

Drug use in pregnancy among parous Scandinavian women

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SUMMARY

The aim of the present study was to investigate the prevalence of drug use in 1945 parous pregnant Scandinavian women, to determine the most common drug categories, and to describe changes in drug use throughout pregnancy. The women were interviewed about drug use by a specially trained midwife at five different occasions during pregnancy: at gestational week 17, 25, 33, 37, and on admission for delivery at three Scandinavian study sites (Trondheim, Bergen and Uppsala). When excluding vitamins and iron supplementation, 1086 (56%) women reported at least one episode of drug use during pregnancy, with an average of 2.6 episodes among the women reporting drug use. Four percent of the women accounted for 18% of the episodes of drug use. Systemic anti-infectives (15%), respiratory drugs (12%), gastrointestinal drugs (11%) and analgesics (11%) were the most widely used drugs among all the pregnant women. The number of women using drugs increased throughout pregnancy.

NORSK SAMMENDRAG

Hensikt med studien var å undersøke forekomsten av legemiddelbruk hos 1945 annen- eller tredjegangsfødende skandinaviske kvinner, å beskrive hvilke legemiddelgrupper som ble hyppigst brukt, og å beskrive hvordan legemiddelbruken forandrer seg i løpet av svangerskapet. Kvinnene ble intervjuet av en spesialopplært jordmor ved fem tidspunkt under svangerskapet: ved gestasjonsuke 17, 25, 33, 37 og ved innleggelse før fødselen på tre skandinaviske studiesteder (Trondheim, Bergen and Uppsala). Når jern- og vitamintilskudd ekskluderes, hadde 1086 (56%) av de gravide minst en episode av legemiddelbruk under svangerskapet, med et gjennomsnitt på 2,6 episoder blant kvinnene som rapporterte legemiddelbruk. Fire prosent av de gravide stod for 18% av episodene med legemiddelbruk. Systemiske antiinfektiva (15%), legemidler med virkning på respirasjonssystemet (12%), gastrointestinale legemidler (11%) og analgetika (11%) var de hyppigst brukte legemiddelgruppene. Andel gravide som rapporterte legemiddelbruk økte i løpet av svangerskapet.

INTRODUCTION

Total avoidance of pharmacological treatment in pregnancy is unrealistic and may be dangerous. In order to gain knowledge on factors influencing pregnant women's drug use and possible teratogenic drug effects, pharmacoepidemiological studies are necessary. In addition, by studying how drugs are used in pregnancy, to what extent and by whom, misuse and misconception can be intercepted.

Most pharmacoepidemiological studies in pregnant women have been performed outside Scandinavia. These studies have shown great variety in the prevalence of drug use between and within countries (1-10). A recently published French study showed that 99% of the pregnant women received prescription for at least

one drug during pregnancy with an average of 13.6 drugs per women (11). Data on drug use in pregnancy from Scandinavian studies are summarised in Table 1. Four of these studies were conducted in Sweden between 1963 and 1980 and included a total of approximately 9000 pregnant women. In these studies, 79% to 93% of the women used drugs during pregnancy including iron and vitamin supplementation (1-4). A prescription based study among primiparous Danish women, showed that 44% of the women were prescribed at least one drug during pregnancy. Antibiotics (29%) and gynaecological drugs (13%) were the most commonly used drugs during pregnancy (7).

Variations between countries in drug use were found in the Drug Utilisation in Pregnancy (DUP) study that included nearly 15,000 pregnant women

Table 1. Overview of Scandinavian pharmacoepidemiological studies of drug use in pregnancy.

Ref.	Place	Period	Number of women	Drug history obtained	Period of pregnancy	Percent of pregnant women talking drugs	Mean number of drugs taken	Most commonly used drugs*
2	22 countries Norway Sweden Denmark Finland	1987-88	14778 (n = 482) (n = 213) (n = 310) (n = 180)	Interview	Whole pregnancy	86	2.9	Analgesic/antipyretic/anti-inflammatory drugs (17%) Anti-infectives (17%)
3	Malmö, Sweden	1963-65	5678	Interview	Whole pregnancy	> 80	5.4	Analgesic (27%) Anti-infectives (7%) Antihistamines (14%)
4	Sweden	1973-74	464	Interview	First trimester	79 (74)*	–	Analgesics (28%)
5	County of Jämtland, Sweden	1971-72	341	Medical files	Whole pregnancy	87	3.1	Analgesic (6%) Anti-infectives (19%) Antihistamines (9%)
6	Malmö, Sweden	1979-80	2436	Interview	First 17 weeks	93 (74)*	–	Analgesics (61%) Antihistamines (13%) Antibiotics (11%)
7	Southwestern Finland	1987-88	5851	Medical records	Whole pregnancy	–	–	Analgesics (12%)
8	Denmark	1991-96	16001	Prescription database	Whole pregnancy	44	2.6	Antibiotics (29%) Gynaecological drugs (13%)

*Disregarding iron and vitamin supplementation

from 22 countries. Women in Norway (32%) and Sweden (45%) had considerably higher use of analgesic/antipyretics than the total study population of pregnant women (14%) (6).

