

ORIGINAL ARTICLE

<https://doi.org/10.61910/ricm.v8i1.437>

Comparison of the use of copper intra-uterine device between women with and without Pelvic Inflammatory Disease

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ABSTRACT

Introduction: Pelvic Inflammatory Disease (PID) is an infection of upper genital tract. Risk factors for this condition include: age ≤ 25 years, new or multiple sexual partners, early onset of sexual activity, history of sexually transmitted infections (STIs) or previous PID. The use of copper intrauterine device (IUD) still presents controversy in literature, as a risk factor for PID. **Objective:** The objective of the present study is to compare the use of copper IUD between people with PID and those without PID. **Methods:** A descriptive observational study was carried out, in which medical records of 30 patients were evaluated. The sample was 15 women with PID and 15 without, between 18 and 40 years old, who were treated at a university outpatient clinic in Belo Horizonte. The pairing was carried out considering the following variables: age, number of pregnancies/births/abortions, active sexual life, previous PID, use of condoms during sexual intercourse, previous history of STIs, previous/current use of oral contraceptives, injectables and another type of IUD other than copper, age at sexual intercourse and multiple sexual partners. **Results:** In the case group, 33.3% of patients have already used a copper IUD and none currently use it. In the control group, 13.3% have already used a copper IUD and 13.3% use it. There was no statistical difference between the previous or current use of IUD between the group with PID and the group without PID. **Conclusion:** No difference was observed between the use of IUD in women with or without PID.

Key words: Pelvic Inflammatory Disease; Copper Intrauterine Device; Risk Factors.

INTRODUCTION

Pelvic Inflammatory Disease (PID) is a mixed polymicrobial infection of the upper genital tract, mainly caused by *Chlamydia trachomatis*¹ and *Neisseria gonorrhoeae*, sexually transmitted agents². Despite not causing high mortality rates, this disease is responsible for generating significant morbidity in the lives of many women, due to its potential to compromise the endometrium, fallopian tubes, ovaries and pelvic peritoneum, resulting in ectopic pregnancy, infertility and chronic pelvic pain, with harmful repercussions on the quality of life of women in reproductive age³. As a result, such impairments also generate a major costly impact on the country's health system and economy³. In this perspective, understanding the details of this disease and its risk factors is essential to prevent it, especially since there are still no proven effective screening methods for the general population⁴.

Clinical diagnosis is the most important practical approach⁵. However, it tends to be difficult due to the broad clinical spectrum of the disease. The time course of PID presentation is typically acute, but a more indolent presentation may also occur over weeks to months. Most women are asymptomatic⁶, presenting only future complications, such as chronic pelvic pain and infertility. Patients with acute disease present lower abdominal or pelvic pain, tenderness in the pelvic organs and evidence of the genital tract inflammation. New onset of pain that worsens during sexual intercourse or with sudden movements may be the only symptom and onset of pain during or shortly after menstruation is particularly suggestive. In some women, the inflammatory process may extend into the liver capsule to cause perihepatitis (Fitz-Hugh Curtis syndrome)².

In Brazil, the commonly used diagnostic criteria, adopted by the Ministry of Health (MS), require the presence of three major criteria, along with either a minor criterion or an elaborate criterion, to establish a diagnosis. The major criteria encompass pain in the hypogastrium, pain upon palpation of the adnexa, and pain upon mobilization of the uterine cervix. Minor criteria include an axillary temperature over 37.5°C or a rectal temperature greater than 38.3°C, the presence of abnormal vaginal contents or endocervical secretion, the existence of a pelvic mass, more than five leukocytes per immersion field in endocervical material, leukocytosis in peripheral blood, elevated C-reactive protein or erythrocyte sedimentation rate (ESR), and laboratory evidence of cervical infection by gonococcus, chlamydia, or mycoplasmas. The criteria developed include histopathological evidence of endometritis, presence of tube-ovarian or Douglas cul-de-sac abscess on imaging study and laparoscopy with evidence of PID⁷. Although, considering the potential for serious complications if PID treatment is delayed or not given⁸, the presumptive diagnosis is sufficient to justify empirical antimicrobial therapy for PID⁵.

Risk factors for PID include age less than or equal to 25 years, new or multiple sexual partners, unprotected sex, sexual intercourse with a symptomatic partner, early onset of sexual activity (before age 15), history of sexually transmitted infections (STIs)⁴ or prior DIP. In addition to these, prolonged use⁹ of the copper Intrauterine Device (IUD) still presents controversies in the literature^{10,11}.

