUROLEPTICS AND ANTIDEPRESSANTS

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ABSTRACT

Objective: This retrospective study was conducted to follow out acute intoxications with neuroleptics and antidepressants in Northeastern Bulgaria (Varna region), to assess the frequency and proportion depending on total non-pharmacological and pharmacological poisoning. **Methods:** The objects of the study are 445 with acute neuroleptic and 148 patients with acute antidepressant intoxications treated in the Clinic of toxicology of the Military medical academy – Varna/Bulgaria. The study is retrospective and covers a period of 20 years (1991-2010). **Results:** Incidence of acute poisoning with neuroleptics is 7.5% of all drug poisoning and 2.5% of general poisoning, while in poisoning with antidepressants, these values are 2,5% and 0,9% respectively. Intoxications occur more commonly in women and the majority of poisonings are in people of working age. **Conclusion:** In recent years, there is a trend of an increase in the absolute number and the proportion of poisonings with neuroleptics and antidepressants. The lethality in these poisonings does not exceed 0.4-0, 7 percent.

KEYWORDS: acute poisoning, intoxication, medicines, neuroleptics, antipsychotics, tricyclic antidepressants.

INTRODUCTION

Drug overdose is the most common cause of acute poisoning according to the data from Poison Control Centers throughout the world.[1] In the USA, 25% of all routine hospital admissions and about 5% of all medical intensive care unit admissions involve some kind of

drug-related adverse event.[2] Poisoning is often referred to as the most frequent method of suicide or suicide attempt, and most cases involve drug poisoning, particularly with psychotropic drugs such as benzodiazepines, antidepressants, and neuroleptics.[3–5]

Neuroleptics, also known as antipsychotic agents and major tranquilizers, are primarily used to treat schizophrenia, manic phase of bipolar disorders, and agitated behavior. However, they are often used to treat nausea, vomiting, headache, and various neurological conditions (chorea, dystonia, spasms, tics, and torticollis). They are divided into two major groups: first-generation (conventional) agents and second-generation (atypical) agents.[22]

The group of antidepressants nowadays has increased considerably and includes tricyclic antidepressants (TCA) and non-tricyclic antidepressants (non-TCA). Besides the treatment of depression, they are also used to treat obsessive-compulsive disorders, panic disorder, alcoholism, obesity, anxiety, and various psychological disorders such as migraine headache syndromes and chronic pain.[15] Over the past decade, the use of antidepressants has skyrocketed across the rich world countries. Astounding increase in antidepressant prescriptions is accounted also in Bulgaria. In many cases, patients are diagnosed with depression without fulfilling the criteria of the disease.[19, 20]

In this context, we aimed to investigate the acute intoxications with neuroleptics and antidepressants in Varna region (Bulgaria) for twenty year (1991-2010) period.

MATERIALS AND METHODS

The objects of the study are 445 with acute neuroleptic and 148 patients with acute antidepressants intoxication treated in the Clinic of toxicology of the Military medical academy – Varna/Bulgaria, respectively. The study is retrospective and covers a period of 20 years (1991-2010). It has been analyzed the history of the disease, medical cards of the patients, received treatment and medico-legal reports from autopsies of deceased patients.

RESULTS AND DISCUSSION

During the period 1991-2010 in the Clinic of toxicology of the Military medical academy – Varna/Bulgaria 17 525 patients with acute intoxication and acute allergic reactions received treatment. Medicated poisoning are 5926 (34,4%) (tabl.1).

Table 1. Total poisoning, total drug poisoning and neuroleptic and antidepressant poisoning during period of 1991-2010.

Period	*Total poisoning (%)*	*Total drug poisoning (%)*	*Neuroleptic poisoning (% of total poisoning)*	*Antidepressant poisoning (% of total poisoning)*
1991-2010	17 252 (100)	5926 (34,3)	445 (2,6)	148 (0,9)

Table 1.

There is a substantial dynamic in the incidence of intoxication with drugs and etiological structure over the period. There is a steady trend in reducing the absolute number of acute drug poisoning, and their share in the causes of hospitalization in the clinic of toxicology. These indicators were highest in the first years of the period, when half of hospitalized patients were with acute drug intoxication and lowest at the end of the period. For the past five years (2006-2010) acute poisoning with drugs was the cause of hospitalization of 908 patients or 18.3% of all hospitalized, and in 2010 we have registered the lowest share of drug intoxication - 15%.