In addition to cultural differences, the differences in methodology give rise to differences in the results. Studies based on prescription data do not include over-the-counter (OTC) drugs, like mild analgesics. As medical records in pregnancy often have incomplete drug registration, studies that use this data source may be underestimating the prevalence of drug use. Studies based on retrospective interview may inherit recall bias. Few studies have investigated changes in drug use during pregnancy.

The aim of the present study was to investigate the prevalence of drug use in parous pregnant Scandinavian women, to determine the most common drug categories, and to describe changes in drug use throughout pregnancy.

MATERIAL AND METHOD

Study population

The data used in this study are derived from the "Successive Small-for-Gestational-Age" (SGA) study, a multicenter study on risk factors for, and impact of being small for gestational age (12).

All pregnant women, expecting their second or third child in one of the three Scandinavian cities Trondheim, Bergen (Norway) or Uppsala (Sweden)

between January 1986 and March 1988, were referred to the study by their primary care doctors at their first antenatal visit. The study included women of caucasian origin who spoke one of the Scandinavian languages and had a singleton pregnancy. Of the 6354 referred women, 432 did not fulfil the inclusion criteria and 200 failed to make the first appointment, leaving 5722 women to be included in the study. These women were assigned to one of three groups. First, a 10 percent random sample was drawn (n=561). Among the remaining, only women with increased risk of giving birth to an SGA child were included in the study (n=1384). The SGA risk criteria were one or more of the following characteristics: a prior low-birth-weight child, previous stillbirth, chronic disease (essential hypertension, renal- or heart disease), pre-pregnancy weight < 50kg or smoking. Hence, the present study population included 1945 pregnant women.

Population characteristics

The women's ages ranged from 18 years to 44 years with a mean age of 29 years (SD 4.5 years). The mean length of gestation was 279 days (SD 15.5 days). In all, 54% of the women were smoking, and 5% reported a chronic disease at study inclusion (high blood pressure 2.9%, cardiac diseases 1.0%, diabetes 0.3% or chronic renal disorder 1.5%). The proportion of women with delivery before 37 weeks of pregnancy was 4%.

Data collection

Data on drug use were collected by structured interviews. The interviews were performed at five different occasions, i.e. at gestational week 17, 25, 33, 37, and on admission for delivery. The timing of the interviews were chosen to monitor important periods of foetal growth (early and late second and third trimester) and at admission for delivery.

The characteristics of maximum three episodes of drug use could be recorded at each interview.

Variables

An episode of drug use was defined as use of a prescription or over-the counter (OTC) drug regardless of type, dosage and duration of use. Hence, usage of the same drug on two different occasions was recorded as two episodes of drug use. The drugs were classified by therapeutical classes according to the Anatomic Therapeutic Chemical Classification of Drugs (ATC) (13) and regrouped into different drug categories (Table 2).

Data analysis

To study changes in drug use during pregnancy, the number of women using drugs during five different time periods was compared: 1) from conception to completed 17th gestational week, 2) from 18th to completed 25th gestational week, 3) from 26th to completed 33rd gestational week, 4) from 34th to completed 37th gestational week and 5) from their last study interview and up to admission for delivery. The time periods chosen reflect the timing of the study interviews. Since the time intervals were of different lengths, the changes in drug use during pregnancy were calculated as percent of women with at least one episode of drug use per pregnancy week per time period. Chi-square statistics were used to test for differences in drug use between each time period. Student's t-test was used to study differences in the mean number of drug use episodes between SGA-risk women and the randomly selected women. The statistical analysis were performed by using Statistical Package for Social Sciences (SPSS), version 9.0.

RESULTS

Drug use during pregnancy

During pregnancy, 1679 women (86%) reported at least one episode of drug use. Excluding vitamin and iron supplements, 1086 women (56%) reported at least one episode of drug use, with an average number of 2.6 episodes among the women reporting drug use (Table 3).

