The risk of using intrauterine devices to benign reproductive system conditions in postmenopausal women: A case control study

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Background: To investigate the effect of using intrauterine devices (IUDs) during the fertile window on women's reproductive system health. **Materials and Methods:** 2,744 postmenopausal women in the Minhang District, Shanghai, China were enrolled. In the IUDs group there were 2,253 women; in the tubal ligation group there were 202 women and there were 289 women in the control group. We selected subjects according to the cases number in different hospital by using step sampling, and, in addition, collected the sociological data and information of the previously used contraceptives by the subjects, which included whether the contraceptives were used appropriately and the effect they had. Kolmogorov-Smirnov test, Levene's test, and logistic regression analysis were used to analyze the data. **Results:** The prevalence rate of benign reproductive system conditions was significantly different among them ($P < 0.05$). Further comparison revealed, the rate in Group 1 was significantly lower than that in Group 2 and Group 3 ($P < 0.05$, respectively). Results of logistic regression analysis show that the risk factors for development of such conditions lie in the women's pregnancy history [odds ratio (OR) = 3.85], reproductive history (OR = 0.5), the use of IUD in fertile window (OR = 0.4), tubal ligation (OR = 1.74), birth control time (OR = 0.9), contraceptive failure history (OR = 1.7), and history of family planning procedures (OR = 1.73). **Conclusion:** IUDs, maybe, can effectively reduce the risk of getting benign reproductive conditions in postmenopausal females.

Key words: Benign reproductive system, contraception, fertile window, intrauterine devices (IUDs)

INTRODUCTION

There are many chosen methods of contraception in China, such as coitus interruptus, condoms, and oral contraceptive, but these methods are associated with relatively high typical use failure rates and low rates of continuation, which in turn contribute to high rates of unplanned pregnancies.[1] Of all reversible contraceptives, intrauterine devices (IUDs) have been shown to have one of the highest rates of satisfaction and continuation and an efficacy that is comparable to sterilization.[2,3] The success of China's family planning policy is mainly due to the IUDs.[4,5] However, the use of IUDs has many side effects, such as pelvic pain, bleeding, and spotting.[6,7] Historically, the use of certain IUDs was associated with increased risk of pelvic inflammatory disease. If expulsion goes unnoticed, women may unexpectedly become pregnant.[8] In addition, greater difficulties of insertion as well as more frequent adverse reactions can affect women's health. The survey conducted in the context of this study investigated the effect of the use of IUDs during the fertile window on women's reproductive system health in postmenopausal duration.

MATERIALS AND METHODS

Data in this study were obtained from residents' health electronic information system. The time span for our

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study was from December 2012 to December 2013. The women were assigned to the IUDs group if they had used IUDs ("T" ring) once as their contraception method of choice during their fertile window stage. The women in the tubal ligation group had had a tubal ligation operation, while in the control group, women used withdrawal for contraception purposes. Health information was collected and the influence of using IUDs during the fertile window on women's reproductive system health was explored by using a retrospective statistical analysis.

Subjects and grouping

All women were ≥45 years old and had been menopausal for at least 1 year, according to the residents' health electronic information system. The three groups (the IUDs group, the tubal ligation group, and the control group) were set according to the method of contraception selected by the women. The subjects were assigned to matching areas; all of the hospitals in these areas were our survey points. We selected subjects according to the number of cases in different hospitals by using step sampling. The above medical institutions fulfilled the task using systematic sampling and cluster sampling according to sample size. All the information concerning the subjects was confirmed by investigators.

Inclusion criteria

The subjects should:
1. Own a Minhang domicile or living in this area,
2. Have their last menstrual period over 1 year before the start of this study,
3. Agree to offer information relevant to the study and take part in laboratory tests after informed consent,
4. Be sexually active, take precautions or have been sterilized (only tubal ligation), and
5. Have been using birth control for over 60 months.

Exclusion criteria

Subjects excluded from the study were those who:
1. Took two or more contraception measures over a period of 60 months, or had sexual activity with males who had vasoligature,
2. Had hysterectomy, bilateral oophorectomy, and colpocleisis before their postmenopausal period,
3. Had had estrogen therapy,
4. Had premature ovarian failure,
5. Had primary infertility and secondary infertility, and
6. Had more than one sexual partner during the experimental period.

The subjects were assigned to the relevant group according to their birth control of choice: Group 1 (IUD), Group 2 (tubal ligation), and Group 3 (coitus during safe days, or coitus interruptus).

Calculating sample size

The effective rate of contraception was more than 99.6% of oral contraceptives and injection contraceptive, and we expected 0.95% confidence. We collected 2,000 samples in all; according to , $n = \frac{\pi_1(100-\pi_1) + \pi_2(100-\pi_2)}{(\pi_1-\pi_2)^2} f(\alpha,\beta)$ π^1 and π^2, respectively, represent the expected effective rate (%) (3-10%) of the two groups (Contraceptive groups and Group 3), $f(\alpha, \beta)$ can be detected by the regular $f(\alpha, \beta)$ number value table, $f(0.05, 0.10) = 10.5$ typically. Considering the difficulty of the investigation, we selected 200 tubal ligation samples, 200 safe period and withdrawal samples, that is, a total of 2,400 samples.

