

INTERNATIONAL COOPERATIVE STUDY ON DRUG USE IN PREGNANCY

RESULTS FROM MALTA

C. Savona-Ventura, E.S. Grech

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INTRODUCTION

The risks of teratogenesis and other adverse effects on the neonate have created a cautious attitude towards the use of drugs during pregnancy. It is generally believed that drug intake in pregnancy is high and variable in different countries, but the quality of prescriptions and use of drugs by the majority of physicians and women has by no means been adequately clarified (1). To identify the pattern of drug use in pregnancy a collaborative network was set up by WHO-IRO to collect comparable data on a population large enough to represent the current situation across various 'cultural' and health care settings. This epidemiological collaboration study allows not only for an international assessment of drug usage during pregnancy and the puerperium, but also enables inter-country differences to be identified. This study attempts to correlate drug usage during pregnancy in Maltese women to the trends identified in the International Cooperative Drug utilization Study (2, 3).

MATERIAL AND METHODS

An international cooperative network was set up involving 131 hospitals representing 19 countries. In each participating country a clinical pharmacology unit and/or an obstetrics department acted as a reference center for

a group of hospitals representing various levels of care. The maximum expected enrolled number of deliveries for each country was 0.1% of the number of live-births per annum. A total of 12605 deliveries were enrolled by December 1989. The Department of Obstetrics and Gynaecology at Karin Grech Hospital (Malta) participated by enrolling 100 deliveries occurring during the period 8 - 16 October 1987 accounting for 1.8% of all the deliveries registered in the Maltese Islands that year. The general organization for the International Cooperative Study has been previously described (4). Women were interviewed in the first week after delivery using a simple structured standardized questionnaire, a method that has been shown to be reliable and accurate for obtaining recalled pregnancy-related events including drug exposure (5). In addition the hospital files were reviewed so that hospital use of drugs could be assessed. A detailed descriptive list of prescribed drugs in Maltese pregnant women has been elsewhere reported (6).

RESULTS

The majority of Maltese pregnant women (99%) received some form of medication sometime during their pregnancy, the larger proportion (96.97%) receiving drugs during the antenatal period while 75.76% and 62.63% received drugs during the intrapartum and postpartum periods. More medications were prescribed however during the latter two periods than during the antenatal period (Table 1). These figure compared to the international trends suggest that during the antenatal period a larger percentage of women receive some form of

prescription when compared to the overall group. The mean number of drugs taken per patient is however less in Maltese patients at any time during pregnancy.

During the antenatal period therefore only 4% of Maltese women received no form of medication. This contrasts with the figure of 13% in the overall group and is similar to the prescribing trends in Ireland (2%), Finland (3%), Brazil (6%), Sri Lanka (1%), India (3), Panama (0%) and Ghana (0%). The percentage of non-drug takers during the antenatal period by participating country is shown in Figure 1. Czechoslovakia and G.D.R. appeared to have the larger percentage of non-drug takers with 36% and 39% respectively.

Drug taking during the antenatal period appears to be more common in Maltese pregnant women when compared to the international mean, though the mean number of drugs taken per woman appears to be markedly reduced. This high drug intake during the antenatal period appears to result from more frequent haematological prescriptions, these accounting for 54.2% of all prescriptions given to 90.6% of all mothers. These figures contrast with those of the international group where haematological prescriptions accounted for 25% of all prescriptions given to 64% of mothers (Table 2). The haematological prescription habits of different countries

