Community pharmacist surveillance of hypertension in pregnancy: Are we ready for prime time?

Nicole W. Tsao, BSc(Pharm), MScPharm; Carlo A. Marra, BSc(Pharm), PharmD, PhD; Larry D. Lynd, BSP, PhD; Jamie M. Thomas, BSc; Ema Ferreira, BPharm, MSc, PharmD

NICOLE W. TSAO

Previous research has shown that when community pharmacists provided education and encouraged medication adherence, this resulted in significant blood pressure reduction for hypertensive patients. Given that hypertensive disorders of pregnancy can affect 5% to 10% of the perinatal population, we hypothesized that community pharmacists can educate and provide postmarketing drug surveillance to this patient population.

Les études antérieures ont montré que les pharmaciens communautaires qui donnent de l'information aux patients et les encouragent à adhérer à leur traitement contribuent à réduire de manière importante la tension artérielle des personnes hypertendues. Puisque les troubles hypertensifs durant la grossesse peuvent toucher 5 à 10 % de la population périnatale, nous formulons l'hypothèse selon laquelle les pharmaciens communautaires pourraient leur donner de l'information et assurer la pharmacovigilance chez cette population.

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ABSTRACT

Background: Hypertensive disorders of pregnancy (HDP) are associated with serious maternal and perinatal complications. For nonsevere hypertension, there is a lack of consensus regarding treatment during pregnancy and while breastfeeding. Further, there is considerable variability in guidelines for antihypertensive drug choices. As part of a Drug Safety and Effectiveness Network (DSEN)-funded project, we piloted a novel surveillance strategy in which community pharmacists recruited pregnant and breastfeeding women to monitor their blood pressure and medication use and to provide education on HDP.

Methods: Participating pharmacists were required to complete a certified training program, identify and recruit patients who were pregnant or breastfeeding, obtain informed consent,

administer a patient questionnaire and complete an initial case report form for enrolled patients. Study outcomes included the feasibility of community pharmacists to enroll patients and carry out study-related documentation and follow-up. The criteria for success in this pilot study included the ability of pharmacists to recruit 10 participants per pharmacy.

Results: 178 community pharmacies across British Columbia agreed to participate in this feasibility study, of which 63 pharmacists completed the study training. Of these, only 21 pharmacists recruited at least 1 patient and 1 pharmacist met the success criteria. Overall, 51 patients were enrolled, 2 withdrew from the study and 7 patients were diagnosed with HDP. Antihypertensive medications used by patients included methyldopa and labetalol.

Conclusions: While postmarketing surveillance is an important tool for the assessment of drug safety in the pregnant and breastfeeding patient population, the feasibility of community pharmacists taking on this role was not successfully demonstrated. *Can Pharm J (Ott)* 2014;147:307-315.

Introduction

Hypertensive disorders of pregnancy (HDP) include gestational hypertension (3.8%), pre-eclampsia (1.3%), preexisting hypertension (0.7%) and preexisting hypertension with superimposed preeclampsia (0.4%).¹ These conditions are associated with serious complications, such

as eclampsia, pulmonary edema and hemolysis, elevated liver enzyme and low platelet syndrome (HELLP syndrome), that affect 5% to 10% of pregnancies.²⁻⁷ The HDP represent 1 of the 2 leading causes of maternal mortality in Canada, accounting for 0.85 maternal deaths per 100,000 live births,⁸ and are the second most common

KNOWLEDGE INTO PRACTICE

- Pharmacists believe that postmarketing surveillance is part of their role, but time commitment and creative efforts to target and engage patients are needed for successful implementation.
- Community pharmacists are well positioned to have an active role in postmarketing drug surveillance for the pregnant or breastfeeding patient population; strategies to improve pharmacist participation should be investigated further.
- Patients with first-time pregnancies are more likely to see value and enroll in a pharmacist-initiated surveillance program of hypertension and medication use in pregnancy and breastfeeding.
- Strong preexisting relationships with patients, help of pharmacy students, in-pharmacy database searching and appointment scheduling are factors facilitating patient enrollment into surveillance programs.

cause of maternal mortality globally (at least 76,000 annually).⁹ Adverse fetal outcomes are associated with maternal hypertension, including earlier gestational age at birth, low birth weight and increased incidence of stillbirths.¹⁰⁻¹²

