Research Article

Pharmaceutical BIOPROCESSING

The relationship between the use of oral contraceptives and the risk of uterine leiomyoma in women of child bearing age of Han Chinese

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Objective: To study the relationship between the use of oral contraceptives and the risk of uterine myoma in women of childbearing age in Han Chinese.

Methods: A case-control study was conducted in 650 women of childbearing age in China who were diagnosed as uterine leiomyoma. The patients were matched according to the ratio of 1: 1, and the questionnaire and health checklist were used to investigate the influence factor of uterine leiomyoma.

Results: There was no significant difference in education level, number of pregnancy, abortion number and genital tract infection between case group and control group (P>0.05). The proportion of one-time pregnancy, body mass index (BMI), the proportion of hypertension and oral contraceptive use in case group were higher than those of the control group (P<0.05). The proportion of oral contraceptives currently used in the case group was higher than that of the control group (P<0.05). Women currently using oral contraceptives have a 1.91-fold greater risk of uterine leiomyoma than women who never used oral contraceptives (OR=1.91, 95% CI:1.22-2.94). Multivariate logistic regression analysis showed that the incidence of uterine leiomyoma in women of childbearing age with oral contraceptives and BMI ≥ 25 kg/m^2 was slightly increased (P<0.05).

Conclusion: Currently, the use of oral contraceptives and BMI ≥ 25 kg/m^2 were the risk factors for the incidence of uterine leiomyoma in Chinese women of childbearing age.

Keywords: chinese women of childbearing age ▪ han ▪ oral contraceptive ▪ uterine leiomyoma ▪ risk factor

Introduction

Uterine leiomyomas are common benign tumors in female genital organs, which can be divided into subserosal leiomyomas, intramural leiomyomas, submucosal leiomyomas, cervical leiomyomas, and broad ligament leiomyomas depending on the growth position. Different types of uterine leiomyomas can be manifested as menorrhagia, low abdominal mass or dysuria, and defecation difficulty and other clinical symptoms [1]. In China, the prevalence of uterine leiomyomas is about 11.21%, and the rate of malignant change is about 0.30%. More than 20% of women over the age of 35 have uterine leiomyomas [2]. Due to slow tumor development and no obvious clinical symptoms, many patients were diagnosed by physical examination, so some patients failed to get early treatment, or even did not receive treatment. The etiology and pathogenesis of uterine leiomyomas is still not very clear. Estrogen is the main promotion factor for the growth of uterine leiomyomas, and progesterone plays a synergistic effect [3]. The occurrence of uterine leiomyomas was the result of mutual interaction among various factors including age, number of births, obesity, smoking, blood pressure, diet, stress, and environment, but whether some of the risk factors can promote estrogen and progesterone to induce uterine leiomyomas has no definitive conclusion

[4,5]. Although the relationship between oral contraceptives and uterine leiomyomas has been widely studied, but differences still exist [6-8]. Compared with those who have never used oral contraceptives, decreased, similar or elevated results of the risk of uterine leiomyomas in women used oral contraceptives have been reported [9]. To further clarify whether oral contraceptives increased the risk of uterine leiomyomas, this case-control study explored the relationship between oral contraceptives and the incidence of uterine leiomyomas in Chinese women of childbearing age, thus providing a reference for the safe use of oral contraceptives as well as monitoring and prevention of adverse reactions of contraceptives.

Subjects and methods

Subjects

A total of 650 Chinese women of childbearing age who were diagnosed with uterine leiomyomas were collected as case group. At the same time, the control groups were 1:1 matched according to the following conditions:

i. Women of childbearing age received examination in the same period

ii. From the same area

iii. Age difference of no more than 1 year old

iv. Without gynecologic cancer.

All subjects in control group (n = 650) were examined by ultrasound to exclude uterine leiomyomas.

Methods

Methods and contents

A case-control study method was adopted. Investigators who passed the uniform training inquired patients in both groups by using structured questionnaires. The contents included general demographic characteristics, fertility history, history of contraception (exposure to oral contraceptives), disease or health status (including history of uterine leiomyomas, recording of diagnosis time, place of treatment, treatment methods and outcomes, etc.). In addition, related health examination and laboratory test were performed at the same time.

