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Choice of Breastfeeding and Physicians' Advice: A Cohort Study of Women Receiving Propylthiouracil

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ABSTRACT. *Objective.* To examine the gap between the current social/medical practice and the evidence-based recommendation in favor of breastfeeding during maternal propylthiouracil (PTU) therapy.

Design. Prospective, observational, cohort study.

Subjects. Women requiring PTU during pregnancy, and endocrinologists and family physicians in Ontario, Canada.

Interventions. Questionnaire.

Main Outcome Measures. Women were interviewed postpartum regarding their choice of infant feeding method and relevant advice received from physicians. Physicians were questioned about their advice to nursing women receiving PTU.

Results. Of 78 women, 66 had live births. Thirty-six required PTU postpartum (group 1), and 30 did not (group 2). Thirty-six healthy women served as controls (group 3). Breastfeeding initiation rates for groups 1, 2, and 3 were 44%, 83%, and 83%, respectively. In group 1, 15 women who breastfed received advice from 22 physicians regarding breastfeeding (20 in favor, 1 against, and 1 equivocal). Eleven who formula fed received advice from 17 physicians (4 in favor, 12 against, and 1 equivocal). A logistic regression analysis of group 1 showed that physicians' advice was the only significant predictor of the woman's choice to breastfeed during PTU therapy (relative risk: 5.48; 95% confidence interval: 1.28–23.40). The physician survey showed that 44% of endocrinologists do not recommend breastfeeding during PTU therapy.

Conclusions. A substantial proportion of the lactating patients on PTU still receive advice against breastfeeding from their physicians. Physicians' advice and attitudes toward breastfeeding during PTU therapy are a major factor in women's final decision to breastfeed. Physicians' compliance with evidence-based data will facilitate breastfeeding in this group. *Pediatrics* 2000;106:27–30; propylthiouracil, breastfeeding, decision-making.

ABBREVIATIONS. PTU, propylthiouracil; CI, confidence interval.

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Propylthiouracil (PTU) is excreted into human breast milk in only small amounts (<.3% of the weight-adjusted maternal dose).^{1–6} Such amounts are not expected to be of clinical importance to the breastfeeding infant. In 1989, Momotani et al⁷ reported the thyroid function of 8 infants exposed to the drug in utero and during breastfeeding. Low thyroxine and high thyroid-stimulating hormone levels in infant serum at birth, attributable to intra-uterine exposure, returned to normal despite breastfeeding, suggesting that maternal PTU therapy poses no substantial risk to the breastfed infant.

Since 1989, the Committee on Drugs of the American Academy of Pediatrics listed PTU as a "maternal medication usually compatible with breastfeeding."^{8,9} Standard reference books also provide similar information.^{1,2,10,11}

Through our daily clinical activities in our fetal and neonatal toxicology counseling service (the Motherisk Program, the Hospital for Sick Children, Toronto, Canada), we suspected that the evidence-based recommendations in favor of breastfeeding during maternal PTU therapy have not been implemented into the current medical practice. Therefore, a study was conducted to reveal how nursing women receiving PTU are advised about breastfeeding, and what proportion of them actually breastfeed their infants. In addition, we surveyed Ontario endocrinologists and family physicians regarding their practice for nursing women on PTU by eliciting their responses to 2 hypothetical case scenarios.

METHODS

Study Setting

Women concerned about the effects of their medications on the fetus or breastfed infant contact the Motherisk program with or without physicians' referrals. Their questions are answered over the telephone by trained counselors or physicians, after demographic and medical information are documented. All cases undergo follow-up interviews to record the outcome of pregnancy¹² or breastfeeding. These procedures have been approved by our research ethics board.

Patients

From January 1990 to September 1997, we identified 78 women residing in Ontario, Canada with concerns about the fetal safety of PTU use during pregnancy. Those who contacted our service regarding the compatibility of PTU during lactation were excluded from the study. Of our potential cases, 66 (84.6%) had live births, 6 (7.7%) had a therapeutic or spontaneous abortion, 5 (6.4%) were still pregnant at the time of interview, and 1 (1.3%) declined to participate. All women with live births were included in the analysis. Of these, 36 (54.5%) required PTU postpartum (group 1). The remaining 30 (45.5%) no

longer required the medication (group 2). In addition, we interviewed 36 age-matched control women (± 1 year) who contacted our program within the same year as their counterparts, and who were not on chronic drug therapy or any known teratogenic or toxic substances (group 3).