The distribution of number of episodes of drug use in pregnancy is presented in figure 1.

Table 2. Drug categories and Anatomic Therapeutic Chemical (ATC) codes.

Name of drug category	ATC codes	Subcategories
Gastrointestinal drugs	A02	Antacid, medication against flatulence and ulcers
	A03	Spasmolytica and anticholinergica
	A06	Laxatives
	A07	Antidiarrhoea and antiseptic and anti-inflammatory medication of the intestine
Cardiovascular drugs	C01	Heart glycosides
	C02	Antihypertensiva
	C03	Diuretics
	C07	Beta blockers
Dermatological drugs	D02	Dermal softeners and protection
	D07	Corticosteroides for dermal use
Urogenital drugs and hormones	G02	Other gynaecological medication
	G03	Sex hormones and ovulation stimulating medication
Topical anti-infectives	D01	Fungicides for dermatological use
	D06	Dermatological antibiotics and chemiotherapeutics
	G01	Gynaecological anti-infectives and antiseptics
Systemic anti-infectives	J01	Antibiotics for systemic use
	J02	Antimycotics
	J03	Chemiotherapeutica for systemic use
	G04	Urological antiseptic and anti-infectives
CNS drugs except analgesics	N01	Anaesthetics
	N02	Anti-migraine drugs
	N03	Antiepileptics
	N05	Psycholeptics
	N06	Other CNS drugs
Analgesics	N02	Narcotics and analgesics/antipyretics
Respiratory drugs except antihistamines	R01	Rhinologica
	R03	Broncodilators and respiratory stimulants
	R05	Expectorants and antitussives
Antihistamines	R06	Systemic antihistamines
Other drugs	B	Anticoagulantia, antihemoragica and medicaments against anemia
	H	Systemic corticosteroides and thyroid medicaments
	L	Alkylating medicaments
	M	Anti-inflammatory and anti-rheumatics, topical medication against pain
	P	Other anthelmintics
	S	Eye and ear medicaments

Table 3. Use of drugs in pregnancy among 1945 parous Scandinavian women.

	Number of users (%)	Average number of episodes of drug used during pregnancy among women using drugs
Total use of drugs	1679 (86.3)	2.9
Use of drugs excluding vitamins and iron	1086 (55.8)	2.6
Use of vitamins	794 (40.8)	
Use of iron	1259 (64.7)	

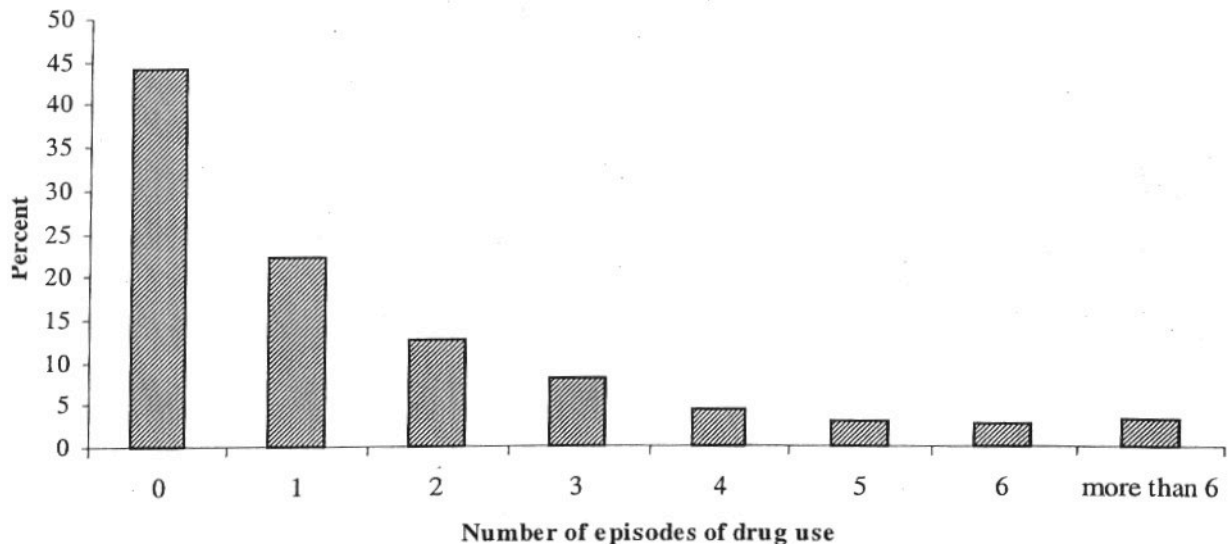


Figure 1. Proportion of women (%) with different number of episodes of drug use in pregnancy among 1945 parous Scandinavian women.

