Medicines Affecting Human Performance

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INTRODUCTION

Many drugs can impair human psychophysical performance. This impairment can be most fateful in cases when it is the cause of a traffic accident because of the driver's inability to react properly in a critical situation, or in cases when a patient, taking a drug, is operating a machine that demands the operator's full performance. In a Spanish study [1], the presence of alcohol, illicit drugs and medicinal drugs among drivers, involved in fatal road accidents between 1991 and 2000, was determined. 4.7% of drivers, killed in the accidents, were under the influence of psychoactive medicinal drugs, the percentage of those under the influence of alcohol or illicit drugs was much higher.

WHICH DRUGS COULD INFLUENCE HUMAN PERFORMANCE?

In general, into the category of drugs, negatively influencing human performance, belong the drugs that directly impair functioning of the central nervous system (CNS) and drugs that affect the function of CNS indirectly by changing blood pressure, lowering blood glucose concentration or affecting vision.

MECHANISMS OF IMPAIRMENT OF HUMAN PERFORMANCE

Most frequently, the impairment of psychophysical performance is due to the main action of the drug. Sometimes, the side effects of the drug, not connected to the main action, are responsible for the impairing effect. Medicinal drugs are frequently taken together with alcohol and illicit drugs and in this case the interaction of both worsens the deleterious effect of each of them [2, 3].

GROUPS OF DRUGS AFFECTING DRIVING ABILITY

There are several factors which make this categorization difficult: the effect on driving ability is dose-dependent and time-related, the development of tolerance and the condition of the subject changes the net effect of drug [4]. Nevertheless, it is generally agreed that there are at least three categories in which drugs can be divided according to their effect on driving ability

[5]; this subdivision is included into the guidelines of European Medicinal Agency (EMEA) [6]. The categories are:

a) Drugs with no or negligible effect on driving ability
b) Drugs with minor or relative disabling capability
c) Drugs with absolute prohibition of driving or handling machines when under their influence

How are pharmacodynamic drug groups divided into these categories? Data about this are supplied by the manufacturer in the documentation for the registration of the drug [6, 7]. There are several methods available to test the influence of drugs on driving ability, but there is no general agreement about which of them to choose as the official measure of this action and how to apply them [5]. So the effect of medicines on driving capability is estimated from other effects of drugs that are better documented.

The last category (*c* – absolute prohibition) contains a few drug groups:
- Antipsychotics (parenteral formulations)
- Opiates
- General anaesthetics
- Muscular relaxants
- Hypnotics/sedatives

More numerous is the second category (*b* – moderate or relative disabling capacity):
- Antipsychotics
- Antidepressants (tricyclic antidepressants – TCA, selective serotonin reuptake inhibitors – SSRI)
- Antiepileptics
- Antiparkinsonics
- Anxiolytics (benzodiazepines)
- Sedatives
- Muscarinic antagonists (also as side effect of other drugs)
- Antihistamines (1st generation)
- Adrenergic antagonists (α, ß – antagonists)
- Antimigraine drugs
- Some chemotherapeutics (chinolones, some antineoplastic drugs)
- Adrenegics (ocular use)
- Vasodilators
- Oral hypoglycaemic drugs

Groups of drugs in this category are not homogenous, some representatives belong to category *c*, some and sometimes to category *a*. This depends on

- patient's adaptation to the effect of drug
- time of the therapy (greater risk at the beginning of therapy)
- changing the dosage
- side effects (not present all the time of therapy, not with all representatives of the group)
- the compliance of the patient (oral hypoglycaemic drugs)

In this category of drugs, the discussion with the patient is very important. The patient should be warned about potential critical situations, the doctor should assess the patient's attitude toward his illness and therapy and his ability to adapt himself to it.

The relation between blood concentration of the drug and its effect on human performance poses no problems in group *c*, as driving should be avoided when under the influence of these drugs; the situation with the drugs in group *b* is more complex as there is a poor correlation between the disabling effect and plasma concentration.

THE SOURCES OF INFORMATION ABOUT DRUG PROPERTIES

For health professionals, the Summary of product characteristics (SPC), supplied by the manufacturer, contains the essential data about the drug. The content and form of SPC is prescribed by the authorities according to the guidelines published by EMEA [6]: 'On the basis of the pharmacodynamic profile, reported adverse reactions and/or specific studies on a relevant target population addressing the performance related to driving or using machines, specify whether the medicinal product has (a) no or negligible influence (b) minor or moderate influence or (c) major influence on these abilities. Effects of the disease itself on these abilities should not be discussed. For situations b and c, special warnings/precautions for use should be mentioned.'

The patient information leaflet (PIL), accompanying the package of the drug ('package leaflet'), contains the information for the patient. It should be written in a language understandable to laymen. The EU directive says: 'the package leaflet shall be compiled in accordance with the SPC and will mention, if appropriate, potential effects on the ability to drive vehicles or to operate machinery' [5]. According to the EU directive the outer packaging of the drug can include symbols or pictograms designed to clarify specific information. In some European countries, the drug packages, containing drugs from groups *b* and *c*, contain pictograms, indicating the danger of driving when under the influence of the particular drug. In Slovenia, the packages of drugs in category *c* are labelled with a filled triangle (▲) and for drugs in the category *b*, with an empty triangle (△).

PROBLEMS

The question is how many patients read the patient information leaflet, look at the labelling on the drug package or care about what they see there. A study, performed in the Netherlands [8] showed that the target group of patients did not care very much about the warnings supplied with the drugs they obtained. Probably, the situation is not very much different in other countries.

So, very much responsibility for proper informing of the patient lies on the doctor prescribing the drug [9], especially for category *b*. He knows his patient and should evaluate and estimate his reactions to therapy and adjust the form of information to the patient's character and mental state.

On the other hand, the general public needs to be made more aware that the side effects of certain prescribed drugs can affect the ability to drive; more should be done to ensure speedier and more specific and co-ordinated research in order to establish appropriate drug testing devices to ascertain their effect on driving ability [10].

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