All international guidelines for the management of HDP agree that persistent, severe hypertension (blood pressure >160 mmHg systolic or >110 mmHg diastolic) must be treated, as the benefits of treatment outweigh the risks.¹³⁻¹⁶ However, there is no consensus on the treatment of nonsevere hypertension (blood pressure 140-159 mmHg systolic, 90-109 mmHg diastolic).^{3,17,18} Even when the decision to initiate treatment for nonsevere hypertension has been made, there is much variability in the choice of therapy. Some antihypertensive medications, such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, are contraindicated during pregnancy, and given that some antihypertensive medications are secreted into breast milk in sufficiently high concentrations to put infants at risk following breastfeeding (e.g., atenolol), caution should be exercised.^{3,19,20}

Community pharmacists are in an ideal position to play an important role in the screening and detection of hypertension, in preventing and monitoring side effects of medications and in increasing adherence to maintain optimum blood pressure control in patients.¹⁵ A previous study has shown that pharmacist-patient interactive activities, such as recommending a change of medication, identifying barriers to adherence and addressing them by providing patient

education, and encouraging and rewarding adherence and blood pressure control, resulted in significant systolic blood pressure reduction when compared with a control group that did not receive the above pharmacy interventions.²¹

As part of a Drug Safety and Effectiveness Network (DSEN)-funded project, we conducted a pilot study to demonstrate the feasibility of pharmacists identifying pregnant and breastfeeding women for active surveillance of post-market drug safety and effectiveness and to determine the proportion of women exposed to antihypertensive medications and other drugs, natural health products (NHPs) and nutritional supplements that could contribute to the risks surrounding hypertension in pregnancy or lactation. As we knew that it was not feasible to have sufficient power or length of follow-up to identify and link specific adverse events to a specific treatment strategy, our objective was to demonstrate the utility of pharmacy-based active surveillance through the number of pregnant/lactating women recruited and the number exposed to either antihypertensive medications or other medications that may increase the risk of pregnancy-related hypertension.

Methods

Pharmacists

Pharmacists eligible for recruitment into the study were identified from an existing database of community pharmacies in British Columbia (BC) that had consented previously to be contacted for community pharmacy-based research. From May to August 2010, all pharmacies from this database were contacted, and individual pharmacists who were interested in participating in this study were included. Each participating pharmacist was required to undergo an accredited educational program that included information about hypertension in pregnancy (i.e., epidemiology, pathophysiology and treatment) and research study procedures. An in-person session was offered in Vancouver, BC, which was videotaped and offered online for those unavailable to attend. Actors playing patients were used to help pharmacists develop interviewing and intervention techniques, including blood pressure monitoring. In addition, pharmacists were oriented to online resources and other information sources to help them assess medication risk in pregnancy and lactation, including the Motherisk Program (Hospital for Sick Children, Toronto,

FIGURE 1 Schematic representation of study procedures

*Patient self-reported as diagnosed by physician.

www.motherisk.org), Reprotox (<https://www.reprotox.org/>), Shepard's, TERIS database, OTIS facts sheets (www.mothertobaby.org/otis-fact-sheets-s13037) and LactMed (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>). Other than the provision of Reprotox software to participating pharmacies, no compensation was provided to the pharmacists.

Participants

The participant sample was derived from pregnant and breastfeeding women who visited participating community pharmacies across rural and urban BC. Potential participants approached pharmacists about the study after seeing display posters near the pharmacy blood pressure monitor, in aisles containing pregnancy and baby care items or at the prescription drop-off or pick-up counters. Some patients were recruited through study advertisements added to prescription bags for patients filling pregnancy- or hypertension-specific medications.

Pharmacists also actively recruited participants by searching their pharmacy database for patients taking pregnancy-related medications such as doxylamine/pyridoxine (Diclectin). These patients were contacted by an initial letter of information and a follow-up phone call from the pharmacist, inviting them to schedule

an appointment to discuss enrolling in the study. Finally, select pharmacies hosted in-pharmacy clinics for pregnant and breastfeeding women to provide information for a healthy and safe pregnancy and to provide information regarding the study. Approached patients were given a letter of information and enrolled to participate in the study after giving informed consent. This study was approved by the Providence Health Clinical Research Ethics Board.

Inclusion and exclusion criteria

The eligibility of each potential participant was determined by her answers to screening questions included on a pharmacist-administered case report form. Inclusion criteria consisted of any patient with confirmed pregnancy or any patient who was breastfeeding. Participants were excluded if they were under the age of 19 or were unable to speak and read English. Blood pressure status was not part of the inclusion or exclusion criteria.