The studying indicators

We collected the sociological data and information of the previously used contraceptives by the subjects, which included whether the contraceptives were used appropriately and the effect they had. Evaluating contraceptive effect used pearl index (PI), PI = (failure times/total months of contraception of all objectives) ×1,200.

Questionnaires were used to collect the data of subjects including fertility circumstances, age of menopause, sexual activity and family planning, history of operations, reproductive tract infection history, and history of malignancies.

Data analysis

Kolmogorov-Smirnov test and Levene's test were used to inspect the normality and homogeneity of variance of all data. Chi-square test was used to detect the prevalence rate of benign reproductive system conditions in different groups. Logistic regression analysis was used to screen the indicators that could influence the benign reproductive system conditions. Demographic indicators were examined by analysis of variance (ANOVA). All statistical tests were two-sided with 0.05 as a cutoff for significance. Statistical analyses were performed using the Statistical Product and Service Solutions (SPSS) (International Business Machines Corporation, IBM, USA) software, version 16.0 and Statistical Analysis System (SAS) (SAS Institute Inc., USA) software, version 9.1.

RESULT

General information

A total of 2,744 women participated in our study from 2012 to 2013 (2,253 in group 1, 202 in group 2, and 289 in control group). Age, menopause age, body mass index (BMI), contraceptive time, and other design quantitative variables can all be considered normal distribution, and dealt as normally distributed variables during calculation. The description of these variables was shown in Table 1. Due to the large sample size (over 2,000), the smaller

differences may lead to significant statistical differences at the baseline.

There were significant differences in age, menopause age, contraceptive time, and BMI among the three groups ($P < 0.05$). Out of all the subjects, the composition rate of women who had never given birth was 4.56% (125/2,744), and of women who had scarred uterus was 14.61% (401/2,744). There was a significant difference among the three groups ($P < 0.05$, respectively).

Contraceptives and state of health after menopause in one-way ANOVA

The distribution of benign conditions was as follows: 61 participants had ovarian cyst (2.2%), 89 participants had a tubal pregnancy (3.2%), 171 participants had uterine fibroids (6.2%), 50 participants had cervical intraepithelial neoplasias (1.8%), 15 participants had vulvalcyst (0.5%), and eight participants had pelvic cyst (0.3%). As far as malignant conditions were concerned, there were three participants with ovarian cancer (0.1%, all in group 1), one participant with oviduct cancer (0.004%, all in group 1), 10 participants with endometrial cancer (0.4%, 7 participants in group 1 and 3 participants in control group), and five participants with cervical cancer (0.2%, 3 participants in group 1 and 2 participants in control group).

Significant differences were found between group 1 and the control group ($P < 0.001$), but no significant difference was found between group 2 and the control group ($P = 0.16$); OR: 1.34 95% CI (0.89-2.02) is shown in Figure 1.

State of health after menopause in multivariate analysis

We have assessed the relationship between benign conditions of the female reproductive system and the use of contraceptives. Whether having benign disease was as dependent variable (1 = Yes, 0 = No), other index was as concomitant variable in unconditional logistic regression model to explore the combined effect of multiple factors in benign disease. We used stepwise regression to screen variables and obtain regression model, $\alpha = 0.05$. The main effect model includes dependent variables of pregnancy

history (OR = 3.85), reproductive history (OR = 0.52), IUD in childbearing period (OR = 0.48), tubal ligation in childbearing period (OR = 1.74), contraceptives service time (OR = 0.99), contraceptive failure history (OR = 1.74), family planning operations history (OR = 1.73). The description was shown in Table 2.

DISCUSSION

This study lasted about 1 year and took full advantage of the Residents health electronic information system. We made

Table 1: The base items between three groups

Indicators	Group I, $n = 2253$	Group II, $n = 202$	Group III, $n = 289$	P^*
Age(years)$^\#$	58.16±5.84	57.50±6.93	62.83±9.12	0.00
Age of menopause (years)	47.03±1.32	46.71±1.53	46.86±1.51	0.00
BMI	23.63±2.99	23.53±3.68	23.60±3.56	0.91
Time of contraception (months)	260.42±73.29	146.26±100.65	204.96±121.63	0.00
Never given birth	114 (5.1)	26(12.9)	41(14.2)	0.00
Scarred uterus	143 (6.3)	28 (13.9)	20 (6.9)	0.00
Benign reproductive system conditions of female	267 (11.9)	59 (29.2)	68 (23.5)	0.00

*Kolmogorov-Smirnov test and Levene's test were used to detect the age; age of menopause; BMI, Time of contraception (m) between different group. And Chi-square test was used to detect the prevalence rate of benign reproductive system conditions in different groups; $^\#$Mean and SD was used express the age; age of menopause; BMI, Time of contraception. BMI (Body Mass Index) = Weight (kg)/Height (m)^2

Table 2: Nonconditional Logistic regression analysis in female benign reproductive system disease

