Use of psychotropic drugs during pregnancy

A report of the international co-operative drug use in pregnancy (DUP) study

F. Marchetti 1, M. Romero 1, M. Bonati 2*, G. Tognoni 2*, and the Collaborative Group on Drug Use in Pregnancy (CGDUP)**

1 Laboratory of Clinical Pharmacology and Epidemiology, Consorzio Mario Negri Sud, S. Maria Imbaro, Chieti, Italy
2 Laboratory for Mother and Child Health, Istituto di Ricerche Farmacologiche “Mario Negri”, Milano, Italy

Summary. Drug Use in Pregnancy (DUP) is an international epidemiological survey of drug use in pregnancy conducted from 1988 to 1990 in 148 maternity wards, representing the general delivery practices of 22 countries. Data on exposure of pregnant women to psychotropic drugs, the indications for their use and their correlation with maternal characteristics are reported.

Of the 14,778 women interviewed, 520 (3.5%) reported 562 courses of psychotropic drugs. Benzodiazepines (BDZ) accounted for the greatest number of the exposures (444/520 women); neuroleptics and antidepressants were prescribed to tiny minorities of women (83 and 17 respectively), mostly in those few countries where the overall prevalence of use of those drugs was highest. Throughout the majority of the other countries, overall rates were in the low range and were rather heterogeneous. With the exception of small clusters of “unexpected” indications, prescriptions of BDZ were found to be consistent with the target symptoms of anxiety and insomnia; chronic use was reported in 31/444 women. The study was not targeted to the detection of malformations; no suspected clustering was found, however, among the 130 women exposed during the first trimester of pregnancy.

The collaborative network now established provides a framework for periodically replicated surveillance to monitor the evolution of this field of knowledge and care in order to provide reliable information for women and society.

Key words: Pregnancy methodological, Psychotropic drugs; drug utilisation

The use of psychotropic drugs in pregnancy, as would be expected, is one of the areas of medicine where subjective factors are most likely to play an important role. On the one hand, we have the mixture of unknown, ex post facts worries and bad methodology, which has characterised the problem of drug assessment in pregnancy [1, 2], and on the other we have the atmosphere of ambiguity which has accompanied the massive diffusion of psychotropic drugs in society (even more than in medicine) [3]. The results are often statements and attitudes (from fear and prohibition to denial), which do not favour rational behaviour in prescribers and users [4].

As is often the case for medical issues, which lie at the border between cultural and societal values, the response of research has not been of increased attention towards the problem: a thorough literature search as far back as the day after the thalidomide-induced epidemics of malformations [5, 6] (at that time a drug with psychotropic indications) produced only an handful of references [7–17] (Table 1). It is apparent that, while documenting that the overall downward trend in the frequency of drug use also includes psychotropics, the data represent settings and populations which are scarcely comparable and do not af-
ford information about the present situation in most countries, other than the three which have produced the epidemiological profile presented in the Table. The large epidemiological survey on Drug Use in Pregnancy (DUP), conducted under the auspices of WHO-EURO in 22 countries [18-20], has provided an opportunity to look at this issue through a representative sample of women being delivered under routine circumstances of hospital care.

Methods and population samples

A total of 14,778 women from 148 maternity wards in 22 countries in four continents was enrolled over the same duration of index periods during 1988-1990. Europe represented the highest final population (10,258 from 121 wards), followed by Asia (2,602 women from 14 wards), Central and South America (1,078 women from 7 hospitals), and Africa (840 women from six hospitals). In each participating country a clinical pharmacology unit and/or an obstetrics department acted as the reference centre for a group of volunteer hospitals representing various levels of care. The reference centre used randomisation techniques to ensure that the study population was closely representative of the health care offered in hospitals in that country. The numbers of deliveries enrolled by each unit varied considerably, with the majority (14 countries) accounting for more than 1.5 per 1000 annual births in the country (at least 10% of the annual births in each participating hospital). Israel, Costa Rica, Japan, Sri Lanka, United Kingdom, Brazil, Ghana and India enrolled less than 1.0 per 1000 annual births. According to a method which has been shown to be reliable for recall of pregnancy-related events, including drug exposure [21], the randomly selected women were interviewed in the first week after delivery by trained medical and/or paramedical personnel, on the basis of a standardised, questionaire, focusing on education, quality of care during pregnancy (tim- ing and number of health checks, morbidity), smoking and drinking habits, and drug consumption. Cross-check questions (on specific “drug” exposure vs indications/problems requiring drugs) were asked for each trimester and overall to help recall: for each affirmative response to a drug question, the brand name of the prescribed drug was requested from hospital records about obstetric history, present delivery (mode, plurality and gestational age) and information about the babies (sex, body weight, Apgar score, malformations, and other major pathological events).

To estimate how representative were, the collected data the rates for a few general variables for each country, such as contraception, mode of delivery, malformations at birth and breastfeeding, were compared with data collected by the representative unit from other specific surveys. Close agreement was found within individual hospitals/countries [20].

The drug products were centrally coded, after careful cross-checking of their contents with the national coordinators, according to the International Pharmaceutical Research Group classifications [22], with marginal adjustments for any products coming from one or the other market. In this report we have analysed all drug prescriptions classified as "psychotropic", namely benzodiazepines, antidepressants and neuroleptics. According to the pre-defined aim of the DUP protocol, data are presented a) first as they relate to the total sample as one population (“women delivering in hospital”), b) then, as they represent the heterogeneity of the cultural and care settings in individual countries, or geographically and historically homogeneous groups of countries.