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Prescription of Hazardous Drugs During Pregnancy

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Abstract

Background: Prescribing drugs to pregnant women requires the balancing of benefits and risks. Only a small proportion of drugs are known to be harmful to the fetus, but for the vast majority of drugs little evidence of fetal safety exists.

Aim: To determine the prescription pattern of potentially and clearly harmful prescription drugs during pregnancy with reference to drug safety categorisation, and to define the drug groups primarily responsible for multiple drug use during pregnancy.

Study design: A retrospective, register-based cohort study.

Methods: Linkage of three nationwide registers in Finland. Data collection included prescription drugs purchased during the preconception period and each trimester in the pregnant cohort, and the corresponding time periods in the non-pregnant controls.

The pregnancy safety categorisation was determined for each drug (Anatomic Therapeutic Chemical [ATC] code) by using the Swedish classification of approved medicinal products (Farmaceutiska Specialiteter i Sverige [FASS]) and if not available, the corresponding Australian (Australian Drug Evaluation Committee [ADEC]) or US categorisation (FDA).

Groups studied: Women applying for maternity support (maternal grants) during the year 1999 (n = 43 470) plus non-pregnant control women matched by age and hospital district (n = 43 470).

Results: In the pregnant cohort, 20.4% of women purchased at least one drug classified as potentially harmful during pregnancy, and 3.4% purchased at least one drug classified as clearly harmful. A significant decline occurred in the number of pregnant women purchasing potentially and clearly harmful drugs during the first trimester when compared with the preconception period, and the decline continued from the first to the second trimester. In the pregnant cohort, 107 (0.2%) women purchased at least ten different drugs during pregnancy. The drugs most commonly purchased in this group were topical corticosteroids and nasal preparations.

Conclusion: The use of hazardous prescription drugs declines during pregnancy but prescriptions of known teratogens and the relatively frequent practice of polypharmacy in epilepsy place emphasis on the need for careful pre-pregnancy counselling. However, drug safety classifications give a very crude estimation of risk and should only be used as general guidelines when planning treatment. Risk

assessment must always be made on an individual basis, and pregnant women with illnesses requiring treatment must be treated adequately.

Introduction

Major congenital anomalies occur in approximately 2–3% of all pregnancies,[1] placing a considerable burden on the affected child, the family and society. In more than half the cases, the aetiology of malformations remains unknown.[1] Only a minor proportion, less than 10%, are estimated to arise from drug teratogenicity.[2] Approximately 30 drugs from several drug groups are known to be teratogenic in man (table I).[1,2] First-trimester exposure to a harmful agent may cause structural malformations, but if first-trimester exposure is avoided, many drugs may be safely used during the second or third trimesters. Some drugs are known to affect the fetus during the later stages of pregnancy. However, the fetal safety of the vast majority of drugs remains unconfirmed and it is possible that many drugs possess a yet-unidentified teratogenic potential.

Drugs can be classified according to fetal safety based on animal data or on available experience and data from human pregnancies. The purpose of drug labelling is to convey information about the level of risk and precautions necessary for drug use during pregnancy. Although several categorisations have been introduced to help clinicians in decision-making (table II), significant differences exist between the systems in the distribution of drugs into risk categories.[3] The US FDA categorisation,[4] established in 1979, is currently under revision.[5] It makes extensive demands for scientific documentation of the safety of each drug and has been criticised for being of questionable value in clinical settings.[3,5,6] The Swedish system, implemented in 1978 in the catalogue of approved medicinal products [Farmaceutiska Specialiteter i Sverige (FASS)],[7] differs considerably from the FDA classification, having a more clinical approach, and covering a considerable number of drugs.[6] A system slightly modified from the Swedish categorisation was adopted by the Australian Drug Evaluation Committee (ADEC) in 1989.[8]

A number of studies report drug use during pregnancy to be extensive.[9-14] In addition to newly marketed drugs, possible drug-interaction effects on pregnancy outcome, including later life and development, are as yet unknown.