C. SAVONA-VENTURA
MD MRCOG SPEC. OBS GYNAE (LEUVEN)
KAREN GRECH HOSPITAL
E. GRECH MD FRCOG
KAREN GRECH HOSPITAL

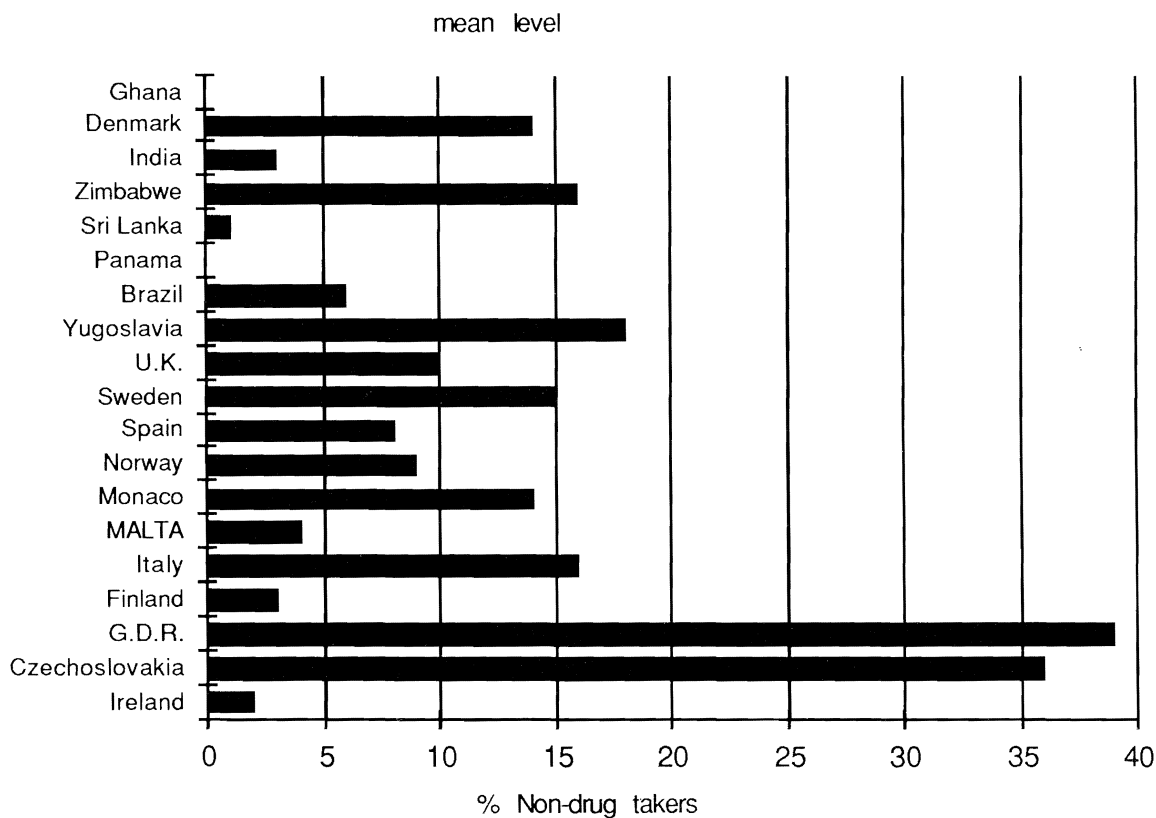


FIGURE 1: POPULATION PROFILE: NON-DRUG TAKERS ANTENATAL PERIOD

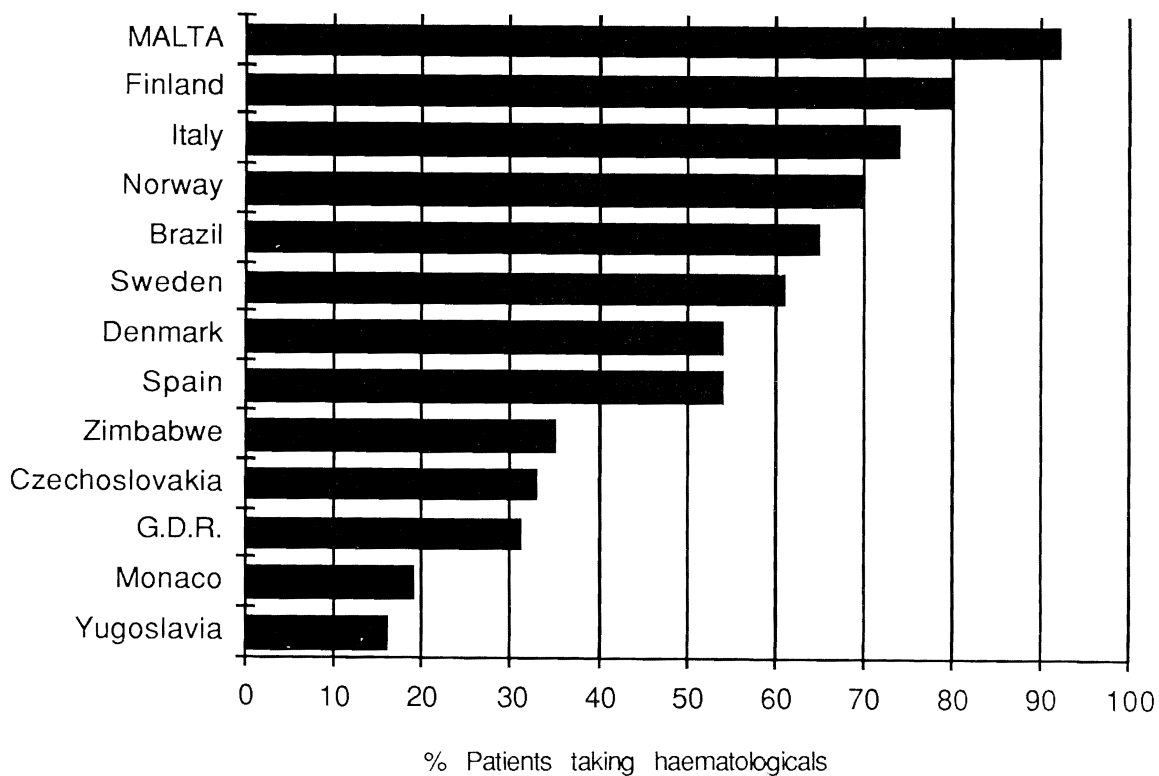


FIGURE 2: PERCENTAGES OF WOMEN TAKING HAEMATOLOGICALS

participating in the study suggests that prescription of haematologicals is most frequent in Malta (Figure II). The intake of all other class of medication appeared to be markedly reduced in the Maltese group, while anti-infective agents appear to have been given to a similar proportion of mothers in both groups (Table 2).

The number of women receiving drugs during the period between hospital admission and delivery appeared to have been reduced from 80.0% in the overall group to 75.76% in the Maltese population with only a minimal decrease in the mean number of drugs taken per patient. these prescriptions were indicated for analgesia or general anaesthesia (67.3% of prescriptions), to augment or delay labour (26.5%) and a minority were prescribed for a variety of indications and included anti-infectives, anti-hypertensives, anti-emetics/antacids, tranquillizers and corticosteroids.

In the third stage of labour and the puerperium until discharge from hospital 62.63% of Maltese women received some form of medication with a mean of 2.19 drugs per patient. This figure contrasts with the higher rate of 79.2% and a mean number of drugs of 2.917 in the overall study population (Table 1). All the Maltese women receiving medication were planning to breastfeed, while only 92.6% of the international group receiving drugs were planning to do so. Initial breastfeeding rates vary from one country to another. In the Maltese population the initial breastfeeding rate was 64%. The medications most frequently prescribed in the Maltese group (Table 3) were the endocrinologicals (49.9% of prescriptions given to 95.2% of women) and the anaesthetics (36.8% of prescriptions given to 80.7% of women), rates which are markedly in excess to those prescribed in the international group (7% of prescription given to 20% of mothers, and 2% of prescriptions given to 6% of women respectively). Identification of these drugs to the principle shows that these prescriptions referred to syntometrin and lignocaine administered after delivery of the child to prevent pos-partum haemorrhage and enable perineal suturing. The relative low rate in the international group may reflect the general inclusion of these drugs as part of the labour process rather than as part of the early puerperium. All other drug classes in the Maltese

group were prescribed at a markedly lower frequency than in the overall international group (Table 3).

