BREASTFEEDING MEDICINE
Volume 2, Number 3, 2007

DOI: 10.1089/bfm.2007.0010

Extent of Medication Use in Breastfeeding Women

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ABSTRACT

Background: **The types of and extent to which medications are used by breastfeeding women have not been thoroughly investigated in the United States. The relationship between medication use during pregnancy and lactation has also been insufficiently investigated.**

Methods: **A survey was given to a cohort of women who delivered their babies at a single center. The participants were asked to record the medications they had taken during pregnancy and subsequently were contacted each month during lactation to determine what medications they had taken.**

Results: **Breastfeeding women took significantly more medications per month than pregnant women ($p < 0.0001$). Women who were breastfeeding also took prescription medications more frequently than women who were pregnant ($p < 0.0001$). The number of medications taken per month showed no trend throughout the course of breastfeeding. The medications most often used by breastfeeding women were multivitamins, nonsteroidal anti-inflammatory drugs, acetaminophen, progestins, antimicrobials, and decongestants. Over a third of the subjects took medications rated possibly or probably unsafe, or had unknown safety.**

Conclusion: **The women in this study took more prescription and nonprescription medications while breastfeeding than they did during pregnancy. Many of the medications taken have unknown safety for the breastfed infant. The results of this study should direct further research toward determining the safety of medications commonly used during lactation and to promote the labeling of these medications.**

INTRODUCTION

PREVIOUS RESEARCH has demonstrated the extent of medication use during pregnancy, as well as the types of medications used and the risks and adverse effects of their prenatal use.[1–6] However, there is a paucity of literature devoted to the subject of medication use during lactation, especially in the United States (U.S.). This is surprising, and increasingly needed, because of the recent increase in prevalence of breastfeeding in the U.S. From 1996 to 2001, national rates of in-hospital breastfeeding as well as breastfeeding at 6 months of age each increased about 2% per year.[7] In groups historically less likely to breastfeed, this increase was even greater.

Existing research on medication use during pregnancy in the U.S. has revealed that half of all pregnant women were prescribed medications that had no evidence of safety with some risk classified. Of all medications prescribed to expectant mothers in the 270 days before delivery, 2.4% were category A, 50% were cate-

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gory B, 37.8% were category C, 4.8% were category D, and 4.6% were category X using the U.S. FDA risk classification system.[2]

In international studies, use of one or more medications during pregnancy ranged from 64%[3] to 84%[1] to 99%[4] of all pregnant patients. The most commonly used medications in pregnant women in Italy were dietary supplements such as vitamins and antianemics-hematologicals, followed by tocolytics, nonnarcotic analgesics, hormones, antibiotics, and topicals.[8]

More precise information is needed regarding the safety (to the infant) of medications taken by the mother during lactation. The most comprehensive study of adverse medication reactions was by Anderson et al.[9] These authors attempted to locate all published cases from 1969 to 2002 using several databases including Medline, Current Contents, Biosis Previews and International Pharmaceutical Abstracts. They found 94 reports of 100 infants. They concluded that none were considered "definitely" associated with the maternal medication, 47% were "probable" and 53% were possible. Only 4% of the reports involved infants older than 6 months.

Information currently available regarding the use of postpartum medications has shown the use of safe medications to be 43.5% of all medication use, medications with possible harmful neonatal effects as 4.8%, and nonclassifiable medications represented 35.8% of all medications taken after pregnancy.[5] However, this study did not specifically pertain to breastfeeding women, and was conducted in a Danish population. Another Danish study of the general postpartum population showed that the most used medication during the 12-week postpartum period was penicillin (in 10.1% of women), with bromocriptine, antibiotics, oxytocics, macrolides, propulsives, sulphonamides, diuretics, and corticosteroids following in descending order of use.[6] The drawbacks in these postpartum studies included the use of prescription databases to obtain information, which does not allow for other agents such as over the counter (OTC) medications, dietary supplements, and alternative medicines. The studies were also of women during the postpartum period, not specifically looking at women who were breastfeeding. This study attempted to gather similar information for the U.S. population in order to progress in the understanding of medication use during lactation, as well as pregnancy.