Drug use according to ATC groups

In all, 299/1945 women (15%) reported using systemic anti-infectives and 225/1945 women (12%) reported using respiratory drugs at least once during pregnancy. Gastrointestinal drugs were used at least once by 219/1945 women (11%), and analgesics (both as prescription and over-the-counter analgesia) by 210/1945 women (11%) during pregnancy (Figure 2).

Among the women using gastrointestinal drugs, antacids were the most commonly used (117/219, 53%). Penicillins were the mostly used systemic anti-infective, used by 110/299 (37%) of the antibiotic users. Mild analgesics were the most commonly used analgesic (183/210, 87%).

Episodes of drug use among subgroups of women

Use of drugs at all study interviews

A total of 76/1945 women (4%) reported at least one episode of drug use at all interviews with an average of seven episodes per woman during pregnancy. The most predominant drugs used by these women were systemic anti-infectives (used by 30/76, 39%), gastrointestinal drugs (28/76, 37%) and analgesics (25/76, 33%). In addition, these women used approximately 7, 6, and 9 times more often CNS-, cardiovascular- and dermatological drugs than the total study population, respectively. Chronic disease was significantly more common among women reporting drug use at all interviews than the rest of the study population (13% versus 5%, $p < 0.01$, chi-square test). There was a non-significant higher proportions of SGA-risk women among women reporting drug use at all interviews than the rest of the study population (78% versus 71%, $p = 0.20$, chi-square test).

Use of drugs among SGA-risk women and randomly selected women

There was no difference in the proportion of women using drugs in pregnancy between SGA-risk women and randomly selected women (56% versus 57%, $p = 0.63$, chi-square test). Analysed according to pregnancy time period, there was no significant difference in the percentage of SGA-risk women using drugs as compared to the randomly selected population in three of the five time periods: conception to 17th gestational week: 29% of the SGA-risk women and 29% of the randomly selected women reported at least one episode of drug use, $p = 0.90$, 18th-25th week: 23% versus 19%, $p = 0.04$, 26th-33rd week: 29% versus 25%, $p = 0.11$, 34th-37th week: 23% versus 17%, $p < 0.01$, last interview to delivery: 18% versus 16%, $p < 0.22$, chi-square test). However, SGA-risk women reported on average a higher number of episodes of drug use among the drug users than the randomly selected women (2.7 episodes of drug use versus 2.3 episodes, $p < 0.01$, Student's t-test).

Changes in drug use during pregnancy

Figure 3 illustrates the changes in drug use according to time in pregnancy. In all, the proportion of women who used drugs increased throughout pregnancy, from 1.7% of the population per pregnancy week in the first time period, to 6.4% per pregnancy week in the last time period ($p < 0.01$, chi-square test).

The proportion of women who used gastrointestinal drugs increased most markedly; from 0.1% of the women per pregnancy week in the first time period to 1.6% per pregnancy week in the last ($p < 0.01$, chi-square test) (Figure 3). The use of respiratory drugs

