ISSN 1671-4083
Shanghai Institute of Materia Medica
Chinese Academy of Sciences
http://www.ChinaPhar.com

Are herbal medicinal products less teratogenic than Western pharmaceutical products?

LEUNG Kwok-Yin[1], LEE Yuk-Ping, CHAN Ho-Yee, LEE Chin-Peng, Mary TANG Hoi-Yin

Department of Prenatal Diagnosis and Counselling, Tsan Yuk Hospital, The University of Hong Kong, Hong Kong SAR, China

KEY WORDS herbal medicine; pregnancy; teratogenicity

ABSTRACT

AIM: To determine the use and teratogenicity of herbal medicinal products (HMP). **METHODS:** A retrospective study was conducted in a University hospital to compare the difference in the pattern of use and fetal outcomes between pregnant women who took HMP and Western pharmaceutical products (WPP). **RESULTS:** From 1995 Jan to 2001 Dec, 61 and 372 women took HMP and WPP one month before or during their current pregnancies respectively. There was an increase in the prevalence of pregnant women who took HMP from 0 % in 1995 to 0.8 % in 2001. Among HMP users, 51.6 %, 82.8 % and 58.6 % of them had low monthly family income (<15 000), low education level (secondary education or below) and were unemployed respectively. In comparison to WPP, pregnant women used smaller number of HMP (1.4 *vs* 3.0, $P<0.01$) at a later gestation (4.8 weeks *vs* 3.1 weeks, $P<0.01$) and within a shorter duration (11.1 d *vs* 47.9 d, $P<0.01$). The prevalence of congenital fetal abnormalities in the group of women who took HMP (3.3 %) was not significantly higher than that who took WPP (0.8 %). There were no and two abnormal fetal karyotypes in the former and latter group respectively. No and ten women in the former and latter group underwent termination of pregnancy for anxiety respectively. The proportions of silent miscarriage in the former and latter group were similar (6.6 % *vs* 5.4 %). **CONCLUSION:** Pregnant users of HMP were from lower socio-economical status. There was no significant difference in the teratogenicity between HMP and WPP.

INTRODUCTION

Despite the potential teratogenicity of some medications, the proportion of pregnant women who took medications was very high, up to 99 % in a recent survey in France[1]. Studies in some countries showed that women took mediations during or prior to pregnancy because of musculo-skeletal pain, vitamin supplements, gastrointestinal discomfort, flu, threaten miscarriage, and infection[2-5]. Not all of them took Western pharmaceutical products (WPP). More than 10 % of pregnant women reported the use of herbal medicinal products (HMP) in Finland, Australia, Nigeria, South Africa and United States[6-10]. Most of them used HMP for dietary supplements[6]. The users in Finland[6] and Italy[8] were from higher socio-economical class. There were no similar studies in Hong Kong Chinese women. We do not know whether there is any racial difference in the use of HMP by pregnant women.

One of thee most frequently cited reasons for us-

[1] Correspondence to Dr LEUNG Kwok-Yin, Consultant. *Department of Obstetrics & Gynaecology, the University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Hong Kong SAR, China*. Phn 852-2855-3913. Fax 852-2517-3278.
E-mail leungky1@ha.org.hk.
Received 2002-09-12 Accepted 2002-10-09

ing HMP in non-pregnant women was a desire to avoid the side effects of conventional treatments[11]. Although consumers often think that herbal medicine products are risk free[12], the evidence available to date implies that some herbal medicinal products are associated with risks[7]. However, the teratogenicity of herbal medicine products was not specified and it is unknown whether HMP is more or less teratogenic than WPP.

The aim of this study is to determine the pattern of use of herbal medicinal products by pregnancy women and whether herbal medicine products are less teratogenic than WPP.

METHODS

This was a retrospective study on fetal outcomes of pregnant women who took HMP and WPP. During the first antenatal visit to Tsan Yuk Hospital, all women who had taken any HMP or WPP one month before or during their current pregnancies were identified on direct questioning by midwives, and were then referred to prenatal diagnosis and counseling department for further management. The name, dosage, duration and purpose of taking medications were then identified as far as possible. Since reproductive risks of most HMP were largely not available, women were counseled as such. On the other hand, women were counseled according to the results of literature search on the reproductive risks of WPP on pregnancy. Nuchal translucency screening, maternal serum screening for Down syndrome and anomaly scan was offered to all women who took either HMP or WPP.

Medical records were reviewed. Main outcome measures included congenital anomalies, miscarriage, and termination of pregnancy. The outcome measures of women who took HMP were compared to that who took WPP. If a woman took both HMP and WPP and her main worry was on HMP (or WPP), she will be put under the group of HMP (or WPP) for analysis. The prevalence of congenital abnomalies in these two groups of women were compared to a control group of pregnant women who were aged below 35, did not take HMP nor WPP and had no risk factors for fetal congenital anomalies. The prevalence in the control group was calculated in a previous study which was performed in our department within the study period in the present study[13].

Statistical analyses SPSS 10.1 was used for statistical analyses. Student's *t* test and *Chi*-square test were used for continuous and nominal data respectively.

