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Drug use in pregnancy: an overview of epidemiological (drug utilization) studies*

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Summary. The need for further information on drug utilization patterns during pregnancy in different countries was assessed by reviewing literature obtained by hand and computer searches for the years 1960–1988.

The 13 identified studies showed that pregnant women used an average of 4.7 drugs. The most commonly ingested medications were vitamins and iron preparations (almost all women), analgesics, antiemetics and antacids.

However, the important variables taken into account differently in each study, such as date of surveillance, country, size of population, personal habits, and physiopathological and demographic characteristics, may it impossible to construct a comprehensive, detailed, up-to-date picture of drug utilization during pregnancy.

The evaluation confirmed the need for systematic permanent surveillance of drug utilization in pregnancy, so as to avoid the use of data based on widely differing contexts, times and methods, in a field where knowledge is often derived from scanty information.

Key words: pregnancy, drug utilization; surveillance

More than 25 years ago the thalidomide disaster gave rise to a decisive change in attitude and practices in drug evaluation, but the area of pregnancy has remained on the edge of the interests of those seeking a satisfactory epidemiological profile of the efficacy/safety balance of drug treatment. The wealth of studies on pharmacokinetic and metabolic aspects of the developing fetus and newborn, and the few major epidemiological studies on malformation risks, have created a cautious attitude. The results of controlled trials of selected pharmacological interventions, e.g. for hypertension and preterm labour, have helped to clarify some controversial areas of prevention and therapy [1]. However, the question of the quality of prescription and use of drugs by the majority of physicians and women has not been adequately covered by the occasional studies available in various countries whose findings were not always officially published (e.g. in Italy), or are reported only in the local language (e.g. in West Germany, 2). In view of the lack of clear guidelines, a tendency to over-medication and over-prescribing, and the spread of highly conservative and even out of date practices among physicians and laymen is an ever-present risk.

Many books deal with drug therapy during pregnancy and in the very early post-natal period (only English books published during the '80s are reported in the references 3–16), but information seems scanty and incomplete in terms of formal studies of the extent and pattern of use of drugs in pregnancy. Data from population surveys are reviewed here, which could be employed as general reference sources.

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Materials and methods

A systematic hand search of the most widely cited literature (according to SCI Journal Citation Reports, 17), plus a computer search using the MEDLINE database of the National Library of Medicine, Bethesda, Maryland, for the years 1960–1988, on the subject of drug utilization during pregnancy identified 48 papers. A detailed analysis identified 14 general papers, and 21 related to specific classes of drugs, a single period of gestation, malformations alone, lacking sufficient data analysis, or repeated or preliminary reports. Thus, a total of 13 original papers in English was selected reporting analytical findings about drugs taken by groups of women throughout pregnancy [18–30].

Results

General analysis

The majority of publications dated from 1973–79 (9/13, 69%), and data had been collected during 1959–76 (10/13, 77%). For only one paper [28] was the year of the study and of publication of findings the same (1982). For the other papers the average delay was 5.3 years (range 2–11; Table 1).

Table 1. Selected studies on drug use in pregnancy

Study No.	Ref.	Place	Period	No. of women	Year of publication
1	18	Houston and Univ. Wisc., USA	1966	240	1967
2	19	Collaborative Perinatal Study (12 hospitals), USA	1959–65	50282	1973
3	20	Edinburgh, UK	1963–65	911	1973
4	21	Houston, USA	1970	156	1973
5	22[a]	Malmö, Sweden	1963–65	5753	1976
6	23	County of Jäntland, Sweden	1971–72	341	1977
7	24	Tucson, Arizona, USA	1975	97	1977
8	25	Gainesville, Florida, USA	1974–76	168	1978
9	26	Tennessee Medicaids, USA	1975–76	2528	1978
10	27	Long Beach, California, USA	1973	153	1979
11	28	Ann Arbor, Michigan, USA	1982	245	1982
12	29	Glasgow, UK	1982–84	2765	1986
13	30	Michigan Medicaids, USA	1981–83	18886	1987