Although there is an understanding that there is an association between copper IUD and PID¹², yet small, related to genital tract manipulation during the IUD insertion procedure, evidence shows that this risk is limited to the first three weeks¹³ after IUD insertion: in an international study, the risk of PID was six times higher during the 20 days after insertion than in later periods; the risk was low and constant for up to eight years of follow-up¹⁴. In a cohort study, it was observed that, after six months, among patients without Chlamydia and Gonorrhea, 0,44% of those who used an IUD developed PID as opposed to the 0,10% corresponding to those who did not use an IUD ($p = 0,008$)¹⁵. It is observed that, although both studies present a correlation between the use of copper IUDs and PID, there are important divergences¹⁶ regarding this association and the risk posed by prolonged use of the intrauterine device, which makes further studies on this topic necessary^{9,17}.

Considering these discrepancies, the aim of this study is to compare the utilization of copper IUDs among women with pelvic inflammatory disease (PID) and those without PID.

METHODS

Study design

A descriptive observational study was carried out, based on analysis of digitized medical records. This study was approved by the Research Ethics Committee (REC) (CAAE: 49582121.30000.5134). The study was perfor-

med at a university outpatient clinic in Belo Horizonte (MG), and the medical records of women who were treated in the first six months of 2021 were analyzed.

Sample

This study was conducted in a single outpatient clinic with women diagnosed with PID, which is a disease with low prevalence. Consequently, the sample size was determined without performing a sample calculation, and a total of 30 women were predetermined.

Considering that PID is uncommon in older women, the age group chosen to be the target of this study was between 18 and 40 years old. Furthermore, since being sexually active is an almost mandatory condition for a patient to have PID, as the ascending route is the primary mode of acquiring the disease, only women who had initiated sexual activity were included. Therefore, the research sample comprised 30 sexually active women, ranging in age from 18 to 40 years.

Procedures

The electronic medical records of all patients treated in the first six months of 2021 were evaluated by two researchers. After applying the eligibility criteria, 15 women were selected to form the “case” group (patients with PID) and 15 women to form the “control” group (patients without PID). To determine the case group and the control group, when it was not specifically described in the medical record, patients with PID were considered to be those who had three major criteria plus one minor criterion or one elaborate criterion, according to the table found in the *Protocolo Clínico e Diretrizes Terapêuticas para Atenção Integral às Pessoas com Infecções Sexualmente Transmissíveis do MS*⁷, in order to avoid deviations in the determination of exposure.

Then, the patients in the case group and the control group were paired, according to the following categorical and quantitative variables: age, number of preg-

nancies/births/ abortions, active sexual life, previous PID, use of condoms during sexual intercourse, previous history of STIs, previous/current use of oral contraceptives, injectables and other types of IUDs other than copper, age at sexual intercourse and multiple sexual partners. The goal of these variables being paired was to ensure greater homogeneity between the groups, leaving only the use of the copper IUD unpaired, so that a more reliable analysis could be carried out, avoiding confusion bias.

It is worth noting that the variables age, number of pregnancies/births/abortions, active sexual life, previous PID, use of condoms during sexual intercourse, previous history of STIs, age at sexual intercourse and multiple sexual partners were determined because they are known risk factors to PID, which could interfere with the analysis. For instance, if pairing had not been performed, we would not know whether PID occurred due to the use of a copper IUD or the presence of multiple sexual partners.

Likewise, it was necessary to pair protective factors. Hormonal contraceptive methods (oral/injectable contraceptives and Mirena IUDs) are known to thicken cervical mucus, being possible protective factors against STIs⁹. Therefore, the previous/current use of oral contraceptives, injectables and other types of IUDs other than copper were also considered variables to be paired, since we would not know if the woman did not acquire PID because she was using a protective factor or whether not using a copper IUD contributes to this outcome.

Statistical analysis

Categorical variables were presented as absolute and relative frequencies and numerical variables as median and interquartile range (IQR). To evaluate possible differences in the distribution of categorical variables, Pearson's Chi-square test was used. Numerical variables were compared using the Wilcoxon test (W). A

significance level of 5% was used and the data were analyzed using the R software version 4.0.3.

RESULTS

Thirty participants were evaluated, of whom 15 (50%) had PID. The gynecological characteristics are presented in Table 1. The average age of the patients included in the study was 31.2 years (standard deviation = 5.3 years). Among the women selected, 76.7% did not have multiple partners. Of the 15 patients with PID, only 2 (6.7%) had a previous history of PID. Regarding the number of pregnancies, 20.0% of patients were nulliparous, while 50.0% had two pregnancies, and 16.7% had one pregnancy. Concerning condom use, 30% of participants reported using it, while 40% did not. The average age at first sexual intercourse was 17.1 years (standard deviation = 2.9 years). Half of the patients had no previous history of STIs, while 30.0% did, and in 20.0% of cases, it was not reported in the medical record.