The aim of the present study was to examine the purchasing frequency of potentially or clearly harm-

Table I. Drugs or drug groups known or strongly suspected to cause developmental defects, and their pregnancy safety categorisation (see table II for an explanation of the safety categories)

Drug	FASS	ADEC	FDA
Agents acting on renin-angiotensin system	D	D	C (I trimester)
			D (II and III trimesters)
Antiepileptic drugs (valproic acid, carbamazepine, phenytoin)	D	D	D
Alkylating agents	D	D	D
Androgens	No code	D	X
Antimetabolites	D	D	D, X
Carbimazole	No code	C	D
Coumarin derivatives	D	D	X
Fluconazole (doses used in systemic mycoses)	B3	B3	C
Lithium	D	D	D
Misoprostol	D	X	X
Penicillamine	No code	D	D
Retinoids	D	X	X
Thalidomide	No code	No code	X

ADEC = Australian Drug Evaluation Committee (Australian categorisation); **FASS** = Farmaceutiska Specialiteter i Sverige (Swedish categorisation); **FDA** = Food and Drug Administration (US categorisation).

Table II. Pregnancy safety category definitions

Category	Pregnancy category definitions
FASS	
A[a]	Drugs taken by a large number of pregnant women with no proven increase in the frequency of malformations or other observed harmful effects on the fetus
B1[a]	Limited experience in pregnant women, no increase observed in the frequency of malformations or other observed harmful effects on the fetus
	Animal studies reassuring
B2[a]	Limited experience in pregnant women, no increase observed in the frequency of malformations or other harmful effects on the fetus
	Animal studies inadequate or lacking
B3[b]	Limited experience in pregnant women, no increase observed in the frequency of malformations or other harmful effects on the fetus
	Animal studies have shown evidence of an increased occurrence of fetal damage
C[b]	May cause pharmacological adverse effects on the fetus or neonate
D[c]	Suspected or proven to cause malformations or other irreversible damage
ADEC	
A-D	Categories A,[a] B1,[a] B2,[a] B3,[b] C,[b] D[c] similar to the FASS definitions
X[c]	High risk of causing permanent damage to the fetus. Contraindicated in pregnancy
FDA	
A[a]	Controlled studies fail to demonstrate a risk to the fetus in the first trimester. Fetal harm appears remote
B[a]	No controlled studies in humans, animal studies indicate no risk; or well-controlled studies in humans show no risk, and animal studies show an adverse effect on the fetus
C[b]	No controlled studies in women, animal studies indicate risk or are lacking
D[c]	Existing evidence of fetal risk in humans, benefits may outweigh risks in certain situations
X[c]	Risk clearly outweighs any possible benefit. Contraindicated in pregnancy

a Drugs grouped as probably safe.

b Drugs grouped as potentially harmful.

c Drugs grouped as clearly harmful.

ADEC = Australian Drug Evaluation Committee (Australian categorisation); **FASS** = Farmaceutiska Specialiteter i Sverige (Swedish categorisation); **FDA** = Food and Drug Administration (US categorisation).

ful prescription drugs during pregnancy, with reference to drug safety categorisation. Another aim was to define the drug groups mainly involved in multiple drug use during pregnancy.

Methods

Register Data

Kela, the Social Insurance Institution of Finland, maintains a nation-wide register with data on all women who have applied for maternal grants. Grants are paid when pregnancy has been ongoing for 154 days and the mother has visited a maternity clinic before the end of the fourth month. Practically all mothers apply for maternal grants. We collected retrospective data on all women who applied for maternal grants in 1999. To rule out the influence of previous pregnancies or lactation, women who had made applications for maternity grants during the 24 months preceding the beginning of this pregnancy were excluded from the study and a total of 43 470 pregnant women were eventually included. In the register data, the estimated date of delivery is recorded; in our study, the beginning of the first trimester was calculated by subtracting 40 weeks from this date. After the child is born, the date of birth is added to the register.

Controls were collected from the Finnish Population Register. For each pregnant woman we randomly selected one female control of the same age and from the same hospital district, who had not applied for a maternity grant during the period beginning 24 months before the pregnancy of the matched case and finishing at the end of 2000. The prevalence of

asthma and thyroid disorders was similar in the two cohorts, whereas chronic diseases, such as psychiatric disorders, epilepsy and hypertension, were more common in the control group.[9] The control group served primarily as a reference group reflecting possible time-related trends in drug prescription and reimbursement policy.