Chemicals taken by a lactating woman postpartum can lead to exposure of the breastfeeding baby through the breastmilk. Research is deficient on the type and quantity of medications that appear in breastmilk, as well as the effects of these chemicals on the child. This research is very important because young infants and newborns may have different medication absorption, distribution, metabolism and excretion than older children or adults.[10] Specifically, medications could affect neurological, endocrine, and pulmonary development.[10] The biological effects of these substances on the infant are largely unknown. However, it has been postulated that the effects could be detrimental or beneficial. Medications present in milk may lead to exposure of the infant to therapeutic effects of the medication.[10] However, in order to research medication effects during breastfeeding, we need to know which medications to study. This study was designed to identify the medications taken by breastfeeding women to inform further research. We hypothesized that, due to the lack of information on safety of medications during breastfeeding, and the false sense of security that results, (1) women take more medications while breastfeeding than while pregnant, (2) women take more prescription medications while breastfeeding than while pregnant, and (3) excluding analgesics and laxatives, the number of medications taken while breastfeeding will increase with time.

MATERIALS AND METHODS

Participants and survey

A cohort of 46 breastfeeding women was recruited from the Milton S. Hershey Medical Center in Hershey, PA, following delivery, and 45 of these women were followed until the cessation of breastfeeding, loss to follow-up, withdrawal from the study, the time of 1 year, or the close of the study in January 2007. Delivery of the baby at the Milton Hershey Medical Center, age of at least 18 years, and a desire to participate were the only inclusion criteria. The Human Subjects Protection Office of the Penn

State College of Medicine approved the study, and subjects signed a consent form prior to participating in the study. Participants in the study were asked to fill out preliminary questionnaires including personal information, demographics, and the medications that they took while pregnant. They were asked to keep a diary of intake of medications, dietary supplements, and herbal products, and were called monthly regarding their use of these products. The PEGASUS study in Germany provided a template for this study, as well as for the questionnaire, which incorporated all types of medications, not just prescription medications.[1] The questionnaire includes the name of medication (including iron, vitamins, or alternative medicines), dosage, start date, end date, reason for medication intake, and whether the medication was prescription or self-medication.

Statistical analysis

Descriptive statistics were prepared for all variables. Count variables and rates are summarized using means and standard deviations or medians and 25th and 75th percentiles if the distributions of the variables were not approximately normal. Categorical variables are summarized using frequencies and percentages. The numbers of self-administered and prescription medications used (1) during pregnancy and (2) while breastfeeding were compared with paired *t*-tests or Wilcoxon signed-rank tests. Similar tests were conducted to compare medication use during pregnancy to medication use while breastfeeding. For the latter comparisons, medication use was reexpressed as number of medications per month to account for different durations of breastfeeding among the women in the sample. To compare the number of women using a class of medications during pregnancy to while breastfeeding, McNemar's test was used. SAS version 9 (SAS Institute, Inc., Cary, NC) was used for all hypothesis testing with the significance level set at 0.05.

RESULTS

Forty-six subjects participated in the study. One subject withdrew from the study at the first telephone call because of the perceived time commitment, so only her pregnancy data were used. Two subjects were lost to follow-up for some time, although contact was eventually reestablished, but for the sake of data accuracy their data were analyzed as if they had stopped breastfeeding at the point of loss of contact. The subjects' ages ranged from 21 to 43 years, with a median age of 32 years. Forty-one (89.1%) of the subjects categorized themselves as White or Caucasian, 2 (4.3%) as Asian Indian, 1 (2.2%) as Puerto Rican, 1 (2.2%) as Cambodian, and 1 (2.2%) declined to answer. Thirty percent of the subjects reported that they had some current medical condition, ranging from one to three conditions with a median of one and a mean of 1.4. One of the subjects delivered twin newborns. Twenty-five (53%) of the babies were male, and 22 (47%) were female. Duration of breastfeeding was very variable, ranging from 0.2 months to over 12 months. Nine women (20%) breastfed for $\geq$12 months. Fifteen (33%) breastfed at least 6 but $<$12 months. Twenty-one (47%) had a duration of $<$6 months.