Acute neuroleptic intoxications were registered in 445 patients. The frequency is not high - 7.5 % of medicated poisoning and 2.5 % of all hospitalized patients in Clinic of toxicology of the Military medical academy – Varna/Bulgaria. In the structure of drug poisoning tends to be an increase in the share of neuroleptic intoxication. In the first 10 years of the period, their share was nearly constant and fluctuating around 6 %. In the last five years of the period, their share rose to 15.75 % (Fig.1).

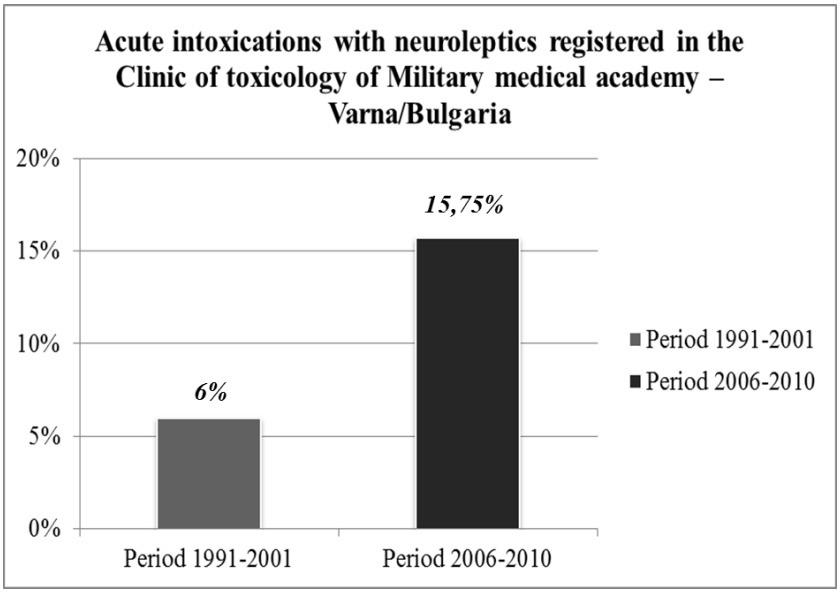

Figure 1. Proportion of acute intoxications with neuroleptics in total drug poisonings.

Figure 1.

Neuroleptics have no significant differences in terms of their efficacy, but they differ greatly in terms of their side effects.[10] Besides accidental or intentional overdose, toxic effects often occur after ingestion of therapeutic doses. Toxic effects include anticholinergic and extrapyramidal syndromes (EPS) as well as CNS and cardiovascular depression.[11] Relatively rare, but severe, idiosyncratic adverse reaction to antipsychotics, is neuroleptic malignant syndrome (NMS), that is characterized with fever, muscular rigidity, altered mental status, and autonomic dysfunction. Second-generation antipsychotics (SGAs) are characterized by lower incidence, lower clinical severity, and less frequent lethal outcome due to NMS than first-generation antipsychotics. Nonetheless, it should be borne in mind that all antipsychotics are able to elicit clinically important NMS.[12]

Acute antidepressant intoxications were registered in 148 patients. The frequency comprises 2.5 % of medicated poisoning and 0,9 % of all hospitalized patients in Clinic of toxicology of the Military medical academy – Varna/Bulgaria. In the last five years of the reported period, there was a double rise in the rate of acute intoxication with antidepressants in a similar way as neuroleptics (Fig.2).

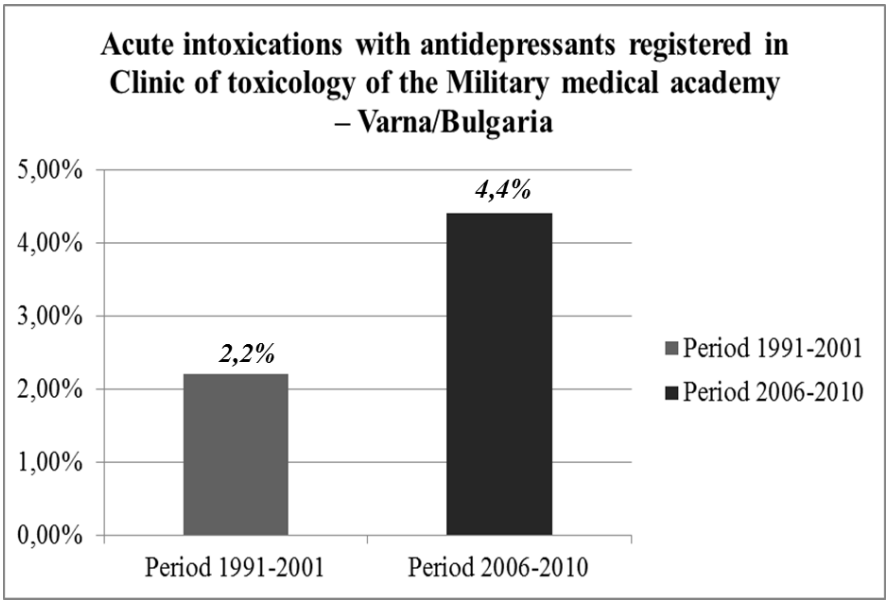

Figure 2. Proportion of acute intoxications with antidepressants in total drug poisonings.