Kela also maintains a nationwide Drug Prescription Register comprising data on 97% of all reimbursed prescriptions. In Finland, almost all prescription-only drugs necessary for treatment of an illness are reimbursable. Some over-the-counter (OTC) drugs are also reimbursable when prescribed by a physician. We used claims data for time-periods comprising 3 months before pregnancy and during pregnancy (divided into three trimesters: weeks 0–12, 13–26, and 27 onwards) for the pregnant cohort and the corresponding periods for the non-pregnant controls.

Drugs were coded according to the Anatomic Therapeutic Chemical (ATC) classification system (year 2000), with the date of purchase recorded. The linkage of all these registers is made possible by the unique identification number (coded in a concealed form for study purposes) assigned to all Finnish citizens and those with permanent residence in Finland.

Drug Safety Categorisation

We linked each individual ATC code to the corresponding pregnancy safety code, primarily using the Swedish categorisation (FASS 1999 or 2000). If this was unavailable, we used the Australian categorisation (ADEC), and when neither was available, we used the US categorisation (FDA). We grouped the drugs as probably safe, potentially harmful, and clearly harmful (table II).

Statistics

Pregnant women served as their own controls for drug-purchase changes during various trimesters. The changes were calculated by using the McNemar test (2-sided) on dichotomic variables (use or no use) for time-dependent association by cross tabulation. Odds ratios (OR) and 95% CI were calculated by cross tabulation using the Chi square distribution These tests were also used when comparing pregnant women with non-pregnant controls. Due to the large sample size and rounding off, some endpoints for the CIs turned equal. All calculations were made with the SPSS statistical package.

Results

The distribution of pregnancy safety categorisations for all 562 different ATC codes recorded in the two cohorts is shown in table III.

Potentially Harmful Drugs

Of the 43 470 pregnant women, 8853 (20.4%) purchased at least one drug which was classified as potentially harmful during their pregnancy versus 15 562 (35.8%) controls (OR 0.5, 95% CI 0.4, 0.5)

Table III. Distribution of pregnancy safety categorisations for the 562 different Anatomic Therapeutic Chemical (ATC) codes recorded in the study

Safety categorisation		n (%)
FASS	A[a]	72 (12.8)
	B1[a]	59 (10.5)
	B2[a]	37 (6.6)
	B3[b]	74 (13.2)
	C[b]	133 (23.7)
	D[c]	53 (9.4)
ADEC	A[a]	15 (2.7)
	B1[a]	4 (0.7)
	B2[a]	3 (0.5)
	B3[b]	3 (0.5)
	C[b]	16 (2.8)
	D[c]	7 (1.2)
	X[c]	1 (0.2)
FDA	A[a]	3 (0.5)
	B[a]	9 (1.6)
	C[b]	29 (5.2)
	D[c]	6 (1.1)
	X[c]	4 (0.7)
No code		34 (6.0)
Total		**562**

a Drugs grouped as 'probably safe' for the purposes of this study.

b Drugs grouped as 'potentially harmful' for the purposes of this study.

c Drugs grouped as 'clearly harmful' for the purposes of this study.

ADEC = Australian Drug Evaluation Committee (Australian categorisation); **FASS** = Farmaceutiska Specialiteter i Sverige (Swedish categorisation); **FDA** = Food and Drug Administration (US categorisation).

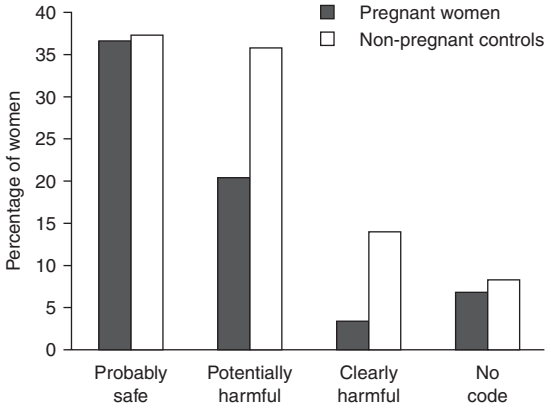

Fig. 1. Percentage of pregnant women (n = 43 470) and non-pregnant controls (n = 43 470) purchasing drugs grouped as probably safe, potentially harmful and clearly harmful during pregnancy.