DISCUSSION

Knowledge of how to handle drugs in pregnancy is still limited and the participating health professional is in any case unlikely to be in possession of all the known facts. Often a woman is merely advised to avoid drugs altogether when she becomes pregnant and if teratogenic drugs have already been taken abortion may be recommended where this is legally permissible. Prescribing habits to pregnant women vary from one country to another. Reliable comparative data on drug usage in pregnancy is largely lacking and even regional or local figures tend to be incomplete or outdated. While drug usage in pregnancy appears to have decreased over the last three decades after the thalidomide experience, it appears that the current level of drug usage is in excess of what one would expect. Drawing on the experience of WHO which has documented the importance of systematic surveys in the extent and quality of drug use in various countries, an epidemiological collaborative study was initiated primarily to assess the pattern of drug use in pregnancy over a predefined period from sample hospitals in different countries (4). The study showed marked intra- and inter-country differences in prescribing habits and the observed drug use profile differed significantly from the picture obtained from the literature, suggesting that practices are continually shifting under the combined influences of variables such as time and country (3).

Prescribing habits in Malta during the antenatal course of pregnancy may be said to be conservative even though a large proportion of women received some form of medication. Pregnant Maltese women received from 1-2 prescriptions during the antenatal period, the larger proportion being haematologicals. All other medications, except the anti-infectives, were prescribed at a marked lower rate. Haematological prescriptions to antenatal patients have been shown to vary from country to country varying from 15% of women in Yugoslavia to 90.6% of women in Malta (3). The value of routine oral iron supplementation in pregnancy remains controversial and it appears that such a widely used therapy

does not seem necessary for the majority of healthy pregnant women in a developed country (7). The incidence of anaemia (Hb under 10 g/dl) in the Maltese pregnant population approximated 0.7% of all deliveries in 1983-1986 (8). The conservative practices regarding other medicaments reflect in part the critical attitude of health care professionals in Malta and also to a similar suspicious attitude by the pregnant woman herself. Patient awareness of the adverse effects of drugs is reflected by reluctance to take medication even when correctly prescribed and by their attitudes towards smoking on discovering they were pregnant when 63.4% attempted to stop (9). Excluding the administration of haematologicals and metabolic-nutritional supplements, all other medicaments were prescribed for a number of medical disorders pre-existing or appearing during pregnancy, to alleviate minor symptoms and to manage specific obstetric problems such as habitual abortion and preterm labour (6).

Intra-hospital prescriptions before and during delivery show an overall similarity to the international group, with the majority of drugs being prescribed to influence the progress of labour and as intrapartum analgesia. The high proportion (75.76%) of women receiving medications and the high mean number of drugs per patient (3.17) reflect the active intrapartum management policy practised in the hospital. The use of intrapartum analgesia and intra-operative anaesthesia in Maltese women has been previously reviewed (10). The use of systemic analgesia and anaesthesia was shown to be associated with depressed Apgar scores of the infants, though this may not have been the result of a direct association with drug usage. A few intrapartum prescriptions were administered for maternal conditions pre-existing during pregnancy or occurring in the intra-partum period. Dexamethasone and salbutamol were administered for foetal indications to delay labour and stimulate lung surfactant production in cases of preterm labour. Other medications given after the birth of the child include the administration of oxytocics to prevent postpartum haemorrhage and local anaesthetics for perineal suturing. Drugs appear to be rarely prescribed to the lactating female in the early puerperium.