Figure 2.

From the group of TCA, one of the most used and the one which most common causes intoxication preparations is amitriptyline.[13] TCA intoxication occurs with high mortality and

morbidity rate. The reason for this lies in their mechanism of action, which includes inhibition of norepinephrine and serotonin (5-HT) reuptake at nerve terminals, direct peripheral α-adrenergic blockage, inhibition of voltage gated sodium channels on the myocardium (membrane stabilizing or quinidine-like effect) and anticholinergic action.[14] As a result of those mechanisms are developed classic symptoms of cardiotoxicity of TCA, which include ventricular dysrhythmias, myocardial depression, and hypotension.[15] On electrocardiography (ECG) is visible widened QRS and changes in QTc, and PR durations due to prolongations of cardiac action potential and refractory period and besides, delay of atrioventricular node (AVN) conduction, and this can be used as a predictive marker on cardiac effects of TCA in emergency department (ER).[16,17] In the Clinic of toxicology of the Military medical academy – Varna/Bulgaria, in most of the patients' cause of acute intoxication with antidepressants is amitriptyline intake. Acute cardiotoxic symptoms were registered in all patients with amitriptyline poisoning and even in rare cases, they were the cause of death.

The most important representatives from the second group (non-TCA) are: SSRIs (e.g. fluoxetine, sertraline etc.), SNRIs (e.g. venlafaxine), MAO A inhibitors (e.g. moclobemid) and so-called atypical antidepressants (e.g. bupropion, trazadone). The most widely used of these groups are the first two. Because they are more selective and do not or slightly interact with histaminic, muscarinic, adrenergic or cholinergic receptors, they tend to have a more benign side-effect profile and have improved compliance and are often considered to be safer.[18, 7] The most important life-threatening clinical conditions, associated with its use, are development of serotonin syndrome and rhabdomyolysis.[19, 20] Serotonin syndrome occurs most often with the use of drugs, which increase the synaptic levels of serotonin and as a consequence activation of serotonin 2A (5-HT_{2A}) receptors in the central nervous system. The triad of clinical features consists of neuromuscular hyperactivity, autonomic hyperactivity and altered mental status, which may present abruptly and progress rapidly.[21] Seizures during intoxications with antidepressants are a well-known complication.[22] There is tend to increase antidepressants use with suicidal purpose in USA.[23] The same situation is in Bulgaria and the main reason for this is most likely due to the fact that the sale of antidepressants and neuroleptics is on plain white prescription forms in pharmacies, which makes them easily accessible. As opposed to psychoactive drugs, such as benzodiazepines and barbiturates, which are prescribed on green forms, the population's access to these drugs is severely restricted and the frequency of intoxication with them is very limited. This

changes the etiological structure of drug intoxication and contributes to a significant increase in the proportion of poisoning with neuroleptics and a small increase in their absolute number. The acute intoxication with neuroleptics and antidepressants are more common in women, the majority of poisonings are in people of working age. The main reasons for poisoning were suicide attempts. Fatal endings are registered only in two patients (0.4 %) with acute neuroleptic and in one patient (0,7 %) with acute antidepressant intake. Lethality in poisoning with neuroleptics and antidepressants is significantly lower compared to the general mortality in acute exogenous intoxication, which is 1.3%, according to our data.

CONCLUSIONS

Incidence of acute poisoning with neuroleptics and antidepressants covers 7.5% and 2,5% of all drug poisoning respectively. In recent years, there is a tendency in increasing the absolute number and its relative share. They are more common in women and in people of working age. The majority are the result of suicide attempts. In most cases, patients do not abuse their prescribed medications. However, some neuroleptics and antidepressants do carry abuse potential. Vulnerable patient populations include those with a history of substance abuse and those in controlled environments. Physicians should be alert when writing prescriptions for such patients, who are prone to abuse. Mortality in these poisonings is not high and is 0.4 and 0, 7 percent, respectively.

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