Diagnostic criteria

The diagnostic criteria were based on the Chinese College of Obstetrics and Gynecology (7th Edition) for uterine leiomyomas including menorrhagia, menstrual prolongation or irregular bleeding; lower abdomen mass, a small number of pain and compression symptoms, or with anemia; uterus increased and hard; intrauterine expansion or deformation; touching intrauterine convex surface by curettage; facilitation of diagnosis by B-ultrasound and / or hysteroscopy.

Quality control

Establish three grade quality control management and evaluation system. Before the survey, all participating researchers were trained and practised. Investigators and clinical examiners are all women and experienced technical service staffs, who can communicate with women of childbearing age easily to obtain real and reliable information. After the investigation, all the instructors were organized to audit the questionnaires term by term. The data acceptance criterion for the person-time pass rate was more than 90%, and the project pass rate was more than 95%.

Pelvic ultrasound examination required that moderate filling of the bladder before examination, the formation of a good "sound-absorbing window", taking a supine position for detection, exposing the lower abdomen, applying couplant on the checking area of the skin. Longitudinal, transection and oblique tomography scan were performed on the basis of requirements to observe and record the uterus, annex, pelvic mass and so on.

Statistical analysis

SPSS 21.0 software was used for statistical analysis. Enumeration data between two groups was compared by chi-square test. Logistic regression analysis was performed in multivariate analysis. $P < 0.05$ was considered statistically significant.

Results

Comparison of general information between two groups

There was no significant difference in education level, number of pregnancy, abortion number and genital tract infection between case group and control group ($P > 0.05$). The proportion of one-time

pregnancy, the BMI, the proportion of hypertension and oral contraceptive use in case group were higher than those of the control group (P <0.05) (**TABLE 1**).

Relationship between oral contraceptives and the incidence of uterine leiomyomas

Women currently using oral contraceptives have a 1.91-fold greater risk of uterine leiomyoma than women who never used oral contraceptives (OR= 1.91, 95% CI: 1.22-2.94) (**TABLE 2**).

Logistic regression analysis of influencing factors of uterine leiomyomas

Multivariate logistic regression analysis showed that the incidence of uterine leiomyoma in women of childbearing age with oral contraceptives and BMI ≥ 25 kg/m^2 was slightly increased (P<0.05) (**TABLE 3**).

Brief summary

There was no significant difference in education level, number of pregnancy, abortion number and genital tract infection between case group and control group (P>0.05). The proportion of one-time pregnancy, the BMI, the proportion of hypertension and oral contraceptive use in case group were higher than those of the control group (P<0.05). The proportion of oral contraceptives currently used in the

Table 1. Comparison of general information between two groups (n=650)

Item	Control group		Case group		X^2	P
	n	%	n	%		
Education level					1.047	>0.05
Primary school or below	50	7.7	48	7.4		
Junior high school	200	30.8	197	30.3		
Senior high school	300	46.2	302	46.5		
Junior college or above	100	15.4	103	15.8		
Pregnancy					0.962	>0.05
0	20	3.1	22	3.4		
1	192	29.5	197	30.3		
2	294	45.2	301	46.3		
≥3	144	22.2	130	20		
Parity					5.735	<0.05
0	32	4.9	29	4.5		
1	568	87.4	577	88.8		
≥2	50	7.7	44	6.8		
Abortion number					0.473	>0.05
0	196	30.2	194	29.8		
1	244	37.5	251	38.6		
≥ 2	210	32.3	205	31.5		
BMI					7.012	<0.05
<25 kg/m^2	477	73.4	402	61.8		
≥ 25 kg/m^2	173	26.6	248	38.2		
Hypertension					6.568	<0.05
Yes	91	14.0	125	19.2		
No	559	86.0	525	80.8		
Genital tract infection					1.492	>0.05
Yes	204	31.4	207	31.8		
No	446	68.6	443	68.2		
Current contraceptive method					8.601	<0.05
Never used	60	9.2	62	9.5		
Oral contraceptives	67	10.3	113	17.4		
Other contraceptive method	523	80.5	475	73.1		

Table 2. Relationship between oral contraceptives and the incidence of uterine leiomyomas