RESULTS

From 1995 Jan to 2001 Dec, 61 and 372 women took HMP and WPP one month before or during their current pregnancies respectively. There was an increase in the prevalence of pregnant women who took HMP from 0 % in 1995 to 0.8 % in 2001. There was also an increase in prevalence of pregnant women who took WPP from 0.4 % in 1995 to 2.4 % in 2001. The unemployment rate was significantly higher in the group of women who took HMP (58.6 %) than that who took WPP (36.0 %) (Tab 1). Among users of HMP, 51.6 % and 82.8 % of them had low monthly family income (<15 000) and low education level (secondary education or below) respectively (Tab 1).

Tab 1. Demographic data of pregnant women who took herbal medicinal products or Western pharmaceutical products. Numbers are expressed as mean (SD) or proportions (percentage). $^{c}P<0.01$ *vs* Western pharmaceutical products.

	Herbal medicinal products	Western pharmaceutical products
Age	30.5±5.1	30.0±4.8
Married	59/61 (96.7 %)	361/372 (97.0 %)
Monthly income <=15 000	16/31 (51.6 %)	82/189 (43.4 %)
Secondary education or below	48/58 (82.8 %)	292/372 (78.5 %)
Unemployed	34/58 (58.6 %)^{c}	134/372 (36.0 %)
Nulliparity (no previous pregnancy)	30/61 (49.2 %)	239/372 (64.2 %)
Positive Down syndrome screening (increase in nuchal translucency, abnormal maternal serum screening or both)	3/61 (4.9 %)	10/372 (2.7 %)
Number of women who took both herbal medicinal products and Western pharmaceutical products	11	13

The reasons why women took HMP were similar to that why women took WPP (Tab 2). Most common reasons included flu, menstrual problem, gastrointestinal problem, and promotion of health. In comparison

Tab 2. Reasons (can be more than one per woman) for taking herbal medicinal products and Western pharmaceutical products in pregnancy.

	Herbal medicinal products	Western pharmaceutical products
Reasons for taking medications		
Flu	23	140
Menstrual problem	8	24
Gastrointestinal problem	8	11
Promotion of health	6	19
Termination of pregnancy	3	7
Chronic medical problems	2	124
Pain relief	2	8
Infection	1	23
Weight reduction	1	36
Subfertility	1	0
Threaten miscarriage	1	0
Vaccination	0	17
Others	0	12
Unknown	8	8

to WPP, pregnant women used smaller number of HMP (1.4 *vs* 3.0, $P<0.01$) at a later gestation (4.8 weeks *vs* 3.1 weeks, $P<0.01$) and within a shorter duration (11.1 d *vs* 47.9 d, $P<0.01$) (Tab 3).

Tab 3. Characteristics of herbal medicinal products and Western pharmaceutical products taken by pregnant women.

	Herbal medicinal products	Western pharmaceutical products	*P* value
Mean number of medications	1.4 (1.0)	3.0 (2.8)	<0.01
Mean duration of medications (number of day)	11.1 (19.3)	47.9 (91.4)	<0.01
Mean gestation age at which medication was taken	4.8 (3.6)	3.1 (3.1)	<0.01

The prevalence of congenital fetal abnormalities in the group of women who took HMP was 3.3 % which was higher, although not significantly than that in the group of women who took WPP (Tab 4). The former prevalence was also higher than the prevalence of congenital fetal abnormalities in the group of women aged below 35 and who did not take any HMP or WPP

Tab 4. Fetal outcomes of women who took herbal medicinal products and Western pharmaceutical products.

	Herbal medicinal products	Western pharmaceutical products
Congenital fetal abnormalities	2/61 (3.3 %)	3/372 (0.8 %)
Termination for fetal abnormalities	2/2 (100.0 %)	3/3 (100.0 %)
Abnormal karyotype	0/7 (0.0 %)	2*/57 (3.5 %)
Termination of pregnancy for anxiety	0/61 (0.0 %)	10/372 (2.7 %)
Silent miscarriage	4/61 (6.6 %)	20/372 (5.4 %)

* 1 case of 46XXp-, and 1 case of 47 XY,+MAR

(2.2 %)[13]. There were two abnormal karyotypes (46XXp- and 47XY,+MAR) in women who took Western pharmaceutical products. No women who took HMP underwent termination of pregnancy because of anxiety. There were no differences in the proportion of silent miscarriage between the two groups.

The two women who took different types of HMP were associated with two different types of fetal congenital abnormalities while all the three women who took different types of WPP were associated with same fetal congenital abnormality-cleft lip and palate (Tab 5). There were no other risk factors for congenital fetal abnormalities other than HMP/WPP in these five cases.

DISCUSSION

There was an increase in the number of pregnant women who underwent prenatal diagnosis because of taking HMP from 0 % in 1995 to 0.8 % in 2001. The latter prevalence was much lower than that found in other countries[6-10]. There were two possible reasons. Firstly, we asked women about the use of HMP in their first antenatal visit rather than throughout the whole pregnancy or during labour as in other studies[6,8-10]. Secondly, women might think that HMP were risk free and so did not inform healthcare professionals about using HMP[12].