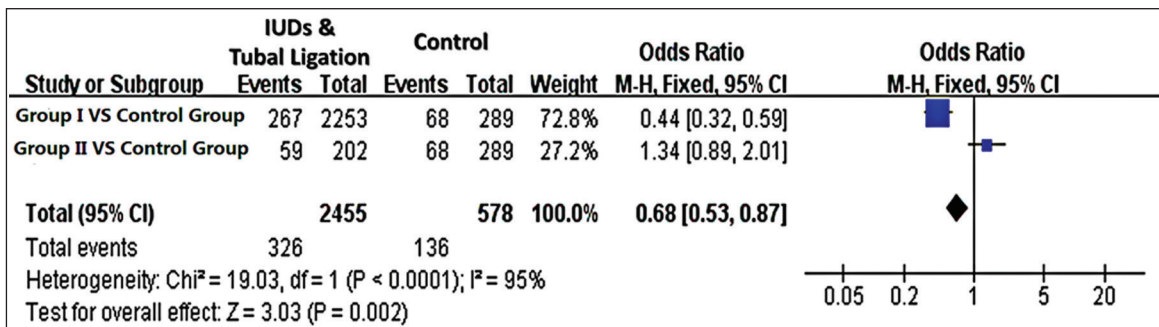| Covariate	β	Correction β	P	OR	95%CI
Gestation	1.35	0.46	0.00	3.85	1.57~9.38
Reproductive	−0.65	0.26	0.01	0.52	0.31~0.88
IUDs	−0.74	0.21	0.00	0.48	0.32~0.72
Tubal ligation	0.55	0.25	0.29	1.74	1.06~2.84
Using time of contraceptives	−0.02	0.00	0.01	0.99	0.97~1.00
Contraceptive failure	0.55	0.13	0.00	1.74	1.34~2.25
Family planning	0.32	0.45	0.01	1.73	1.57~1.94

Figure 1: Risk of the reproductive system diseases

the best of each basic medical unit in the area and collected the contraception and health condition of postmenopausal women. Despite comprehensive contraceptive availability, IUDs are an increasingly used long-acting reversible contraceptive method worldwide due to their superior effectiveness, low cost, safety, reliability, convenience, reversibility, and cultural acceptance.[9,10] Results of this study suggest that using IUDs can affect the reproductive system health in postmenopausal women. Compared with the rhythm method, IUDs can reduce the risk of suffering benign reproductive system conditions in postmenopausal women. In addition, birth control time, pregnancy/ reproductive history, contraceptive failure history, and family planning operation history may affect the women's health during the postmenopausal period as well. There were several papers reporting that the contraceptive failure history and family planning operation history can significantly increase the risk of getting benign reproductive conditions in postmenopausal females.[11-14]

The groups of this study was set according to the contraception, there were significant difference among three groups in age, menopause age, the and time of contraception. This result may be related to the family planning policy and the strict principle of screening condition. On the one hand, the family planning policy led to the women in group 1 to be younger than that in group 3, on the other hand, because of the strict principle in screening objective, the final number was only to the minimum. However, the multiple-factor analysis suggested that these three indexes above were not effective in women reproductive system benign diseases. In a word, they still had a good comparability.

Single factor analysis suggests that IUDs may reduce the risk of benign reproductive system conditions in postmenopausal women (by at least 50%) and tubal ligation may increase the risk, but the difference does not have statistical significance ($P > 0.05$). Consistent with the above results, multiple factors analysis additionally show that contraceptive failure and the resulting pregnancies can increase the risk of suffering from reproductive diseases as well. Felix *et al.* showed that using IUDs may affect endometrial cancer (EC) risk, they combined individual level data from four cohort and 14 case-control studies, in total 8,801 EC cases and 15,357 controls, compared with never use, reduced risk of EC was observed for inert IUDs [pooled-OR = 0.69, 95% confidence interval (CI) = 0.58-0.82].[15] Arnes M's research[16] suggested that Levonorgestrel-impregnated IUD maybe effective at reducing the occurrence of hyperplastic endometrial polyps. The same as Arnes M, Orbo A obtained the similar conclusion, his study showed that in the first trial of its kind, women treated with the levonorgestrel intrauterine system (LNG-IUS)

showed histologically normal endometrium after 6 months of therapy for endometrial hyperplasia.[17]

In addition to such conclusion, giving birth can reduce the risk of reproductive system conditions (OR = 0.31-0.88). The declining estrogen levels more than 1 year postmenopause typically lead to atrophy of the vagina, cervix and uterine body, and the cervix may become very stenotic.[5] In fact, contraceptive methods, contraceptive failures, pregnancy, and fertility are related to each other closely and the importance of contraceptive methods cannot be underestimated.

Future work will involve a larger sample survey and district coverage. Moreover, we will analyze more benign conditions and put more emphasis on malignancies.

CONCLUSION

IUDs, maybe, can effectively reduce the risk of getting benign reproductive conditions in postmenopausal females.

Conflicts of interest
There are no conflicts of interest.

AUTHOR'S CONTRIBUTION

Study concepts and Study design: HZh; XZh. Data acquisition and Data analysis/interpretation: XZh; LX. Statistical analysis: LCh. Manuscript writing and editing: XZh. Manuscript revision/review: XZh. Manuscript final version approval: HZh.

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