The condition of oral contraceptives	Control group		Case group		OR(95%CI)	P
	n	%	n	%		
Never used	309	47.5	312	48	1.00	>0.05
Once used	274	42.2	225	34.6	1.32 (0.95-1.86)	<0.05
Currently used	67	10.3	113	17.4	1.91 (1.22-2.94)	<0.05

Table 3. Logistic regression analysis of influencing factors of uterine leiomyomas

Variable	β	SE	Wald X^2	OR(95%CI)	P
BMI (<25 kg/m² VS ≥25 kg/m²)	0.542	0.328	4.873	1.452 (1.205-6.61)	<0.05
One-time pregnancy (Y vs N)	0.118	0.072	1.054	1.067 (0.942-1.383)	>0.05
Hypertension(Y vs N)	0.367	0.241	6.682	1.394 (1.025-1.941)	<0.05
Currently oral contraceptives(Y vs N)	0.614	0.272	7.033	1.845 (1.106-2.783)	<0.05

case group was higher than that of the control group (P<0.05). Women currently using oral contraceptives have a 1.91-fold greater risk of uterine leiomyoma than women who never used oral contraceptives (OR=1.91, 95% CI: 1.22-2.94). Multivariate logistic regression analysis showed that the incidence of uterine leiomyoma in women of childbearing age with oral contraceptives and BMI ≥ 25 kg/m² was slightly increased (P<0.05).

Discussion

Uterine leiomyomas often occur in women of childbearing age [10]. Foreign research indicated that the prevalence of uterine leiomyomas was more than 25% in women of childbearing age in developed countries [11]. At present, the etiology and pathogenesis of uterine leiomyomas are still not very clear. The occurrence of uterine leiomyomas was the result of mutual interaction among various factors including age, number of births, obesity, smoking, blood pressure, diet, stress, and environment. A Japanese control study of uterine leiomyomas found that BMI was significantly higher in case group than control group, indicating that overweight increased the risk of uterine leiomyomas. Uterine leiomyomas were more likely to occur in hypertensive patients and the proportion of hysterectomy also increased significantly [12,13]. The risk of uterine leiomyomas increased with the extension of the history of hypertension, especially in patients with more than 5 years history of hypertension [14].

Among the many factors, whether oral contraceptives increase the risk of uterine leiomyomas, the conclusions of different populations are still controversial. World Health Organization (WHO) on the "medical standard selection of contraceptive methods" shows that the uterine leiomyomas is not an absolute contraindication to the use of oral contraceptives and oral contraceptives may not cause uterine leiomyomas growth. Compared with those who have never used oral contraceptives, decreased, similar or elevated results of the risk of uterine leiomyomas in women used oral contraceptives have been reported [15]. Currently taking oral contraceptives were at 0.4 times more likely to have uterine leiomyomas than those who had never used before, while those once taking oral contraceptives had a similar risk with those never taking oral contraceptives [16]. A study by the Oxford Family Planning Association (FPA) in 535 cases of uterine leiomyomas showed that the risk of leiomyomas decreased with the stop time of oral contraceptive increased. When the stop time of oral contraceptive was more than 12 years, the risk of leiomyomas decreased to 0.5. A case-control study in Italy showed that the use of oral contraceptives did not raise the risk of leiomyomas. It has been reported [17] that long-term use of oral contraceptives increased the risk of uterine leiomyomas in women.

The multivariate analysis of this study showed that the risk of uterine leiomyomas increased slightly in Chinese Han women of childbearing age with BMI ≥ 25 kg/m² as well as the current use of oral contraceptives. This study found no relationship between the number of pregnancy, parity, reproductive tract infection, hypertension and the risk of uterine leiomyomas in Chinese women of childbearing age which should be focused on in the future research. For those who used oral contraceptives, health screening should be carried out, and the indications and contraindications of oral contraceptives should be correct understood. Regular follow-up, including blood pressure and body mass measurement should be carried out after use. Early prevention and early treatment can be achieved by strengthening the monitoring of uterine leiomyomas in women with high BMI and long-term oral contraceptives. High quality services of family planning should be carried out and the safe use of contraceptives should be enhanced to improve the reproductive health of Chinese Han women.

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