Data Collection

Information regarding the following characteristics was documented during the interviews: initial choice of feeding method; sources and nature of advice on feeding methods; duration of breastfeeding; and demographic data, such as annual family income, maternal and paternal education, and marital status. Information on the infants' medical conditions, including thyroid-related diseases, was also recorded.

The women were questioned in an open-ended manner as to why they initially chose to breastfeed or formula feed. Subsequently, close-ended questions for specific reasons were asked. The women were allowed to list multiple reasons for both question types. The sources of information on feeding methods were identified by asking whether they received information or advice from a physician. Advice from physicians were categorized into 3 groups according to maternal reports: breastfeeding, formula feeding, or equivocal. To quantify the overall trend of the advice, a cumulative score¹³ was calculated for each woman by summing up a number assigned to each category: +1 for advice in favor of breastfeeding, -1 for advice against breastfeeding, and 0 for equivocal advice. (For example, if a woman received advice from 3 sources recommending breastfeeding, the cumulative advice score is +3; if she received 2 conflicting pieces of advice and 1 equivocal piece of advice, the score is 0.)

Physicians' Survey

To directly examine physicians' attitude toward PTU therapy during lactation, a survey letter was sent to all Ontario endocrinologists ($n = 92$) and randomly selected family physicians ($n = 300$) listed in the 1997 edition of the *Canadian Medical Directory*. These populations were targeted because the majority of advice received by the mothers came from these 2 sources. Two scenarios were presented: 1) a lactating woman requires 300 mg/day of PTU and has no preference for a feeding method, and 2) a woman on the same dose wishes to breastfeed. Physicians were asked to indicate whether they would recommend breastfeeding in each scenario. They were also questioned on whether they had to provide such advice in the past year. If the physician was unsure of their recommendation, they were asked to select from a list of options which information sources they would consult to obtain an answer (reference books, literature searches, colleagues, or other).

Data Analysis

Results among the 3 groups were compared using analysis of variance, Kruskal-Wallis test, or χ^2 analyses. Where there was a significant difference among the 3 groups ($P < .05$), the results were compared between 2 groups using unpaired Student's t test (2-tailed) or χ^2 analysis. For comparisons between 2 groups, Fisher's exact test was also used, where appropriate. The Mann-Whitney U test was used to compare the cumulative scores of the physicians' advice between the PTU-receiving mothers who chose

to breastfeed and those who chose to formula feed. A logistic regression analysis was performed to evaluate independent predictors of the mother's choice on the feeding method. The relative risks of choosing to breastfeed were estimated. The factors for which the P values on univariate analysis were $< .05$ were entered in the model. Also, an exploratory stepwise logistic regression analysis was used to identify other potential factors independently associated with the women's choice of feeding methods. Data are expressed as means \pm standard deviation or proportions, unless otherwise stated. A P value of $< .05$ was considered significant.

RESULTS

Subject Demographics (Table 1) and Choice of Feeding Methods

Demographics of the 3 groups were similar (Table 1). However, $>80\%$ of women in groups 2 and 3 who were not receiving PTU started breastfeeding, whereas only 44% in group 1 initiated breastfeeding (group 1 vs group 2, $P < .01$; group 1 vs group 3, $P < .01$). Although 2 infants nursed by women in group 1 were hyperthyroid at birth, all attained euthyroid status within 1 month. No other adverse effects that were considered related to the PTU therapy were observed in the infants.

Subgroup Analysis of Group 1 (PTU-Exposed Women): Physicians' Advice and Breastfeeding Initiation (Table 2)

Of the 36 women in group 1, 10 women did not seek advice from physicians. The remaining 26 (72.2%) women received advice from 39 physicians (20 endocrinologists, 16 family physicians, and 3 pediatricians). According to the maternal reports, 24 physicians (61.5%) advised to breastfeed, 13 (33.3%) advised not to breastfeed, and 2 (5.1%) gave equivocal advice.

Of 18 women who received advice in favor of breastfeeding by at least 1 physician, 15 (83.3%) initiated breastfeeding. In contrast, of the 8 women who did not receive advice in favor of breastfeeding, none breastfed ($P < .01$). The mean cumulative advice scores were +1.3 (95% confidence interval [CI]: +.9,+1.6) for the breastfeeding women, and -0.7 (95% CI: -1.5,+0.2) for the formula-feeding women ($P < .01$). Twelve of 20 women (60.0%) who chose to formula feed indicated physicians' advice against breastfeeding or their concern about the medication as the primary reason for not breastfeeding.