[a] The findings of this study were reported in five different papers [22, 31–34]. The report noted here is the first to describe the study plan

Table 2. Data colleted in selected studies of drug use in pregnancy

Study No.	Drug history obtained	Obstetrical history	Demographic characteristics	Life habits	Mothers taking drug (%)	Mean No. of drugs taken
1	Prospective recording during pregnancy – Interview	Yes	No	Yes	> 89	5.4
2	Prospective recording during pregnancy – Interview	Yes	Yes	Yes	94	3.8
3	Interview at delivery	No	No	Yes	97	4[a]
4	Interview at delivery	No	No	Yes	100	10.3[b]
5	Prospective lists	Yes	Yes	No	> 80	5.4
6	Medicaid files	No	Yes	No	87	3.1
7	Interview at delivery	Yes	No	Yes	100	4.7
8	Prospective recording during pregnancy – Interview	No	Yes	No	100	11
9	Medicaid files	No	Yes	No	82	5.1
10	Prospective recording during pregnancy – Interview and diary	No	No	No	83	3[c]
11	Interview at delivery and antepartum charts	Yes	Yes	Yes	98	2.9
12	Prospective recording during pregnancy – Interview	No	Yes	Yes	35[d]	?
13	Medicaid claims	No	Yes	No	100	5.5

[a] Iron not-included; [b] including labor and delivery medications; [c] mode, iron and vitamins not included; [d] Iron and vitamins not included

All the reports originated from developed countries: nine (69%) from U.S.A. and four (31%) from Western Europe (two from the U.K. and two from Sweden). The studies involved a total of 82,525 women (range in the single studies 97–50,282), 88% of them from U.S.A. The imbalance in the numbers enrolled is reflected in the criteria for collecting data or including women (Table 2).

Systematic comparison of the present findings and previous surveys was attempted in only three studies [26, 28, 30], although, in view of the methodological differences in collecting data, as well as in the data themselves, the discussion had to be limited to the average number of drugs taken.

The changing patterns of drug use during pregnancy in the same country were formally analyzed in two studies [22, 29], which compared recent results with those obtained, respectively, 10 and 20 years earlier in Sweden [34] and U.K. [29]. However, in that case too "... important differences in the methods of the studies limit the possibility of making precise comparisons" [29].

Interviews with the woman were the most widely used approach (nine studies, 69%) to obtain the drug exposure history, as compared to other sources of such information (Medicaid files or diary). Data were collected prospectively in six studies (46%), five by periodical interview and one by diary. A retrospective survey was made by interview at delivery in four studies (31%) and from Medicaid files in three (23%).

The different approaches affected the size of samples. In fact 59,361 women (72% of the overall population) underwent prospective recording of drug intake. For

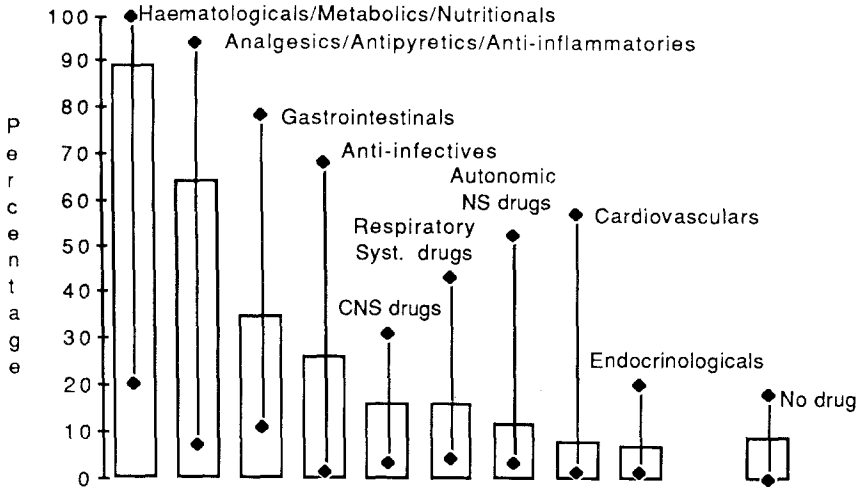

Fig. 1. Median percent (Â) and range (◆) of women enrolled in selected studies according to the most common classes of medication taken

21,755 women (26%) the drug history profile was defined by reviewing Medicaid files or charts, and for only 1,409 (2%) by interview at delivery.