[figure 1]. The number of pregnant women purchasing potentially harmful drugs during the first trimester was significantly lower when compared with the preconception period (11.2% vs 17.9%; OR 0.6, 95% CI 0.6, 0.6; $p < 0.05$). Furthermore, the decline continued from the first to the second trimester (OR 0.7, 95% CI 0.7, 0.7; $p < 0.05$) but there was no significant difference between the second and the third trimester ($p = 0.2$) [figure 2a]. Of the individual drugs used with increased frequency in the third trimester, nimesulide, the only one considered harmful, was purchased by seven pregnant women in the second trimester and by 12 in the third trimester. The most frequently purchased potentially harmful drugs during the different trimesters are presented in table IV.

Clearly Harmful Drugs

Of the pregnant women, 1478 (3.4%) purchased at least one drug classified as clearly harmful during their pregnancy versus 6075 (14%) controls (OR 0.2, 95% CI 0.2, 0.2) [figure 1]. The number of pregnant women purchasing clearly harmful drugs during the first trimester was significantly lower than during the preconception period (3.2% vs 5.5%; OR 0.6, 95% CI 0.5, 0.6; $p < 0.05$), and declined further from the first to the second trimester (OR 0.1, 95% CI 0.1, 0.2; $p < 0.05$). There was no significant difference between the second and the third trimester ($p = 0.9$) [figure 2b]. Three women purchased isotretinoin, a potent teratogen, in the preconception period, and one during each pregnancy trimester. Two women purchased combination preparations containing misoprostol, a drug strongly suspected to cause developmental defects, in the first trimester. Drugs classified as clearly harmful and purchased during the different trimesters are presented in table V.

Polypharmacy

In the pregnant cohort, 107 (0.2%) women purchased ten or more different drugs during the period of pregnancy (mean 12.0, range 18; 10–28), and 29 (0.1%) women purchased five or more drugs during each trimester.

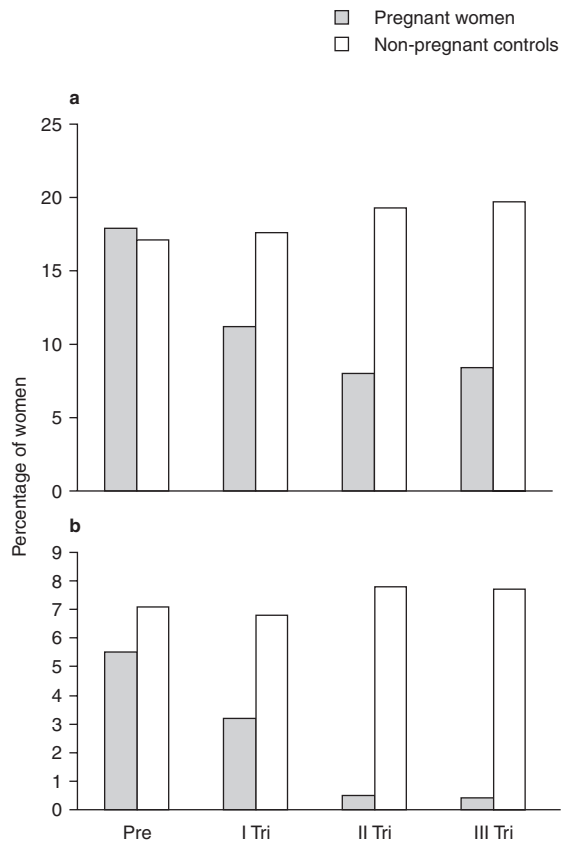

Fig. 2. Percentage of pregnant women (n = 43 470) and non-pregnant controls (n = 43 470) purchasing drugs grouped as: (**a**) potentially harmful and (**b**) clearly harmful. Time-periods correspond to preconception (3 months before the first trimester) and pregnancy trimesters. **Pre** = preconception; **tri** = trimester.