Study procedures

The study procedures are diagrammed in Figure 1. Study participants completed a patient questionnaire at baseline in which they self-reported demographic information and medical history including prenatal care, breastfeeding practices

MISE EN PRATIQUE DES CONNAISSANCES

- Les pharmaciens estiment que la pharmacovigilance fait partie de leur rôle; mais pour y parvenir, ils ont besoin de temps et d'efforts créatifs afin de cibler et de mobiliser les patients.
- Les pharmaciens communautaires occupent une place privilégiée pour assurer activement la pharmacovigilance chez les femmes enceintes ou qui allaitent. Il faudrait examiner plus avant des stratégies afin de renforcer le rôle du pharmacien.
- C'est lors de la première grossesse que les patientes auraient probablement le plus d'intérêt et seraient le plus susceptible de s'inscrire à un programme de surveillance par le pharmacien de l'hypertension et des médicaments durant la grossesse et l'allaitement.
- Plusieurs facteurs pourraient influencer l'inscription des patientes aux programmes de surveillance, notamment l'établissement de relations professionnelles solides avec les patientes, l'aide des étudiants en pharmacie, la possibilité d'accéder à partir de la pharmacie à des bases de données et la prise de rendez-vous.

and history of illness. At baseline, the pharmacist reviewed the patient's BC PharmaNet profile for a complete 14-month prescription medication history. The pharmacist also completed a case report form by interviewing the patient. The case report forms asked about possible adverse drug reactions relating to antihypertensive medications as well as use of NHPs or over-the-counter medications on a regular basis.

Blood pressure measurement

Twenty-five pharmacies were given a Microlife 3AC1-PC (Microlife AG; Widnau, Switzerland) ambulatory blood pressure monitor specifically designed to measure blood pressure during pregnancy. Pharmacists were trained on the proper use of this monitor and were instructed to take participant blood pressure readings from both the Microlife blood pressure monitor and the in-pharmacy blood pressure machine when possible.

Pharmacist education

Pharmacists provided patients with education on how to self-monitor blood pressure and interpret readings, complications of hypertension during pregnancy, common over-the-counter medications and NHPs to avoid during pregnancy or breastfeeding and over-the-counter and NHPs that may affect blood pressure.

Follow-up

Patients who were previously diagnosed with hypertension or were found to have hypertension during the study period were contacted at 3 and 6 months after enrollment to complete a follow-up questionnaire and case report form. The 3- and 6-month follow-ups documented changes in blood pressure status, based on patient self-report of most recent measurement at the time of follow-up and changes in any antihypertensive medications, including starting new medications, discontinuing medications and changing doses and regimens. Pharmacists completed the follow-up case report forms in person or by phone, and study coordinators completed the follow-up patient questionnaire by phone with patients.

Data analysis

Due to the nonexperimental design of this study, no inferential statistics were used. Data were summarized using proportions or means where appropriate.

Outcomes

Study outcomes included the feasibility of community pharmacists to enroll eligible patients and to carry out study-related documentation and follow-up. This outcome was defined by the number of participants that pharmacists recruited and by the proportion of participants who had a hypertensive disorder with or without antihypertensive treatment. Our criteria for success in this pilot study were determined as the ability to recruit 10 participants per pharmacy and the ability to recruit at least 1 participant with a hypertensive disorder per pharmacy.

Any pharmacists' interventions and patient outcomes were also of interest in this study, including patients' blood pressure status, antihypertensive medications, adverse drug reactions and any changes to these outcomes at 3 and 6 months.

Sample size

Every year, there are approximately 80,000 pregnancies in BC, 40,000 of which continue to a completed delivery (the remainder ending in spontaneous or therapeutic abortion). Approximately 83% of women in BC initially breastfeed, with this number declining to 19% at 9 months postpartum.²² We therefore estimated that 60,000 to 80,000 women would meet our study inclusion criteria each year in BC. Of these, approximately 5% to 10% would have HDP. As such,

TABLE 1 Pharmacist level of study participation

Pharmacist enrollment	<i>n</i>	%
Pharmacists approached for participation	713	–
Agreed to participate in study	178	25.0
Completed study-related training	63	8.8
In-person training	21	3.0
Online training	42	5.9
Total pharmacists enrolled	63	8.8