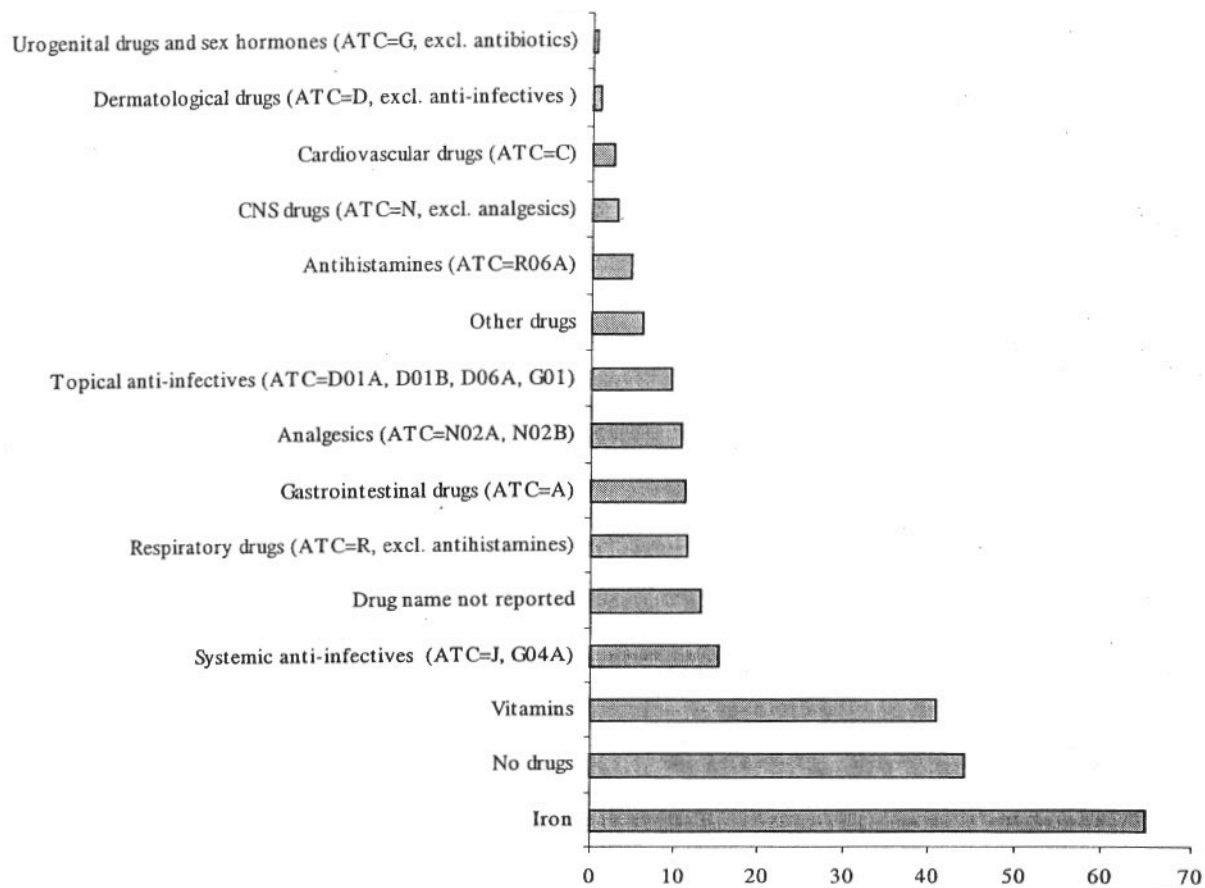


Figure 2. Proportion of women (%) using different drug categories in pregnancy among 1945 parous Scandinavian women.