Between the participants, only 23,3% said they had already used the copper IUD before the time of the research. Around 93,0% of the group analyzed were not using this IUD at the time of data collection, while 6,7% were. Moreover, none of the included patients currently use or have ever used an IUD other than copper. Regarding other contraceptive methods, 80.0% have previously used oral or injectable contraceptives, and 63.3% have discontinued their use.

The table 2 presents the comparison of variables with the presence of PID. In the present study, patients in the case and control groups had a similar average age of 31 years ($p=0,863$). This occurred in the same way in relation to the number of pregnancies, with a median of two pregnancies per woman ($p = 0,065$). The age at sexual debut (sexarche) was also similar, with a median of 18.5 years in the case group and 17.0 years in the control group ($p > 0.999$). Regarding

the presence of multiple partners, 26.7% of the control group reported having multiple partners, while 86.7% of the case group denied having multiple partners ($p = 0.135$).

Between the case patients, 13,3% had a previous history of PID and 33,3% had a history of a previous STI, while none of the control group had a previous PID ($p = 0,232$) and 26,7% had a previous STI ($p > 0,999$). The use of condoms was reported by 40% of the control patients, while 26,7% of the case group stated that they did not use them ($p= 0,345$).

As shown in table 2, in the case group, 33,3% of patients have already used a copper IUD and none currently use this device. In the control group, 13,3% have already used a copper IUD ($p = 0,397$) and 13,3% use it ($p = 0,503$). Regarding the use of other contraceptive methods, 80,0% of both groups stated that they had already used it and, currently, 60% of the control group and 66,7% of the case group denied using it ($p > 0,999$).

It is noteworthy that in all categorical and quantitative variables the p-value was greater than 0,05, which means that there was no significant difference between the case group and the control group.

Table 1 – Descriptive analysis of quantitative and categorical variables that were paired

Variable	n = 30
Age in Years, median (IQR)	31,0 (27,0 – 35,8)
Pregnancies, n (%)	2,0 (1,0 – 2,0)
0	6 (20,0)
1	5 (16,7)
2	15 (50,0)
3	3 (10,0)
4	0 (0,0)
5	1 (3,3)
Births, n (%)	2,0 (1,0 – 2,0)
0	7 (23,3)
1	7 (23,3)
2	14 (46,7)
3	2 (6,7)
Abortions, n (%)	0,0 (0,0 – 0,0)
0	24 (80,0)
1	5 (16,7)
2	0 (0,0)
3	0 (0,0)
Multiple sexual partners, n (%)	
Yes	4 (13,3)
No	23 (76,7)
Uninformed	3 (10,0)
Previous history of PID, n (%)	
Yes	2 (6,7)
No	26 (86,7)
Uninformed	2 (6,7)
Current diagnosis of PID, n (%)	
Yes	15 (50,0)
No	15 (50,0)
Report of condom use, n (%)	
Yes	9 (30,0)
No	9 (30,0)
Uninformed	12 (40,0)
Previous history of STI, n (%)	
Yes	9 (30,0)
No	15 (50,0)
Uninformed	6 (20,0)

History of previous copper IUD use, n (%)

Yes	7 (23,3)
No	22 (73,3)
Uninformed	1 (3,3)

Current copper IUD use, n (%)

Yes	2 (6,7)
No	28 (93,3)

Previous use of another IUD other than copper, n (%)

Yes	0 (0,0)
No	30 (100,0)

Current use of an IUD other than copper, n (%)

Yes	0 (0,0)
No	30 (100,0)

Previous use of oral or injectable contraceptives, n (%)

Yes	24 (80,0)
No	3 (10,0)
Uninformed	3 (10,0)

Current use of oral or injectable contraceptives, n (%)

Yes	11 (36,7)
No	19 (63,3)

IQR: IQR: interquartile range; n: sample number; PID: Pelvic Inflammatory Disease; STI: Sexually Transmitted Infection; IUD: Intrauterine Device.

Table 2- Comparison of quantitative and categorical variables with the presence of PID