TABLE 2 Number of patients enrolled per pharmacist

Enrolled	Number of pharmacists	%
≥10 patients	1	1.59
2-9 patients	11	17.46
1 patient	9	14.29
0 patients	42	66.67

TABLE 3 Participants' reasons for visiting the pharmacy on the day they enrolled in the study

Reason for visiting pharmacy	Number of participants*	%
Fill a prescription	22	44.9
Purchase over-the-counter medications	5	10.2
Purchase other pharmacy products	6	12.2
Patient visited pharmacy specifically to enroll in study	10	20.4
Other	6	12.2

*Two participants chose not to respond regarding their reason for visiting the pharmacy on the day of study enrollment, *n* = 49.

approximately 3000 to 8000 women fit these criteria per year.

Using recruitment strategies successfully applied in studies examining pharmacist interventions for osteoarthritis and for emergency contraception,^{23,24} we anticipated that we would be able to recruit approximately 120 pharmacies to participate in this study and that each pharmacy would be able to recruit 10 participants within a 6-month period. This means approximately 1200 pregnant or lactating participants would be enrolled into this study. We anticipated that, of these, 60 to 100 women would have hypertension and might be receiving an antihypertensive agent.¹

Results

Of 178 community pharmacists across BC who agreed to participate in this study, 63 completed study-required training, and of these 21 enrolled at least 1 patient (Tables 1 and 2). The distribution of patient enrollment by number of pharmacists is outlined in Table 2, with most participating pharmacists enrolling no patients (67%) and only 1 pharmacist recruiting 10 or more patients. Table 3 documents the reasons why participants were attending the pharmacy on their day of enrollment. Most of the time, participants were enrolled into the study by the pharmacist while filling a prescription.

Fifty-one pregnant or breastfeeding women were enrolled into the study between August 2010 and July 2011 and were included in the baseline data analysis. Two participants withdrew from the study. The demographic information of the participants is summarized in Table 4; 14% ($n = 7$) of the participants reported having been diagnosed with hypertension by their physician. One woman was determined to have severe hypertension at study enrollment, 2 had nonsevere hypertension and 4 women had controlled blood pressure (Table 4). Of these 7 women, 1 was lost to follow-up; of the 6 women who remained in the study, 100% completed the 3-month questionnaire, 50% completed the 3-month case report form, 83% completed the 6-month questionnaire and 67% completed the 6-month case report form.

At baseline, 3 women were taking antihypertensive medications: 1 was on methyldopa, 1 on labetalol and 1 on methyldopa and hydrochlorothiazide. During the study period, there were no changes to any patients' antihypertensive medications that required pharmacist intervention and there were no reported adverse events associated with any antihypertensive medications taken by enrolled participants. At the 3-month follow-up, 1 patient discontinued methyldopa postdelivery and 1 patient initiated methyldopa, as instructed by their physicians. No changes in antihypertensive medications were found at 6-month follow-ups.

At baseline, a pharmacist did identify a patient with untreated hypertension and instructed the patient to see her physician. Upon follow-up, it was determined that this patient's untreated hypertension led to induced labor. There were also 2 cases of a pharmacist identifying a patient with prehypertension before her physician was aware of it. In these cases, after the physicians were notified, active monitoring was initiated for both patients, but no pharmacotherapy was required. At 3- and 6-month follow-ups, only 2 of 6 patients were able to self-report their blood pressure status and no changes were found from baseline.

Discussion

This was the first pilot study to assess the feasibility of community pharmacists' identification of pregnant and breastfeeding women and active surveillance of postmarket drug safety and effectiveness in this patient population. A total of

178 community pharmacists agreed to participate; however, only 21 pharmacists enrolled any patients and only 1 pharmacist met the objective of enrolling 10 patients in 1 year. Each pharmacist was initially projected to enroll approximately 10 patients over a 6-month period, but recruitment resulted in only 51 patients in total enrolled after 1 year.

Upon study close, pharmacists were asked to comment on various aspects of their experience participating in this study. Most often, pharmacists reported time constraints as the primary reason that patient enrollment and follow-up opportunities were missed. Many pharmacists reported shortage of staff and lack of management support as other important impediments to recruitment success. Less common, but still reported, were the lack of remuneration, discomfort with study activities and a lack of perceived value of the research project. The pharmacists were unable to keep records of number of patients approached to enroll in the study, number of patients declined and reasons for declining, rendering it difficult to pinpoint the exact reasons for low participant enrollment. Pharmacists recognized the value of active surveillance for this population, as approximately one-quarter of pharmacists who were invited to enroll ($n = 713$) agreed to participate, and more than half of these pharmacists believed that postmarketing surveillance should be a cornerstone of pharmacy. However, results of participant recruitment suggest that pharmacists' ability to implement effective surveillance programs varies, depending on a number of factors.