Table IV. Number of pregnant women (n = 43 470) purchasing individual drugs categorised as potentially harmful. Only the most commonly purchased drugs are presented

Preconception	n (%)	I trimester	n (%)	II trimester	n (%)	III trimester	n (%)
Ibuprofen	719 (1.7)	Pivmecillinam	627 (1.4)	Pivmecillinam	629 (1.4)	Pivmecillinam	573 (1.3)
Fluconazole	707 (1.6)	Chorionic gonadotropin	328 (0.8)	Fluticasone propionate (nasal)	380 (0.9)	Labetalol	565 (1.3)
Clomifene	681 (1.6)	Clomifene	287 (0.7)	Labetalol	215 (0.5)	Fluticasone propionate (nasal)	292 (0.7)
Naproxen	566 (1.3)	Ibuprofen	271 (0.6)	Budesonide (inhalation)	214 (0.5)	Budesonide (inhalation)	234 (0.5)
Nafarelin	457 (1.1)	Fluconazole	243 (0.6)	Fluticasone propionate (inhalation)	206 (0.5)	Beclometasone (inhalation)	200 (0.5)
Tizanidine	376 (0.9)	Fluticasone propionate (nasal)	241 (0.6)	Beclometasone (inhalation)	192 (0.4)	Fluticasone propionate (inhalation)	195 (0.4)
Buserelin	328 (0.8)	Budesonide (inhalation)	169 (0.4)	Beclometasone (nasal)	180 (0.4)	Aciclovir	147 (0.3)
Fluticasone propionate (nasal)	322 (0.7)	Fluticasone propionate (inhalation)	167 (0.4)	Mometasone (nasal)	131 (0.3)	Beclometasone (nasal)	132 (0.3)
Diclofenac	318 (0.7)	Beclometasone (inhalation)	144 (0.3)	Budesonide (nasal)	112 (0.3)	Nifedipine	120 (0.3)
Pivmecillinam	317 (0.7)	Labetalol	131 (0.3)	Hydrocortisone butyrate (topical)	111 (0.3)	Budesonide (nasal)	117 (0.3)
Ketoprofen	284 (0.7)	Diclofenac	121 (0.3)	Ibuprofen	74 (0.2)	Mometasone (nasal)	91 (0.2)
Chorionic gonadotropin	271 (0.6)	Beclometasone (nasal)	118 (0.3)	Piroxicam (topical)	72 (0.2)	Hydrocortisone butyrate (topical)	76 (0.2)
Tolfenamic acid	197 (0.5)	Tizanidine	115 (0.3)	Hydroxyzine	70 (0.2)	Ursodeoxycholic acid	60 (0.1)

Table V. Number of pregnant women (n = 43 470) purchasing individual drugs categorised as clearly harmful

Preconception	n (%)	I trimester	n (%)	II trimester	n (%)	III trimester	n (%)
Doxycycline	918 (2.1)	Follitropin α or β	595 (1.4)	Carbamazepine	77 (0.2)	Carbamazepine	84 (0.2)
Follitropin α or β	690 (1.6)	Doxycycline	282 (0.6)	Valproic acid	63 (0.1)	Valproic acid	64 (0.1)
Estradiol	187 (0.4)	Estradiol	175 (0.4)	Oxcarbazepine	30 (0.1)	Oxcarbazepine	30 (0.1)
Norethisterone	158 (0.4)	Carbamazepine	72 (0.2)	Doxycycline	21 (0.0)	Phenytoin	5 (0.0)
Cyproterone[a]	101 (0.2)	Menotropin	69 (0.2)	Azathioprine	5 (0.0)	Azathioprine	4 (0.0)
Leuprorelin	79 (0.2)	Valproic acid	64 (0.1)	Phenytoin	5 (0.0)	Vigabatrin	3 (0.0)
Tetracycline	77 (0.2)	Buserelin	33 (0.1)	Vigabatrin	3 (0.0)	Warfarin	3 (0.0)
Menotropin	75 (0.2)	Norethisterone	30 (0.1)	Cyproterone[a]	3 (0.0)	Doxycycline	2 (0.0)
Carbamazepine	74 (0.2)	Tetracycline	28 (0.1)	Chlortetracycline(ocular)	2 (0.0)	Lithium	1 (0.0)
Valproic acid	59 (0.1)	Oxcarbazepine	23 (0.1)	Lithium	2 (0.0)	Tetracycline	1 (0.0)
Lymecycline	36 (0.1)	Cyproterone[a]	22 (0.1)	Isotretinoin	1 (0.0)	Isotretinoin	1 (0.0)
Enalapril	35 (0.1)	Enalapril	16 (0.0)	Interferon-β	1 (0.0)	Cyproterone[a]	1 (0.0)
Oxcarbazepine	27 (0.1)	Other renin/angiotensin antagonists[b]	13 (0.0)	Ethosuximide	1 (0.0)		
Other renin/angiotensin antagonists[c]	23 (0.1)	Lymecycline	7 (0.0)				
Misoprostol[d]	12 (0.0)	Azathioprine	5 (0.0)				
Simvastatin	9 (0.0)	Vigabatrin	4 (0.0)				
Warfarin	7 (0.0)	Lynestrenol	3 (0.0)				
Lovastatin	5 (0.0)	Interferon-β	3 (0.0)				
Azathioprine	5 (0.0)	Phenytoin	3(0.0)				
Phenytoin	5 (0.0)	Lithium	3 (0.0)				
Vigabatrin	5 (0.0)	Misoprostol[d]	2 (0.0)				
Lithium	4 (0.0)	Simvastatin	2 (0.0)				
Megestrol	3 (0.0)	Leuprorelin	2 (0.0)				
Isotretinoin	3 (0.0)	Warfarin	1 (0.0)				
Interferon-β	3 (0.0)	Quinine[e]	1 (0.0)				
Quinine[e]	2 (0.0)	Isotretinoin	1 (0.0)				