CONCLUSION

This study has shown that, except in the case of the prophylactic administration of haematologicals during the antenatal period and the intrapartum prescriptions to manage labour actively, the majority of pregnant women and health care professionals in Malta have a conservative attitude towards drug prescription in pregnancy and lactation using medications only when they are considered essential.

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Collaborative Group on Drug Use in Pregnancy

Study Secretariat and Data Management
M Bonati and G Tognini (Co-ordinators);
T Castoldi and D Miglio (Secretaries); R Bortolus, S Cernignani, P Colombo, I Dapsy, G Fellin, F Marchetti, I Negrello, M Romero (Data Management).

Advisory Board

M.N.G.Dukes, I. Lunde, M. Wagner (WHO-EURO, Copenhagen, Denmark);
P.K. Lunde (IUPHAR, Oslo, Norway).

TABLE 1 : DRUG THERAPY DURING DIFFERENT CONSIDERED PERIODS

DRUG THERAPY	Maltese Population		International study		
	No of drug takers	Mean no of drugs /patient (%)	No of drug takers	Mean no of drugs /patient (%)	
Started before and continued during pregnancy	4	(4.04) 1.75	526	(4.2)	1.481
Started during pregnancy	95	(95.96) 1.86	10840	(87.0)	2.849
During pregnancy up to hospital admission for delivery	96	(96.97) 1.77	10829	(87.7)	2.897
Between hospital admission & delivery	75	(75.76) 3.17	9966	(80.0)	3.423
In the puerperium:					
-all women	62	(62.63) 2.19	9867	(79.2)	2.917
-breast feeders	62	(62.63) 2.19	9132	(73.3)	2.958
Whole pregnancy	99	5.57	12463		7.587

TABLE 2 : MEDICATIONS GIVEN DURING PREGNANCY UP TO HOSPITAL ADMISSION FOR DELIVERY

CLASS	MALTESE POPULATION		INTERNATIONAL STUDY	
	No of mothers	(%)	No of mothers	(%)
Haemetologicals	87	(90.6)	7004	(64)
Metabolic - nutritionals	28	(29.2)	5959	(54)
Autonomic nervous system drugs	7	(07.3)	2405	(22)
Anti-infections	19	(19.8)	2136	(19)
Analgesics, antipyretics	3	(03.1)	1890	(17)
Immunologicals	0	(-)	1676	(15)
Gastrointestinals	6	(06.3)	1364	(12)
Endocrinologicals	2	(02.1)	995	(09)
Central nervous system drugs	1	(01.0)	631	(06)
Cardiovasculars	3	(03.1)	496	(04)
Respiratory system drugs	2	(02.1)	392	(04)
Miscellaneous	2	(02.1)	345	(03)
Coadjuvants	0	(-)	333	(03)
Anaesthetics	0	(-)	37	(-)
Unknown, unclassified	0	(-)	480	(04)
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Total number of women receiving drugs	96		10929	

TABLE 3 : DRUGS TAKEN IN BREASTFEEDING (Current or planned) WOMEN

CLASS	MALTESE POPULATION		INTERNATIONAL GROUP	
	No of women	(%)	No of women	(%)
Autonomic nervous system	6	(9.7)	5302	(58)
Analgesics, antipyretics	3	(4.8)	3702	(40)
Metabolics, nutritionals	0	(-)	3098	(34)
Anti-infections	4	(6.5)	2963	(32)
Haemetologicals	0	(-)	2578	(28)
Endocrinologicals	59	(95.2)	1852	(20)
Gastrointestinals	2	(3.2)	943	(10)
Anaesthetics	50	(80.7)	584	(06)
Central nervous system drugs	2	(3.2)	596	(06)
Cardiovasculars	2	(3.2)	236	(02)
Immunologicals	3	(4.8)	266	(03)
Coadjuvants	-	(-)	174	(02)
Miscellaneous	0	(-)	145	(01)
Respiratory system drugs	0	(-)	93	(01)
Unknown - unclassified	-	(-)	9	(-)
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Total	62		9132	

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