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Analysis on the Risk Factors for Ectopic Pregnancy in Intrauterine Device Users: A Case-Control Study

Jian Zhou[1], Yue-Hua Yang[1], Zhi-Ming Sun[1], Ying Li[2,*]

1 Jiangsu Institute of Planned Parenthood Research, Nanjing, Jiangsu, China;
2 School of Public Health, Nanjing Medical University, China.

*Corresponding author. Tel: +86-25-86576000; Fax: +86-25-86503625; E-mail: liying2008@qq.com

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Case Study

Abstract

Objective: To assess the influencing factors of ectopic pregnancy (EP) in intrauterine device (IUD) users for promoting the safe use of IUD.

Methods: 29 EP cases were collected and 1:1 matched controls in IUD users by case-control study.

Results: The data showed that pregnancies had significant association with EP, two pregnancies and three or more pregnancies were increased the risk of EP, adjusted odds ratio [AOR]=14.39, 95% CI: 2.37, 87.49 and AOR=14.87, 95% CI: 2.27, 97.38, respectively. The risk of EP in women of previous abdominal or pelvic surgery was also significantly increased (AOR=4.43, 95% CI: 1.04, 18.92). While no significant association have been seen with age, first or second time use IUD, periods of insertion, types of IUD, and copper surface area of IUD.

Conclusion: The results suggested that the number of pregnancies significantly increased the risk of EP; there was no significant association between the risk of EP and copper surface area and shape of IUD used. Therefore, it is beneficial to reduce the risk of EP by the prevention of unwilling pregnancy and induced abortion.

Keywords: Intrauterine device; Ectopic pregnancy; Case control study; Risk factors.

1. Introduction

As long-term contraceptive, IUD has become the most commonly used method in China [1]. The number of women using IUD in China accounted for about 70-80% of worldwide. IUDs can prevention and control of pregnancy. Meanwhile, they can inevitably cause health risks, such as EP in IUD users, which belong to serious adverse outcomes. That harms themselves are difficult to eliminate, need surgery to alleviate the damage, so the safety of IUD is especially important. In this study, a case-control study was designed to identify potential risk in order to reduce the incidence of EP, and to provide a reference for the safe use in IUD users.

2. Methods

This study was conducted at sentinel hospitals (county) of contraceptive adverse reaction surveillance in China. The study protocol was approved by Jiangsu Institute of Planned Parenthood Research. All subjects gave signed informed consent.

From Jan to Dec 2014, EP cases with IUD were enrolled as subjects in the case group (EP group) at sentinel hospitals. Women using IUD at the same sentinel hospital matched for age (± 3 years), time of inserting IUD (± 3 months), using IUD without any event were added to the control group.

The information of research was collected from all subjects (from interview and medical records) which included socio-demographic features, history of contraception, birth history, surgical history, history of pelvic inflammatory disease(PID), IUD product information, insertion period, individual biological characteristics, placing IUD operation information.

Data was entered into computers by two independent staff. Univariate logistic regression was analyzed to the difference of the risk factors between the two group, including the crude odds ratio (OR) and 95 % confidence interval (CI). A multivariable logistic regression analysis was used to adjust for confounders and calculate adjusted odds ratio (AOR). All statistical analysis was performed with SAS software, version 9.3 (SAS Institute, Inc., Cary, NC). Significance level was set at $P<0.05$.

3. Results

29 EP cases and 29 controls among IUD users were collected in this study. The diagnoses of EP were made on the basis of history, ultrasonography and level of β-human chorionic gonadotropin. The case included 12 left tubal pregnancies, 15 right tubal pregnancies, 2 cases of unknown. The average age of EP group was 29.86 ± 4.99 years, while the control group was 30.14 ± 4.82 years, two groups of age distribution could be compared without statistically significant. Meanwhile the difference between two groups was not statistically significant in occupation, education level, marital status, marriage age.