a Cyproterone and estrogen combination.

b Lisinopril, perindopril, ramipril, quinapril or losartan.

c Lisinopril, captopril, ramipril, quinapril or losartan.

d Diclofenac and misoprostol combination.

e Combination products containing quinine and meprobamate or diazepam.

In this subgroup of 107 women, the drugs most frequently purchased during pregnancy (defined by the third level ATC code) were dermal corticosteroids (85% of pregnant women in this subgroup), decongestants and other nasal preparations for topical use (74%), adrenergic inhalants (67%), and other inhaled drugs for obstructive airway diseases (63%), followed by penicillins (62%), other β-lactam antibacterials (59%), gynaecological anti-infectives (50%), anxiolytics (38%), corticosteroids for systemic use (38%), antihistamines (32%) and NSAIDs (31%).

The number of pregnant women purchasing two or more antiepileptic drugs concurrently was 23 (7.4% of the 309 pregnant women with an epilepsy diagnosis) during the preconception period and remained essentially the same throughout the pregnancy trimesters. Among the 21 antiepileptic drug combinations purchased by the pregnant women, four included three different antiepileptic drugs, and seven contained valproic acid.

Discussion

Principal Findings

We found that during the first trimester, 11.2% of pregnant women purchased at least one drug classified as potentially harmful and 3.2% purchased at least one drug classified as clearly harmful. However, potentially or clearly harmful drugs were purchased less frequently during each pregnancy trimester than during the preconception period.

Strengths and Weaknesses of the Study

The strength of our study lies in the combination of three nationwide registers, which made it possible to analyse drug prescription data in two large cohorts. The data derived from the maternal grants register and the prescription register enabled us to estimate accurately the time of drug purchase related to length of gestation, because ultrasound is performed before application for maternal grants. The control cohort reflected general Finnish trends in drug prescription and reimbursement policy.

A weakness is the absence of data as to any harmful effects of these drugs on pregnancy outcome. Secondly, caution should be used in interpreting our results in terms of actual drug use – we were only able to record drug purchase. Compliance could be lower in pregnant women, who may fear harming their unborn children.[15] Thirdly, only those drugs prescribed and reimbursed could be analysed.