This study has shown two racial differences in the use of HMP in pregnant women. Firstly, unlike women in Finland[6] and Italy[4], Hong Kong Chinese women who took HMP had lower family income, lower education level and were unemployed. A possible explanation is that HMP is something traditional to Hong

Tab 5. Types of congenital fetal abnormalities in women who took herbal medicinal products or Western pharmaceutical products.

Name of products	Gestational age/week	Reasons for taking the products	Types of congenital abnormalities
A combination of herbal medicinal products*	8	Gastric discomfort	Megacystitis and umbilical cord cyst
Herbal medicinal products: unknown nature	2-3	Reduce 'heat'	Body stalk anomaly
Steroid injection	5	Skin problem	Cleft lip and palate
Fluconazole	5	Vaginal moniliasis	Left cleft lip and palate
Tetracycline, amoxil, minoxidil	3	Urogential infection	Left cleft lip and palate

Radix scrophulariae; fructus aurantii zmmaturns; radix trichosanthis; fructus ziziphi; cortex magnoliae officinalis; radix rehmanniae; semen pruni; rhizome anemarrhenae; radix glycyrrhizae; endothelium corneum gigeriae galli; radix ophipogonis; radix astragali seu hedysari; radix bupleuri; radix scutellariae.

Kong Chinese women, but not to Caucasian women. Secondly, unlike Finland[6], flu and menstrual problem, instead of dietary supplements, were the two most common reasons for taking HMP by Hong Kong Chinese Pregnant women.

The prevalence of congenital fetal abnormalities in the group of pregnant women who took HMP (3.3 %) was not significantly higher than that in the group of pregnant women who took WPP (0.8 %). However, the interpretation of this apparent difference should be cautious. Firstly, more pregnant women who took HMP had lower socio-economical status which is a risk factor for congenital abnormalities[14,15]. Secondly, the number of women who took HMP was much smaller than that of women who took WPP in our study. Under reporting of HMP is possible[12]. Thirdly, on literature search, we are not aware of any teratogenicty associated with any of the HMP listed in the case having fetal megacystitis and umbilical cord cyst (Tab 5). Fourthly, no women who took HMP underwent termination of pregnancy because of anxiety while 2.7 % of women who took WPP did so. Whether congenital abnormalities were present in the latter group was unknown.

In Hong Kong, pregnant users of herbal medicinal products are from lower socio-economical status. There were no significant difference in the teratogenicity of herbal medicinal products and Western pharmaceutical products.

REFERENCES

1 Lacroix I, Damase-Michel C, Lapeyre-Mestre M, Montastruc JL. Prescription drugs during pregnancy in France. Lancet 2000; 356: 1735-6.
2 Henry A, Crowther C. Patterns of medication use during and prior to pregnancy: the MAP study. Aust N Z J Obstet Gynaecol 2000; 40: 165-72.
3 Splinter MY, Sagraves R, Nightengale B, Rayburn WF. Prenatal use of medications by women giving birth at a University hospital. South Med J 1997; 90: 498-502.
4 Donati S, Baglio G, Spinelli A, Grandolfo ME. Drug use in pregnancy among Italian women. Eur J Clin Pharmacol 2000; 56: 323-8.
5 Aviv RI, Chubb K, Lindow SW. The prevalence of maternal medication ingestion in the antenatal period. S Afr Med J 1993; 83: 657-60.
6 Hemminki E, Mantyranta T, Malin M, Kopponen P. A survey on the use of alternative drugs during pregnancy. Scand J Soc Med 1991; 19: 199-204
7 Ernest E. Herbal medicinal products during pregnancy: are they safe? BJOG 2002; 109: 227-35.
8 Gharoro EP, Igbafe AA. Pattern of drug use among antenatal patients in Benin City, Nigeria. Med Sci Monit 2000; 6: 84-7.
9 Mabina MH, Pitsoe SB, Moodley J. The effect of traditional herbal medicines on pregnancy outcome. S Afr Med J 1997; 87: 1008-10.
10 Pastore L. Home remedies used during pregnancy. The Cochrane Library 2000; 3: 529.
11 Palinkas LA, Kabongo ML. San Diego Unified Practice Research in Family Medicine Network. The use of complementary and alternative medicine by primary care patients. A SURFNET study. J Fam Pract 2000; 49: 1121-30.
12 Eisenberg D, David RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, *et al*. Trends in alternative medicine use in the United States; 1990-1997. JAMA 1998; 280: 1569-75.
13 Leung WC, Lee CP, Tang MHY. Evaluation of routine obstetric ultrasound examination in detecting fetal structural abnormalities in low risk pregnancies. HKJGOM 2000; 1: 28-32.
14 Vrijheid M, Dolk H, Stone D, Abramsky L, Alberman E, Scott JE. Socioeconomic inequalities in risk of congenital anomaly. Arch Dis Child 2000; 82: 349-52.
15 Basso O, Olsen J, Christensen K. Recurrence risk of congenital anomalies-the impact of paternal, social, and environmental factors: a population-based study in Denmark. Am J Epidemiol 1999; 150: 598-604.