All subjects recorded a medication intake during pregnancy, and 96% recorded a medication intake while breastfeeding. The average number of different medications per subject (obtained by taking the total number of different medications taken during pregnancy or while breastfeeding and dividing by 46 or 45, respectively) was 3.1 during pregnancy and 4.9 while breastfeeding. The average number of medications per month (obtained by taking the total of different medications taken by each subject during pregnancy or while breastfeeding and dividing by 9 months or the duration of breastfeeding, then totaling and dividing by 46 or 45 corresponding to pregnancy or breastfeeding data) was 0.3 during pregnancy and 1.1 while breastfeeding ($p < 0.0001$). Excluding iron, minerals, folic acid, and other vitamins reduces the average number of medications taken during pregnancy and lactation to 1.6 and 4.0, respectively, and the average number of medications taken per month to 0.2 and 0.9, respectively. Table 1 shows the number of different medications per month recorded by the women during pregnancy and while breastfeeding. Of all medications taken during pregnancy, 21% were prescribed, and 79% were self-administered; while breastfeeding, 33%

Table 1. Recorded Average Number of Medications Taken per Month by Pregnant and Lactating Women

Average number of medications per month	*0.0*	*0.1–0.9*	*1.0–1.9*	*2.0–2.9*	*>/=3.0*
During pregnancy (n = 46 [%])	0 [0]	46 [100]	0 [0]	0 [0]	0 [0]
While breastfeeding (n = 45 [%])	2 [4]	22 [49]	14 [31]	3 [7]	4 [9]

were prescription, and 66% were self-administered.

Similar calculations were performed with the data gathered regarding the number of prescription medications taken by the subjects during pregnancy and while breastfeeding. The average number of different prescription medications per subject (obtained by taking the total number of different prescription medications taken during pregnancy or while breastfeeding and dividing by 46 or 45, respectively) was 0.7 during pregnancy and 1.6 while breastfeeding. The average number of prescription medications per month (obtained by taking the total of different prescription medications taken by each subject during pregnancy or while breastfeeding and dividing by 9 months or the duration of breastfeeding, then totaling and dividing by 46 or 45 corresponding to pregnancy or breastfeeding data) was 0.1 during pregnancy and 0.4 while breastfeeding ($p < 0.0001$).

The various classes of medications recorded are illustrated in Figure 1. The most frequent preparations during pregnancy are vitamins, acetaminophen, folic acid, iron, and antacids, and while breastfeeding are multivitamins, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, progestins, antimicrobials, decongestants, antitussives, and antihistamines. A comparison of the medication classes used in breastfeeding and pregnancy shows a significant difference in analgesic usage (breastfeeding (BF) > pregnancy (P), $p = 0.003$), as well as antimicrobials (BF > P, $p = 0.02$), ENT meds (BF > P, $p = 0.004$), contraceptives (BF > P, $p = 0.01$), and vitamins (the only class used significantly greater in pregnancy, with $p = 0.04$).

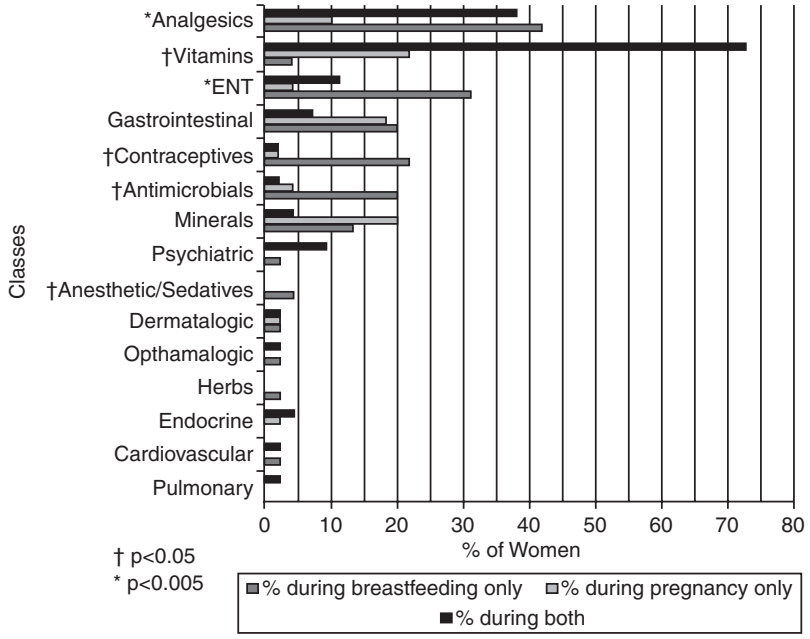

FIG. 1. Classes of medications taken by women during breastfeeding and pregnancy.