Comparison with Previous Studies

Great cultural variations prevail concerning drug use during pregnancy.[10] In addition, the differences in methodology of study design, in classification of drugs, and in variables, such as socio-economic status or residence, often make comparison of results difficult. A Danish study based on registers and FASS categorisation of drugs reported 18% of pregnant women as being exposed to potentially or clearly harmful drugs during pregnancy.[16] In that study, the proportion of prescriptions for drugs classified as potentially harmful decreased during pregnancy, as in our findings. In a French study based on prescription records of 1000 pregnant women, 60% purchased drugs known to be harmful according to the FDA categorisation.[13] A recent, register-based study from The Netherlands reported 10% of prescriptions for pregnant women being classified as potentially harmful.[17] Studies based on interviews after childbirth may be biased, due to under- or over-reporting of past drug use; such studies are usually also based on a relatively small number of interviewees. Prospectively collected data – before the outcome of pregnancy is known – is the ideal method of gathering reliable data on drug use, and both prescription and OTC drugs can be included. This method demands well-organised, continuous data collection.[18]

Drug Categorisation and Relevance to Clinical Settings

Drug safety categorisations provide a very rough estimate of risk for adverse fetal effects. Relying on classification in individual risk assessment may lead to oversimplification. In addition to exposure, teratogenicity depends on dose and the time period of exposure. In counselling situations, risk assessment should always be made individually.[19] For example, pivmecillinam was purchased frequently by the pregnant cohort during the first trimester. Pivmecil-

linam is labelled by FASS as category C due to its potential for lowering serum carnitine levels.[20] However, no adverse fetal events have been reported, and pivmecillinam is considered relatively safe during pregnancy.[21] Among drugs known to cause fetal harm, the most frequently purchased during the first trimester were tetracyclines. Tetracyclines may cause permanent discolouration of the infant's deciduous teeth when used after the 16th week of gestation, but no evidence exists of teratogenic risk during first-trimester exposure.[22]

After the preconception period the number of pregnant women purchasing clearly harmful drugs declined sharply, and declined again after the first trimester. Among infertility treatments, most gonadotropins do not have a categorisation in the FASS or the ADEC system and were therefore coded with the FDA categorisation, which codes them as clearly harmful (X category). Overestimation of exposure may occur as these drugs are used to stimulate ovulation, with exposure rarely occurring during the period of organogenesis.

Meaning of the Study: Implications for Clinicians

Pregnancies often occur unplanned and several weeks may pass before a woman realises she is pregnant. Because organ development begins during the fifth week of gestation (calculated from the last menstrual period), harmful exposure may occur by accident. Of the known teratogens, isotretinoin, a potent teratogen comparable with thalidomide, was purchased by three women in the pregnant cohort during the preconception period and by one during each trimester. With its relatively long half-life and individual variability in pharmacokinetics, the safety margin before conception must be adequate.[23] Women should also be counselled never to restart a previously prescribed medication without medical consultation.

Among drugs used increasingly during the second or third trimesters, nimesulide was the only one considered harmful. Even though numbers were small, the number of pregnant women purchasing nimesulide during the third trimester almost doubled. Nimesulide use during the last trimester has been associated with end-stage renal failure and fetal death,[24] and should be avoided during pregnancy. Renewing a prescription can be done over the phone, meaning that the physician may be unaware of pregnancy; this gives the pharmacist the important task of conveying information about drug-related risks during pregnancy.

Drug groups responsible for multidrug use were relatively innocent. Thus far, no evidence exists that dermal corticosteroids, inhaled asthma medications, nasal preparations, or β-lactam antibacterials would pose any appreciable teratogenic risk.[22] The use of systemic corticosteroids in certain situations is well-founded, but anxiolytics and NSAIDs are probably prescribed and used with less well-defined indications.

A relatively large proportion of pregnant women with epilepsy purchased two or more antiepileptic drugs simultaneously. Polypharmacy may increase teratogenic risk considerably, and the principal goal should be monotherapy.[25] All women with epilepsy who are planning a pregnancy are recommended to take folic acid supplementation. Because folic acid is not reimbursable in Finland, the frequency of folic acid supplementation in this subgroup of pregnant women could not be analysed.

Conclusion

Our results show that prescriptions for potentially or clearly harmful drugs decrease during the first trimester, but many women are still exposed during the period of organogenesis. Effort should be put into tailoring prescribed medication to the safety of eventual pregnancy, and women should be reminded of possible drug-related hazards to the fetus. However, drug safety classifications give a very crude estimation of risk and should only be used as general guidelines when planning treatment. Risk assessment must always be made on an individual basis, and pregnant women with illnesses requiring treatment must be treated adequately.

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