Factors	Case Group		Control Group		OR [95% CI]	AOR [95% CI]
Pregnancies						
1	2	6.90	15	51.72	Reference	Reference
2	13	44.83	7	24.14	13.93 [2.45, 79.21]	14.39 [2.37, 87.49]
≥ 3	14	48.28	7	24.14	15.00 [2.65, 84.78]	14.87 [2.27, 97.38]
Previous Pelvic Surgery						
No	19	65.52	26	89.66	Reference	Reference
Yes	10	34.48	3	10.34	4.56 [1.10, 18.86]	4.43 [1.04, 18.92]
Uterus Position						
Middle	8	27.59	8	28.57	Reference	Reference
Anteversion	17	58.62	12	42.86	0.71 [0.21, 2.41]	0.62 [0.15, 2.55]
Retroversion	4	13.79	8	28.57	0.35 [0.09, 1.45]	0.36 [0.08, 1.52]
First-Time User						
Yes	15	51.72	13	44.83	Reference	Reference
No	14	48.28	16	55.17	0.76 [0.27, 2.13]	0.59 [0.17, 1.99]
Period Insertion of IUD						
Menstrual Interval	25	86.21	24	82.76	Reference	Reference
After Induced Abortion	2	6.90	3	10.34	0.64 [0.10, 4.17]	0.69 [0.10, 4.88]
Suckling Period	2	6.90	2	6.90	0.96 [0.13, 7.37]	0.86 [0.10, 7.10]
Shapes of IUD						
Open Frames	17	58.62	17	58.62	Reference	Reference
Closed Frames	11	37.93	10	34.48	1.10 [0.37, 3.27]	1.17 [0.38, 3.61]
Fixed	1	3.45	2	6.90	0.50 [0.04, 6.05]	0.53 [0.04, 6.75]
Copper Surface Area of IUD						
<300 mm^2	24	82.76	24	82.76	Reference	Reference
≥ 300 mm^2	5	17.24	5	17.24	1.00 [0.26, 3.91]	0.93 [0.23, 3.74]

Table 1. Risk factors for EP in IUD users.

The results of the analysis were shown in Table 1. The data revealed that history of abdominal or pelvic surgery was associated with risk of EP (AOR=4.43, 95% CI: 1.04, 18.92). Two pregnancies and three or more pregnancies had a significant higher risk of EP (AOR=13.93, 95% CI: 2.45, 79.21; AOR=15.00, 95% CI: 2.65, 84.78) compared with pregnancy only once. However, there were no significant correlated between the risk of EP and factors including uterus position, first or second time use IUD, period insertion of IUD, shapes of IUD and copper surface area of IUD.

4. Discussion

EP is the leading cause of maternal mortality in the first trimester of pregnancy [2]. It has been accounted for about 1-2% of all naturally pregnancies [3]. In the past decades, the occurrence of EP has been on the rise in many countries [4,5].

IUD is widely used as a long-acting contraceptive in China, but whether to increase the risk of EP is still controversial. Some study found that past use of IUD can mildly increase the risk of EP [6,7]. The main reason may be pelvic infections, which could cause an ectopic implantation among past IUD users [8]. According to guideline of ACOG, IUD use does not increase the absolute risk of EP. But 'if pregnancy does occur with an IUD in place, the pregnancy is more likely to be ectopic' [9]. The EP incidences after using different IUD were different. In 1987, WHO pointed out that the highest incidence of EP was IUD release of progesterone, which may affect tubal peristalsis. While TCu380A and MLCu375 IUD with larger copper showed the lowest rate of EPs [10]. Skjeldestad found that copper IUD can prevent 91% EP; the results suggested that when Cu^{2+} concentration increased in the uterine cavity and fallopian tube, intrauterine pregnancy not only can be prevented, EP also can be prevented [11]. Our study suggests that there was no significant association between copper surface area, shape of IUD and the risk of EP.

In our study the risk of EP for women who conceived two or more pregnancies was 14 times fold than those who only pregnancy once and the association was statistically significant. Our results demonstrated that the risk of EP was positive correlated with pregnancies, which is similar to findings of two study [12,13]. Induced abortion is only a remedy for contraceptive failure, and it should not be used as a routine birth control method. But recently the times of induced abortion increased gradually especially in young unmarried women without childbearing demand. But whether induced abortion increase the risk of EP is still in arguments. Some study believed that induced abortion did not increase the risk of EP [12,14]. But other study showed that there was a positive correlation between the number of abortion and EP [15,16]. On the one hand, some researchers believed that induced abortion may lead to some complications such as endometrial lesion

and intrauterine adhesion, which may affect the implantation of fertilized egg in the uterus and reduce the pregnancy rate finally. And on the other hand, some researchers believed that EP was related not to abortion itself, but rather to intrauterine infection after abortion. Induced abortion may increase the risk of RTI and the risk was also increased with the number of induced abortion [17-19].

5. Conclusion

The study suggested that the number of pregnancies significantly increased the risk of EP; there was no significant association between the risk of EP and copper surface area or shape of IUD used. Therefore, it is beneficial to reduce the risk of EP by the prevention of unwilling pregnancy and abortions.

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