Variable	Do you have PID?		p- value ^w
	Yes (n=15)	No (n=15)	
Age in years, median (IQR)	33,0 (28,5 – 35,0)	31,0 (26,5 – 36,5)	0,863
Pregnancies, n (%)	2,0 (1,5 – 2,0)	2,0 (0,5 – 2,0)	0,065
Births, n (%)	2,0 (1,0 – 2,0)	1,0 (0,0 – 2,0)	0,429
Abortions, n (%)	0,0 (0,0 – 0,5)	0,0 (0,0 – 0,0)	0,345
Sexarche (n=16), n (%)	18,5 (15,2 – 20,0)	17,0 (15,8 – 19,0)	>0,999
History of previous copper IUD use, n (%)			
Yes	5 (33,3)	2 (13,3)	
No			
Uninformed			
Multiple sexual partners, n (%)			0,135
Yes	0 (0,0)	4 (26,7)	
No	13 (86,7)	10 (66,7)	
Uninformed	2 (13,3)	1 (6,7)	
Previous history of PID, n (%)			0,232
Yes	2 (13,3)	0 (0,0)	
No	13 (86,7)	13 (86,7)	
Uninformed	0 (0,0)	2 (13,3)	
Report of condom use, n (%)			0,345
Yes	3 (20,0)	6 (40,0)	
No	4 (26,7)	5 (33,3)	
Uninformed	8 (53,3)	4 (26,7)	
Previous history of STI, n (%)			>0,999
Yes	5 (33,3)	4 (26,7)	
No	7 (46,7)	8 (53,3)	
Uninformed	3 (20,0)	3 (20,0)	
Previous use of oral or injectable contraceptives, n (%)			>0,999
Yes	12 (80,0)	12 (80,0)	
No	1 (6,7)	2 (13,3)	
Uninformed	2 (13,3)	1 (6,7)	

Current use of oral or injectable contraceptive, n (%)			>0,999
Yes	5 (33,3)	6 (40,0)	
No	10 (66,7)	9 (60,0)	
History of previous copper IUD use, n (%)			0,397
Yes	5 (33,3)	2 (13,3)	
No	10 (66,7)	12 (80,0)	
Uninformed	0 (0,0)	1 (6,7)	
Current use of copper IUD, n (%)			0,503
Yes	0 (0,0)	2 (13,3)	
No	15 (100,0)	13 (86,7)	

^w Wilcoxon test; IQR: interquartile range; n: sample number; PID: Pelvic Inflammatory Disease; STI: Sexually Transmitted Infection; ^a Pearson's Chi-square test; n: sample number; PID: Pelvic Inflammatory Disease; IUD: Intrauterine Device.

DISCUSSION

Based on the data collected in the present study, it is possible to compare the use of copper IUD between women with and without PID. Among women with PID, 33,3% of them have already used a copper IUD and none currently use this device. Among women without PID, 13.3% have previously used a copper IUD, and 13.3% currently use it. Therefore, it is evident that there is a higher prevalence of previous copper IUD use among women with PID. However, there was no statistically significant difference between the groups, suggesting that the copper IUD alone is not a contributing factor to PID.

This result may contribute to future more robust research that studies the relationship between the use of copper IUDs and PID in the long term¹⁸. This is because, despite various studies have been carried out to try to understand whether there is any direct association between the use of the copper IUD and PID¹⁹, no clear conclusion was stipulated, because of the limitations of this research¹⁵.

Among the limitations of performing this type of study, firstly, the difficulty in diagnosing PID by professionals stands out¹⁷. Although there are Ministry of Health criteria for diagnosis, it is a disease that can be asymptomatic and manifest its complications late or even be confused with other illnesses, making the prevalence is underestimated and, in studies, it is difficult to identify patients with a less advanced clinical condition¹⁵.

Another significant limitation that hinders the direct analysis of IUD use as a risk factor for PID is the presence of various confounding factors. These factors include the use of hormonal contraceptive methods, which can thicken cervical mucus and make it more challenging to acquire sexually transmitted infections (STIs), as well as other risk factors for PID (age up to 25 years, new or multiple sexual partners, unprotected sex, sexual intercourse with a symptomatic partner, early onset of sexual activity, history of sexually transmitted infections or previous PID)²⁰. With this issue in mind, our study aimed to balance the sample by ensuring that the case and control patients were a similar as possible in all aspects, except for the presence of PID and the use of copper IUD.

Our results showed that the pairing was performed properly and that the methodology was correctly used, considering that in all these variables the p-value was greater than 0,05, which means that there was no significant difference between the case group and the control group. Considering that the pairing was successful, it is possible to analyze the use of copper IUDs specifically, since both groups were aligned in relation to other possible causes of PID.

CONCLUSION

No difference was observed in the use of the IUD between women with and without PID. Thus, the copper IUD does not appear to be an isolated contributing factor to PID. This conclusion is drawn from the absence of differences in the use of the copper IUD between the groups after accounting for confounding factors. However, further studies with larger sample sizes and multivariate analysis are necessary to confirm this finding.

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FINANCIAL SUPPORT: SCIENTIFIC INITIATION SCHOLARSHIP PROGRAM (PROBIC) FROM THE FACULTY OF MEDICAL SCIENCES OF MINAS GERAIS (FCMMG).

THE AUTHORS DECLARE THAT THERE IS NO CONFLICT OF INTERESTS IN RELATION TO THIS ARTICLE.