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Drug Abuse Monitoring: Which Pharmacoepidemiological Resources at the European Level?

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Abstract – Monitoring the potential for abuse and dependence of psychoactive substances falls within the scope of international conventions on narcotic drugs. At the European level, this monitoring is based on activities controlled by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) for substance abuse in general and by the European Medicines Agency (EMA) for marketed drugs, in the context of pharmacovigilance. If France has set up in the early 1990s an original system to assess potential for abuse of psychoactive substances, with specific tools combining both the evaluation of the use of these substances (illicit substances or diverted drugs), and the consequences of that use in terms of morbidity and mortality, there is no equivalent in other European countries. Indeed, unlike the USA, who, for several decades, organized this type of surveillance, with a multisource approach (sentinel systems, databases, medical and administrative data, databases for seeking care in relation abuse), we have not found in other European countries integrated system for identifying a signal of drug abuse, or to assess the impact of measures for minimizing the risk of abuse. However, some recent examples show a growing concern about drug addiction, based on a pharmacoepidemiological approach using pharmacovigilance databases or medical administrative data. These examples illustrate the interest of these approaches in the field of drug of abuse.

Abbreviations: see end of article.

1. Introduction

In 2007, the number of deaths and complications related to drug abuse in the USA exceeded that of those related to illegal substances such as heroin or cocaine.[1] This situation led the USA to strengthen both their drug abuse monitoring system, and secondly, to establish risk management plans to minimize diversion of prescription drugs.[2-5] Several pharmacoepidemiological tools, including analysis of "doctor shopping" in prescription databases, data collection about substance use in specialized structures, identification of adverse events related to drug abuse in pharmacovigilance systems, or multi-source approach combining several data sources have been widely described in the literature.[6,7] In the USA, the number of people abusing prescription drugs exceeds those who admit abusing cocaine, hallucinogens, inhalants and heroin. As an example, increased medical use of opioids in USA is directly correlated with increased abuse as well as subsequent morbidity and mortality. Actually, the level of use of opioid analgesics in North America is the highest in the world.[8] According to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), abuse of prescription drugs is also increasing in Europe, although literature on the extent of the phenomenon remains scarce, limiting the understanding of the problem at the European level.[9,10] As highlighted in the recent review of

Bramness *et al*., the share of research on substance abuse is particularly weak in Europe compared with the USA.[11] The purpose of this article is to review the characteristics of pharmacoepidemiology data regarding abuse of marketed drugs available in Europe.

2. Organization of control and monitoring of drugs with abuse potential

Internationally, narcotics and psychotropic drugs are included in specific schedules related to international conventions established by the United Nations, namely the 1961' Single Convention on Narcotic Drugs, as amended by the 1972 Protocol, and the 1971' Convention on Psychotropic Substances. The objective of these conventions is to ensure adequate availability of narcotic drugs and psychotropic substances for medical and scientific purposes worldwide, while ensuring that such drugs are not diverted for illicit purposes. These conventions give the rules of the international monitoring of narcotic and psychotropic drugs production, prohibiting any use without prior authorization from national authorities. In essence, these international agreements limit exclusively possession and production of scheduled substances to "medical and scientific" use. These conventions also insure the availability of drugs (for example analgesic opioids and drugs for opiate maintenance treatments) for medical and scientific purposes (while preventing runoff on illicit market). The World Health Organization (WHO) is responsible for the evaluation of pharmacological properties and the potential for abuse of the substances within these international conventions. WHO relies on the skills of its Expert Committee on Drug Dependence, and has an advisory role on the international scheduling of certain substances. WHO also promotes drug safety monitoring (including narcotic and psychotropic drugs for medical use), under the coordination of the Uppsala Monitoring Centre (UMC) located in Sweden. This Collaborating Centre for Drug Monitoring is in charge of the promotion and coordination of drug safety activities from the national pharmacovigilance systems around the world. Information on adverse drug reactions recorded by national systems are transmitted to the UMC and registered in a common database, VigiBase™, accessible without any restrictions for members of the WHO Programme. Reports of drug abuse or misuse included in VigiBase™ are considered for the evaluation of the potential for abuse of some medications.

These international agreements apply at the state level and therefore concerned all European countries, but not at the level of the European Union. Actually, 2 different institutions are involved in the regulation of psychotropic or narcotic drugs in Europe: the EMCDDA, in charge of the surveillance of drugs and drug addiction, and the European Medicines Agency (EMA), responsible for the benefit-risk assessment of medicines for human (and veterinary) use.

Originally founded to fight against the use and trafficking of illicit drugs, the EMCDDA aims to provide information necessary to understand the phenomenon of drug abuse, including diversion of prescription drugs.[11] EMCDDA presents information related to the status of psychotropic and narcotic drugs in the 28 Member States and Norway in the European Legal Database on Drugs (ELDD).[12] This database includes drugs marketed in Europe, and their status as available through official sources (including national drug regulatory agencies). Each European state being sovereign for more strictly control drugs (for example by classifying a drug as a narcotic, restricting or tight control of prescription and / or delivery, or by limiting its accessibility), this database allows to compare national legislations.

The objectives of the EMCDDA were primarily focused on illicit substances recently spread throughout the European territory. Gradually, misuse and abuse of prescription drugs appears to be an increasing part of abuse phenomenon. The exchanges of information between the EMCDDA and EMA began in 1995 at the creation of the two institutions, but have evolved recently towards a more effective cooperation. The EMA is a key partner in the early warning system for new substances (EWS) and participates in the risk assessment of these substances. Cooperation between the EMCDDA and EMA takes place in the framework of Decision 2005/387/ JHA of the Council of the European Union on the information exchange, risk assessment and control of new psychoactive substances. According to this decision, "substances whose medical value is established and acknowledged... are not subject to control measures based on this decision. Regulatory and appropriate public health measures should be taken with regard to substances with established and recognized medical value that are being misused." Similarly, "... in addition to what is provided for under the pharmacovigilance systems as defined in Directives 2001/82 / EC and 2001/83 / EC, the exchange of information on psychoactive substances which are the subject of abuse or misuse should be increased and should ensure appropriate cooperation with the European medicines Agency."

The European pharmacovigilance database at the EMA – EudraVigilance - and the EMCDDA database on new substances are used to allow the exchange of information. The two institutions have signed a new agreement in September 2012, strengthening cooperation and under which they agree to exchange the information they receive on drug abuse.

3. Pharmacovigilance and addictovigilance

In 2010, the European Parliament and the Council of the European Union launched the reform of the pharmacovigilance system with the adoption of the Directive 2010/84/UE and the EU regulation 1235/2010. The new law, implemented in July 2012,