Table 2. Most Common Medications Recorded by Subjects During Breastfeeding and Pregnancy

During pregnancy	*# Women (n = 46 [%])*	*While breastfeeding*	*# Women (n = 45 [%])*
multivitamin	43 [93%]	multivitamin	33 [73%]
acetaminophen	21 [46%]	NSAIDs	32 [71%]
folic acid	17 [37%]	acetaminophen	26 [58%]
iron	8 [17%]	progestins	11 [24%]
antacids	6 [13%]	antimicrobials	10 [22%]
antihistamines	4 [9%]	decongestants	10 [22%]
antimicrobials	3 [7%]	antitussives	9 [20%]
SSRIs	3 [7%]	antihistamines	8 [18%]
calcium	3 [7%]	opioids	6 [13%]
progestins	2 [4%]	SSRIs	5 [11%]
decongestants	2 [4%]	calcium	5 [11%]
PPIs	2 [4%]	laxatives	5 [11%]
thyroid hormones	2 [4%]	expectorants	4 [9%]
dermatologics	2 [4%]	other ENT	4 [9%]
estrogens	2 [4%]	other GI	3 [7%]
NSAIDs	1 [2%]	folic acid	3 [7%]
laxatives	1 [2%]	iron	2 [4%]
expectorants	1 [2%]	PPIs	2 [4%]
other GI	1 [2%]	β-antagonists	2 [4%]
β-antagonists	1 [2%]	thyroid hormones	2 [4%]
ophthalmologics	1 [2%]	Mother's Milk tea	2 [4%]
H2 antagonists	1 [2%]	ophthalmologics	2 [4%]
leukotriene inhibitors	1 [2%]	dermatologics	2 [4%]
insulin	1 [2%]	anesthetics/sedatives	2 [4%]
antiemetics	1 [2%]	H2 antagonists	2 [4%]
stimulants	1 [2%]	antacids	2 [4%]
other analgesics	1 [2%]	leukotriene inhibitors	1 [2%]
steroids	1 [2%]	insulin	1 [2%]
other antidepressants	1 [2%]	estrogens	1 [2%]
antitussives	0 [0%]	antiemetics	1 [2%]
opioids	0 [0%]	stimulants	1 [2%]
other ENT	0 [0%]	other analgesics	1 [2%]

NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitor; PPI, proton pump inhibitor; ENT, ear, nose, throat; GI, gastrointestinal.

Table 2 details the most common medications used. The most common mineral taken by pregnant women is iron (73% of all minerals), followed by calcium (27%). Conversely, the most common mineral taken in breastfeeding is calcium (71% of all minerals), then iron (29%). Systemic antimicrobials (antibiotics and antivirals) were used by three (7%) of the subjects in pregnancy, and 10 (22%) in breastfeeding. Herbal preparations were used by two subjects exclusively while breastfeeding, and consisted only of Mother's Milk Tea (which contains Fennel seed, Anise seed, Coriander seed, spearmint leaf, Lemongrass leaf, Lemon Verbena leaf, Althea root, Blessed Thistle leaf, and Fenugreek seed), a putative lactation aid.

The median number of medications taken by month after delivery is shown in Figure 2. No trend over time was noted, either with the data as presented before processing, or with analgesics and laxatives subtracted out, as those would likely be used sooner after delivery.

DISCUSSION

The most frequent preparations taken while breastfeeding are multivitamins, NSAIDs, acetaminophen, progestins, antimicrobials, decongestants, antitussives, and antihistamines. While multivitamins, acetaminophen, and ibuprofen have been judged to be safe in lactation, further research may need to be directed toward use of other NSAIDs, antimicrobials,

