MEDICINAL DRUGS AND DRIVING SAFETY: A GRADED-LEVEL SYSTEM FOR LABELING

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Introduction

It is widely recognized that many medicinal drugs possess the potential for seriously impairing a person's ability to safely operate motor vehicles. That belief is supported mainly by a vast literature concerning drug effects on skills related to driving and simulated or actual driving as measured in a variety of experimental situations. But also clinical case reports and a limited number of epidemiological surveys support views of a drugs and driving problem.

Individuals who drive after using prescription or over-the-counter (OTC) drugs are not generally those who engage in risky behaviors for recreational purposes. If their driving performance becomes dangerously impaired, they view the occurrence as a definitely unwanted drug side-effect. Given a choice between impairing and non-impairing medication they will certainly choose the letter.

Ideally, physicians and pharmacists should be fully informed of these effects and select or dispense only safe drugs for their patients. And when that is impossible, they should advise the patients of the risks as well as the ways to minimize them. Unfortunately, that ideal is almost never realized in practice.

There is a world wide need for a system to inform prescribing doctors, pharmacists and patients about the potentials of a drug to impair driving skills.

Although a specific system for labeling medicinal drugs with respect to possible effects upon driving performance and safety has been implemented in The Netherlands and Scandinavia for more than a decade, their inadequacies are widely recognized. The existing systems are dichotomous (warning - no warning), while the adverse effects of drugs within the same therapeutic class are known to vary substantially.

Package Warning Systems

The Netherlands:

A joint initiative by the Royal Dutch Societies for the Advancement of Pharmacy (KNMP) and of Medicine (KNMG) led to the world's first warning system in 1973. All drugs registered for prescription sales in The Netherlands were divided on the basis of pharmacological considerations into two categories:

1. those likely to interfere with patients' ability to drive safely and 2. those not. According to an agreement between two professional societies and the Dutch Regulatory Authority, pharmacists filling a prescription were to affix a yellow/black label to drugs in the first category which conveys the message "This drug can affect your driving ability".
Prescribing physicians were allowed to change the ordinary procedure by annotating their prescriptions with either the Latin abbreviation d.s.m. (da sine monitione) or d.c.p. (da cum prohibitione). In the former case the pharmacist must withhold the usual label and in the latter, he must replace it with a red/white label declaring "Operating a motor vehicle is not allowed while taking this drug". Strictly speaking this is not a legally binding prescription but its legal consequences would be almost escapable for any patient who ignored the physician's advice and precipitated a traffic accident. In any case, Dutch physicians' understandable reluctance to alter the normal procedure has led to a situation where it is followed almost without exception.

Drugs entering the market since 1973 have been reviewed by a committee of the KNMP. In the beginning it was a relatively easy task since all drugs within certain therapeutic categories (e.g. antidepressants, antihistamines, anxiolytics etc.) were sure to acquire the label. Lately, however, certain manufacturers of antihistamines have successfully challenged the concept of class-warning by offering these drugs were unimpairing. This late development has revealed one of the weaknesses of the Dutch system.

Another problem with the Dutch system is that it appears ineffectual on the level of individual patients' reactions. Two surveys conducted in pharmacies where drivers had just acquired labeled medication revealed that 70% did not plan to alter their driving habits in reaction to the warning. It is unknown whether the others actually did anything to conform with their feelings that they should. It may be suspected that many did not.

Finally it has recently been shown, that many Dutch pharmacists hardly use any yellow/black warning label at all. Labels with patients' instructions and warning for using the drug properly are generated automatically by computerized systems for medication surveillance.

The Nordic Countries:

Another package label warning system has introduced in Norway in 1981 and adopted by Denmark, Finland, Iceland and Sweden in 1983. It is very similar to The Netherlands'. It was created by an expert committee and is maintained by the Nordic Committee on Medicines. A label showing a red triangle is invariably affixed by pharmacists to all drugs within a category entitled "especially hazardous" (i.e., sedative-hypnotics, opioid analgesics, antihistamines, antiepileptics and centrally active muscle relaxants). At the request of the prescribing physicians, the label is affixed to all drugs within another category entitled "potentially dangerous" (i.e., neuroleptics, antidepressants and anticholinergics).

Until 1986 pharmacists dispensing medication presenting the label were required to provide the recipients with a leaflet describing its meaning. The latter equipment was eliminated out of a belief that everyone knows the meaning. However, only two years before a study of Finns who received labeled medication revealed that about 1/3 were unaware of its significance and only 20% altered their driving habits in accordance with the warning.

Both the Dutch and the Nordic warning systems have been criticized on the basis that the information they provide is unrelated to the known differences between effects of drugs and doses of drugs.
Dichotomous warning systems are generally ignored by physicians, pharmacists and patients. It would be far better to provide physicians and pharmacists at least with a rank ordering of drugs within therapeutic classes known to be hazardous for drivers.