Two pharmacists in distinct practice environments were relatively successful in implementing the study. These pharmacists recruited patients based on 2 different patient recruitment strategies. One pharmacist, at an independent pharmacy in a rural community, relied on strong preexisting relationships with patients and the help of a pharmacy student in completing the extra study-specific tasks. The other successful pharmacist at a large chain pharmacy relied on database searching and calling patients to schedule appointments at the pharmacy. Without remuneration or infrastructure support, these pharmacists were able to creatively adapt their pharmacy practices to implement the surveillance strategy.

In this study, patient participation was biased toward women previously diagnosed with

TABLE 4 Baseline demographics of participant population

Parameter	Number of participants (total <i>N</i> = 51)	%
Mean age, 30.5 years (SD 5.1 years)		—
Pregnant	39	76
First trimester	17	33
Second trimester	15	29
Third trimester	7	14
Breastfeeding	12	24
Hypertensive*	7	13.7
Severe (>160 mmHg/>110 mmHg)	1	2.0
Nonsevere (140-159 mmHg/90-109 mmHg)	2	3.9
Controlled (<140 mmHg/<90 mmHg)	4	7.8
Antihypertensive use	3	5.9
Methyldopa	2	3.9
Labetalol	1	2.0
Hydrochlorothiazide	1	2.0
Mean duration of antihypertensive use (months)	12.3	—
Comorbid conditions		
Gestational diabetes	2	3.9
Asthma	9	17.6
Hypothyroidism	2	3.9
Autoimmune disorder	3	5.9
Musculoskeletal condition	2	3.9
Mood disorder	1	2.0
Genetic disorder	1	2.0
Other	2	3.9
Ethnicity [†]		
Aboriginal	1	2.1
Asian	6	12.5
Black	1	2.1
Caucasian	39	81.3
Hispanic	1	2.1
Education completed		
Less than high school	2	3.9
High school	12	23.5
Vocational school	1	2.0
Some college	20	39.2
University degree (BSc, BEd, etc.)	12	23.5
Graduate degree (MA, PhD, etc.)	3	5.9
Annual household income reported [‡]		
<\$40,000	13	38.2
\$40,000-\$70,000	9	26.5
>\$70,000	11	32.4

*Patient self-reported as diagnosed by physician.

[†]Three participants chose not to respond, *n* = 48.[‡]Seventeen participants chose not to respond, *n* = 34.

hypertension. Our results show that 14% of the patients recruited were hypertensive, compared with the 5% to 10% expected in the population.²⁵ Mean blood pressure readings in our study were within normal ranges (<120 mmHg/<80 mmHg). It is notable that our study also included more participants who were primigravida (53%) compared with first-time pregnancies in the general population (44%).²⁵ The participating pharmacists reported difficulty recruiting pregnant or breastfeeding women who were experienced mothers or were normotensive. Patients without blood pressure concerns, understandably, did not see the value in a drug surveillance program limited to antihypertensive medications. The normotensive women who enrolled in the study were typically in a higher education bracket (70% had at least some college education) or, as noted above, were more likely to be primigravida.

While postmarketing surveillance is an important tool for the assessment of drug safety in the pregnant and breastfeeding patient population, the feasibility of community pharmacists taking on this role was not successfully demonstrated. These results suggest the need for additional research with lessons learned from our study. Future studies should focus on 1) pharmacists' use of case-finding techniques to boost enrollment by targeting patients who would benefit most from drug surveillance²⁶; 2) pharmacists' development of patient monitoring and follow-up plans and documentation of identified adverse drug reactions and actions taken to resolve/report adverse drug reactions; and 3) built-in remuneration strategies, buy-in from pharmacy management and support staff to allow dedicated time for surveillance activities and documentation. ■

From the Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences (Tsao, Marra, Lynd, Thomas), University of British Columbia, Vancouver; and the Faculty of Pharmacy (Ferreira), University of Montreal, Montreal, Quebec. Contact cmarra@mun.ca.

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