Fifteen women in group 1 who breastfed were

TABLE 1. Demographics and Feeding Methods

	Group 1	Group 2	Group 3	P Value
<i>n</i>	36	30	36	
Postpartum PTU therapy	Yes	No	No	—
Maternal thyroid status	Hyperthyroid	Euthyroid	Euthyroid	—
Postpartum maternal age (y)	29.3 \pm 4.6	30.4 \pm 4.6	30.3 \pm 4.2	.49
Parity (number)				
1	13	12	14	.48
2	13	15	14	
≥ 3	10	3	8	
[Range]	[1-7]	[1-4]	[1-6]	
Family income				
<\$40 000	13	11	6	.62
\geq \$40 000	16	14	13	
Breastfeeding initiation (number [%])	16 [44.4%]	25 [83.3%]	30 [83.3%]	<.01
Breastfeeding duration (mo)	4.8 \pm 5.3	5.3 \pm 5.7	7.3 \pm 5.6	.07

TABLE 2. Subgroup Analysis of Group 1

	Breastfed	Formula Fed	P Value
<i>n</i>	16	20	—
Maternal age (y)	30.6 ± 4.0	28.2 ± 4.9	.11
Parity (number)			
1	7	6	
2	5	8	.69
≥3	4	6	
[Range]	[1–6]	[1–7]	
PTU dose (mg/d)	171.3 ± 97.8	213.9 ± 149.3	.34
Family income			
<\$40 000	3	10	.034
≥\$40 000	10	6	
Maternal education			
≤Secondary	5	7	.81
Postsecondary	11	13	
Physicians' advice			
Breastfeeding	20	4	<.01
Formula feeding	1	12	
Equivocal	1	1	

advised by 22 physicians regarding breastfeeding (20 in favor of breastfeeding, 1 against, and 1 equivocal); 11 who formula fed received advice from 17 physicians (4 in favor of breastfeeding, 12 against, and 1 equivocal; $P < .01$).

The women in group 1 were further categorized according to the year they contacted our program. The breastfeeding initiation rate of the women who contacted our program before 1994 was 23%. However, an upward trend was observed in 1994 and onward, with a breastfeeding initiation rate of 78.6%.

Multiple Logistic Regression Analysis of Group 1

The 26 patients who received advice from physicians were included in the analyses; the remaining 10 were excluded. An exploratory stepwise logistic regression analysis indicated that physicians' advice was the only independent factor associated with the women's choice of feeding methods; all factors listed in Table 2 were included in the analysis (results not shown). In the univariate analysis, family income and physicians' advice were significantly different for women who breastfed, compared with those who formula fed. These 2 independent variables were included in a logistic regression model as predictors of the mother's choice of feeding method. Physicians' advice was found to be the only significant predictor of the feeding method ($P = .017$). Namely, women who received physician advice in favor of breastfeeding were more likely to breastfeed than to formula feed (relative risk: 5.48; 95% CI: 1.28–23.40).

Survey of Physicians

Results of the physician surveys are summarized in Table 3. Five endocrinologists and 7 family physicians were excluded on the basis that they were no longer in clinical practice or at the mailing address listed in the directory. Response rates were 72.4% (63/87) for the endocrinologists, and 37.5% (110/293) for the family physicians. Of all physicians who indicated that they would not recommend breastfeeding in scenario 1, 2, or both, 81.4% listed drug amount found in the breast milk as the primary reason for not recommending breastfeeding. Eighty family physicians and 5 endocri-

TABLE 3. Survey of Physicians

	Endocrinologists	Family Physicians
	Number [Percentage]	
<i>n</i> *	63	110
Gave advice within the last y	47 [74.6]	1 [0.9]
Response to case 1		
A healthy, lactating woman on 300 mg/d of PTU has no preference as to formula or breastfeeding. Would you recommend breastfeeding?		
Recommend	32 [50.8]	12 [10.9]
Against	28 [44.4]	29 [26.4]
Breastfeeding		
Unsure	3 [4.8]	68 [61.8]
Response to case 2		
A healthy, lactating woman on 300 mg/d of PTU expresses the wish to breastfeed exclusively. Would you recommend breastfeeding?		
Recommend	44 [69.8]	14 [12.7]
breastfeeding		
Against	15 [23.8]	20 [18.2]
Breastfeeding		
Unsure	4 [6.3]	76 [69.1]

* Response rates were 72.4% (endocrinologists) and 37.5% (family physicians).

nologists who were unsure of the compatibility of PTU with breastfeeding provided information sources they would consult. Of the family physicians, reference books were quoted most commonly (56/80; 66%), followed by colleagues (48/80; 60%), other (46/80; 57.5%; Motherisk would be consulted by 32 of the physicians), and literature searches (22/80; 27.5%). Of the 5 responses listed by the endocrinologists, literature searches were chosen by all. Three (60%) would also consult reference books and colleagues. Two of these 3 would also consult an additional source (eg, Motherisk). Interestingly, ~1 in 4 endocrinologists, who are otherwise against breastfeeding during PTU therapy, indicated that they would change their advice from against to in favor of breastfeeding if the patient expressed a desire to breastfeed.