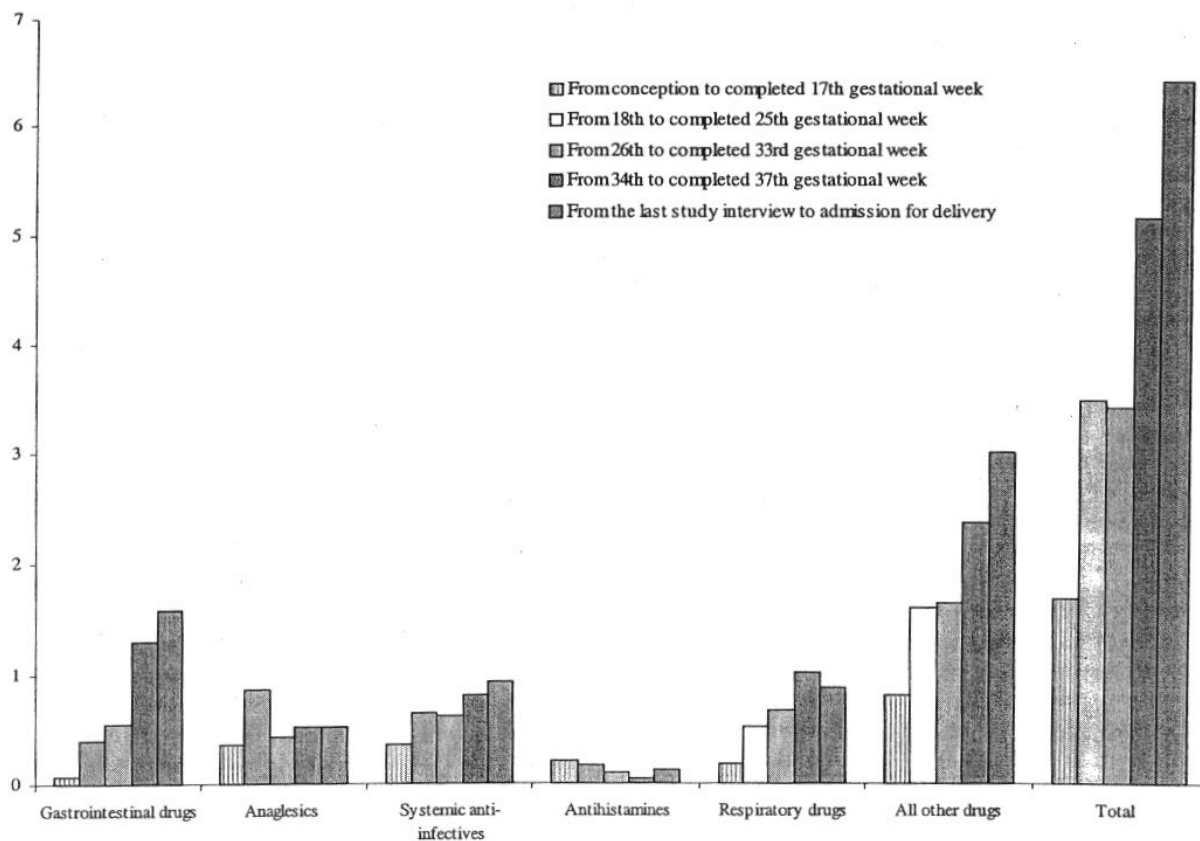


Figure 3. Proportion (%) of women using drugs per week according to drug category and pregnancy time period among 1945 parous Scandinavian women.

increased from 0.2% of the women per pregnancy in the first time period to 1.0% per pregnancy week from 34th to 37th gestational week ($p < 0.01$, chi-square test) (Figure 3).

DISCUSSION

In this study, 56% of the women reported at least one episode of drug use during pregnancy. When including iron and vitamin supplementation the proportion of drug users increased to 86%. Systemic anti-infectives (15%), respiratory drugs (12%), gastrointestinal drugs (11%) and analgesic/antipyretic (11%) were the most commonly used drugs. These results are in agreement with results from previous Scandinavian pharmacoepidemiological studies among pregnant women (Table 1).

In our study, four per cent of the women reported at least one episode of drug use at all study interviews. These women accounted for 18% of all episodes of drug use. Not surprisingly, these women had a higher prevalence of chronic disease before pregnancy. Also, a slightly larger proportion of SGA-risk women belonged to this subgroup. This is likely to be due to chronic disease being a criterion for being in the SGA-risk group.

The proportion of women using drugs increased throughout pregnancy. This increase may be attributed to an increased prevalence of pregnancy related discomfort. Another possible explanation is that physicians may be more reluctant to prescribe drugs during the three first months of pregnancy including the organogenesis period. The increased use of gastrointestinal drugs, especially antacids, throughout pregnancy has also been reported from Denmark (7) and the Netherlands (14). The use of antihistamines was mainly before 18th gestational week, and may suggest that antihistamines are used to alleviate nausea, as nausea is most common early in pregnancy.

This study reports the use of drugs among parous women in 1986-88. Our findings may not reflect today's drug use in pregnancy. However, to our knowledge no previous Scandinavian study has reported

changes in drug use during pregnancy. The results may also serve as reference for future studies on drug use in pregnancy. It provides us with more knowledge about the extent of drug use and changing trends in drug use in pregnancy in a Scandinavian population.

About one third of our study population was randomly selected from the general population of parous pregnant women, while the remaining had at least one risk factor of giving birth to a small-for-gestational age (SGA) child. A higher proportion of SGA-risk women reported drug use after the completed 17th gestational week, therefore the percentage of women using drugs in this study may be higher than in the general population. On the other hand, as only three drugs could be registered per interview, the number of episodes of drug use per user in this study might be underreported. Underreporting, however, could only be the case for maximum 43 women (2%) who reported use of three drugs at one of the study interviews. Thus, there is no reason to believe that underreporting would have influenced our conclusions.

In this population more than half of the women smoked at study entry. Since smoking has been associated with drug use in other studies, the estimated prevalence of drug use in our study may be higher than the general population of pregnant women (15,16). There was, however, no difference in drug use between smokers and non-smokers in our study.

The fact that none of the women were pregnant for the first time, may effect the way they use drugs, though several studies have not shown parity to be a factor related to drug use (15,16).

CONCLUSION

The majority of pregnant women in this study reported at least one episode of drug use in pregnancy. The number of episodes of drug use, however, was low, but increasing throughout pregnancy. Four percent of pregnant women accounted for 18% the episodes of drug use. Few drug utilisation studies have been conducted in Norway, and our results may be useful as a comparison for future studies.

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