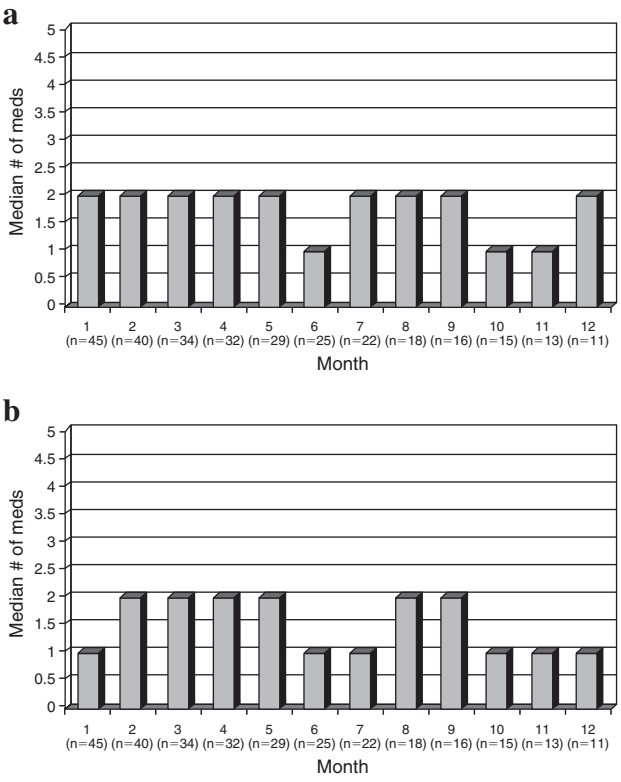

FIG. 2. (**a**) Median number of medications taken, by mouth, while breastfeeding. (**b**) Median number of medications taken, by mouth, while breastfeeding, excluding analgesics and laxatives.

decongestants, antitussives, and antihistamines and their distribution in breastmilk and effects on the nursing child. It is interesting to note the switching of frequency of acetaminophen with NSAIDs as the new mothers went back to taking ibuprofen and naproxen for their ailments. The nursing mothers also took more OTC cold medications, which accounts for the significant number of decongestants, antitussives, and antihistamines. Further study should be directed toward these medications.

The results of the study supported the hypotheses that women take more total medications and more prescription medications during breastfeeding than during pregnancy (see "Results"). This may be due to several reasons; however, it is likely that women feel a greater sense of security in taking medications during breastfeeding. There are fewer warnings against specific medications in lactation, and there is an assumption that medications will not affect a baby in the same way while breastfeeding as during pregnancy.

The classification of medication safety during lactation is very speculative. For purposes of this study two of the sources used to determinethe safety in lactation of the medications taken while breastfeeding were Epocrates Rx[11] and Tarascon Pharmacopeia.[12] Using these sources, 16 (36%) of the women were taking medications that had been deemed possibly or probably unsafe in breastfeeding. These were naproxen, pseudoephedrine, aspirin, diazepam, mesalamine, doxycycline, diphenhydramine, and codeine. Seventeen (38%) were taking some medication that was labeled as safety unknown. This is much higher than the data gathered by the previous studies in postpartum women, and is very concerning. Other sources[13,14] may not consider these substances as being potentially unsafe. The review by Anderson et al.[9] illustrates the low number of case reports of maternal drugs possibly causing adverse effects in the nursing infant.

With regard to the third hypothesis, the data showed neither an increase nor a decrease in the number of medications taken per month over the course of breastfeeding. While medication use may be greatest at first because the woman has just given birth and may be using analgesics and laxatives, there is also the possibility that over time, the breastfeeding mother develops a comfort level with taking medications as no adverse effects are seen, and so takes more over time. Further research following a larger cohort of women may be effective in investigating this, and a delineation of this type of data according to type of delivery, vaginal versus Caesarean, might be informative.

This study had several potential sources of bias. The greatest was recall bias. This was present to some extent for the breastfeeding data, since the woman had to either remember to write the medication down, or remember the medication it until the principal investigator called her each month. However, it was even greater for the data gathered concerning medications during pregnancy, because the data was collected retrospectively rather than prospectively. The subjects were asked to recall 9 months of information rather than simply 1 month at a time. Some women also may not have been willing to disclose all of the med-

ications that they took either during pregnancy or during delivery specifically for sensitive medical conditions such as sexually transmitted infections or illicit drug withdrawal.

CONCLUSION

The women in this study took more medications overall and more prescription medications while breastfeeding than during pregnancy.

The descriptive portion of the study revealed that multivitamins, NSAIDs, acetaminophen, progestins, antimicrobials, and decongestants were the most used medications while breastfeeding, and that vitamins, acetaminophen, folic acid, iron, and antacids were the most used during pregnancy. Thirty-six percent of breastfeeding women took at least one medication that is rated possibly or probably unsafe, and 38% took at least one medication with unknown safety. The results of this study should direct further research toward determining safety in lactation of medications commonly used during lactation.

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