Data concerning obstetric history (abortions, stillborns, neonatal deaths, and delivery data) were collected in only five studies (39%). The demographic characteristics of the study population were reported in eight papers (62%) and life habits (smoking, alcohol, coffee, tea and/or cola consumption) were investigated in seven studies (54%). Only two papers took partial account of all three variables [19, 28].

Drug use profile

A median of 4.7 drugs was taken by each woman, with a range of 2.9 to 5.5 in comparable studies. The most commonly used classes of drugs are reported in Fig. 1. Iron and vitamins, alone or in combination, dominated prescriptions throughout pregnancy, being taken by almost all women, with some differences from one study to another.

Analgesics/antipyretics/anti-inflammatories were the second most widely taken class of drugs, particularly mild analgesics (mostly aspirin) for relief of headaches and musculoskeletal discomfort. Antiemetic and antiacid therapy were taken by about a quarter of the overall population. Of the many different anti-infective agents (including tetracyclines, sulphonamides, chloramphenicol), penicillin derivatives led the list, ampicillin being the most frequently used. The remaining classes of drugs (each taken by 10–20% of women) included a piecemeal array of compounds, such as psychotropic agents (particularly the minor tranquilizers, diazepam), antihistamines, and diuretics.

The pattern of use during the different trimesters is hard to define. One paper affirms "... the drug exposure rate increased, rather than decreased, as pregnancy advanced" [28], whereas another paper reports "... overall drug use (excluding vitamins) did decrease during pregnancy, ..." [30]. Probably vitamins are a "confounding variable" in these sentences. The two selected Swedish studies done at different times noted that "... a marked and significant reduction in the use of psychotropic drugs and antihistamines can be seen" [34]. This suggests that the variable "year study performed" may be another confounding variable for correct evaluation of the epidemiological pattern of drug use, not only because of the presence of different drugs on the market, or changes in their therapeutic indication(s), but other potential sources, too, i. e., women's habits and health policy.

Similarly, since the incidence of self-administration can be affected by country, time and type of study, it is difficult to assess; i. e., "... self administered drug was used at some stage during pregnancy by 64.4% women in the previous study [20] compared with only 8.8% in the recent one [29]".

Discussion

The survey has suffered from major limitations, but it does at least give a hazy outline of what classes of drugs are used, and when, in pregnancy. The general profile emerging from the piecemeal information where important covariables are randomly considered (country, region, hospital, obstetric history, delivery data, newborn data, maternal habits and education, drug therapy in different periods of pregnancy), and the findings of different completed studies, cannot be viewed as a whole. There appears to be a challenging need for a research protocol (intra- and inter-country) about drug use in pregnancy, including comparative variables.

Drawing on the experience of the WHO-DURG (World Health Organization – Drug Utilization Regional Group), which has documented the importance of systematic surveys in the extent and quality of drug use in various countries [35], an epidemiological collaborative study is now under way [36] to assess the pattern of drug use in pregnancy through standardized interviews of women admitted for child delivery to sample hospitals over a predefined period in different countries; to establish a permanent research network with centres where obstetric and perinatal care is delivered; to assure a readily available resource to test/validate therapeutic or prophylactic measures, and drug safety issues. Twenty-three countries

from Europe, America, Asia, and Africa are already collecting data.

When the findings become available, the scanty and incomplete information on the topic will, it is hoped, be greatly strengthened. The exercise may be repeated in the same and other countries in the future to give a constantly updated picture of drug utilization during pregnancy, which is amongst the least developed areas for which no comprehensive surveillance program is yet available.

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