Formation of a "Task Force"

Deficiencies of the existing warning systems were recognized by many experts in human psychopharmacology. In 1987 a special "Task Force" was organized in The Netherlands at the expressed wish of the Chief Inspector for Drugs. It had unofficial status and functioned merely to advise the Dutch Government. Nonetheless its membership included representatives of the major national traffic safety and drug regulatory agencies, along with others from professional associations of physicians and pharmacists, patient/consumer groups, traffic safety organizations, the Dutch association of pharmaceutical manufacturers and scientific institutions engaged in drugs and driving research.

The "Task Force" considered the need for a package label warning system, deficiencies with present systems and how a better system might be achieved. The "Task Force" has been disbanded and its final report will be publicly issued by the end of this year. Yet, the work it began continues now at the Institute of Drugs, Safety and Behavior of the University of Limburg.

Concept of a Graded-Level Warning System

The Institute has undertaken a 14-month study, beginning in January 1989, under a contract jointly funded by the Dutch Ministeries of Health and Transportation. The goal of the study is to determine whether the current state of knowledge about the effects of drugs on driving would support the creation of a graded-level warning system. The Institute collaborates in this effort with the Royal Dutch Society for the Advancement of Pharmacy, which as mentioned earlier, is charged with implementing the present system.

The study consists of two parallel lines of activity. The first is an extensive literature review to compare, and in so far as possible, quantitatively discriminate, among the performance impairing properties of drugs within all the major classes thought to be hazardous for drivers. A rank ordering of drugs within each therapeutic class will be attempted based upon the investigator's conclusions from the literature.

Yet, it is recognized that however carefully the investigators attempt to retain an unbiased and objective perspective, their unsupported conclusions would not stand alone as the basis to accept or reject the concept of a graded-level warning system. For that reason the second line of activity involves an attempt to solicit to the consensus of an internationally recognized group of experts in the field of drugs and driving.

Some experts have been polled to first determine how many agree with the desirability and feasibility of a graded-level package label system. Most have agreed that the state of knowledge in the field allows the construction of such a system. Finally over 40 experts have been asked to place the drugs with which they are familiar within the following categories:
Category A: Drugs likely to possess strong adverse effects on driving performance as determined from studies wherein such impairment has been frequently observed.

Category B: Drugs likely to possess moderately adverse effects on driving performance as determined in the same manner.

Category C: Drugs likely to produce any important effects on driving performance as determined in the same manner.

Category D: Drugs which have not been sufficiently studied to allow categorization on the basis of experimental evidence but which possess essentially the same pharmacological activity as other drugs that are known to adversely affect driving performance.

Category E: Drugs which have not been sufficiently studied to allow categorization on the basis of experimental evidence but which possess no pharmacological activity known to affect driving performance.

The results of this study will indicate the feasibility of the proposed graded-level warning system if a high degree of consensus is achieved by the experts and that consensus is supported by the conclusions from the literature survey.

The study is ongoing and the design of the new system will be presented next year. Examples of its application for two categories of psycho-active drugs will be given: antihistamines and anxiolytics. Note that experts' response to the questionnaire is still in process and consensus has to be achieved yet. The figures show preliminary results of the categorization within both classes of drugs that have been reviewed by at least five different experts. As shown in the figures the difference between the "old" and "new" drugs is clearly demonstrated.

Future Outcome

It seems that some improved system for informing physicians and pharmacists and warning patients about the possible effects of medicinal drugs on driving performance must eventually emerge from the intense efforts presently underway. Package inserts and patient information leaflets should contain the information on the category A - E for each (psychotropic) drug. In addition a red triangle symbol, like presented in the Nordic system, should also apply in the new graded-level warning system on drugs of the categories A, B and D. Patient counseling by the pharmacist will be needed to inform the patient about the effects of combined drug use as presented by the patient's drug history as available in most pharmacy computerized medication surveillance systems. Physicians will communicate with pharmacists based on computer technology using the pharmacy computer. The development of "expert systems" will support the health care professionals in providing the dispensing information.

The Netherlands was the first country in the world to inaugurate a package label system. It follows Dutch tradition to initiate a program of research aimed at improving the system. Yet after 1992, it will not longer be possible for the Netherlands or another member state of the European Community (EC) to
act with the same independence as before in pursuing a national drug regulatory policy. If the Dutch agencies decide to require drug manufacturers to submit new drugs to standard screening procedures that will categorize their effects on patients' driving performance, they will shortly have to convince their EC partners to do the same. Nobody expects this to be an easy task but few would say that it is impossible.

**ANTIHISTAMINICA**

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