DISCUSSION

Published studies indicate that breastfeeding by mothers on PTU is unlikely to affect the infant's thyroid function.^{5–7} Hence, there is a wide consensus that the drug is compatible with breastfeeding.^{1,2,8–10} Although the American Academy of Pediatrics classifies PTU as compatible with nursing, no data have demonstrated how breastfeeding women receiving PTU are advised and what proportion of them actually breastfeed. This study has found that mothers on PTU therapy had a lower breastfeeding initiation rate than did mothers who were not on any chronic medication. This finding is consistent with our previous results with antiepileptics.¹⁴

As previously described, only women who contacted the Motherisk Program regarding the fetal safety of PTU use were included in the study. The safety of PTU during lactation was not discussed with these women. Women who called regarding the safety of PTU during breastfeeding were excluded, because this subgroup of women may display a greater interest in breastfeeding than the general population. However, a

limitation of the study is that our selected study group may represent a more anxious subpopulation with greater concerns about medication use than women on PTU who did not contact our program. Thus, they may take a more cautious approach when deciding whether to breastfeed.

All women who formula fed during PTU therapy did not receive physicians' advice in favor of breastfeeding. Although their family income was lower than the family incomes of those who chose breastfeeding, our logistic regression analyses indicated that physicians' advice was the only significant predictor of women's decision to breastfeed. We conclude that the advice and attitude of physicians toward breastfeeding during PTU therapy are important modifiable factors. Although differences in clinical consequences of these choices (ie, breastfeeding or formula feeding while on PTU) are not entirely clear, it is doubtful that those infants who are formula fed benefit from the well-documented advantages of breast milk.¹⁴

To validate the results derived from maternal reports, the current medical practice has to be examined directly. To this end, we surveyed endocrinologists and family physicians by eliciting their responses to the 2 case scenarios. Our results indicate that presently approximately one third of the endocrinologists do not use the widely accepted recommendation in favor of breastfeeding during PTU therapy. Family physicians showed a similar trend but the majority of them have indicated that they were unsure what to recommend. Overall, the results of the physicians' survey corroborate maternal reports. The fact that 1 in 4 endocrinologists would change their advice and recommend breastfeeding if the woman wished to breastfeed suggests that the decision-making process of these physicians seems to be influenced by the attitudes of the patients.

The study noted an increase in the percentage of women who chose to breastfeed over the years. This increase may be attributable to an increase in the public awareness of breastfeeding. Although these results are encouraging, a large proportion of physicians still currently advise women against breastfeeding while on PTU.

PTU is only 1 of many drugs considered compatible with breastfeeding by the American Academy of Pediatrics. As demonstrated by this study, the current recommendations have not been incorporated successfully into the medical community. This raises the question of whether women are receiving inaccurate advice regarding the safety of other medications during breastfeeding, and thus, choosing not to breastfeed. It is important to note that the list of medications that are considered contraindicated with breastfeeding is short.⁹ The advice given by physicians is influenced by their attitudes and personal beliefs.^{15,16} This may be explained partially by our study, which showed that physicians are often not aware of the evidence-based safety of a drug.

This study focused on family physicians and endocrinologists, because these were the 2 subpopulations consulted the most frequently for advice on PTU use during lactation. Although the American Academy of Pediatrics publishes recommendations on the safety of

medications during breastfeeding, women may be consulting the physician responsible for prescribing the medication (eg, endocrinologists and psychiatrists) rather than their child's health care provider (ie, pediatrician) for information about breastfeeding while on the drug. Thus, more effort should be made to educate physicians in other relevant disciplines on the current recommendations regarding drug use during breastfeeding and on breastfeeding promotion in general.

A substantial proportion of physicians continue to advise against breastfeeding for women receiving PTU. This finding indicates several possibilities. First, physicians may not be aware of the current recommendations. Second, despite their knowledge of the experts' recommendations in favor of breastfeeding, they may choose to make a cautious medical judgment. If there is mere ignorance on the part of the physicians, effort should be made to disseminate the evidence-based knowledge. In contrast, if the current evidence is not convincing enough for the majority of health professionals, more research should be encouraged to further strengthen the foundation of the medical practice.

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