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Original Article

# Prevalence of Infections After In-Office Hysteroscopy in Premenopausal and Postmenopausal Women

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**ABSTRACT** **Study Objective:** To estimate the incidence of infection after diagnostic and operative hysteroscopic procedures performed in an in-office setting with different distension media (saline solution or $CO_2$).

**Design:** Prospective, multicenter, observational study (Canadian Task Force classification II-2).

**Setting:** Tertiary women's health centers.

**Patients:** A total of 42,934 women who underwent hysteroscopy between 2015 and 2017.

**Interventions:** Of the 42,934 patients evaluated, 34,248 underwent a diagnostic intervention and 8686 underwent an operative intervention; 17,973 procedures used $CO_2$ and 24,961 used saline solution as a distension medium. Patients were contacted after the procedure to record postprocedure symptoms suggestive of infection, including 2 or more of the following signs occurring within the 3 weeks after hysteroscopy: fever; lower abdominal pain; uterine, adnexal, or cervical motion tenderness; purulent leukorrhea; vaginal discharge or itchiness; and dysuria. Vaginal culture, clinical evaluation, transvaginal ultrasound, and histological evaluation were completed to evaluate symptoms.

**Measurements and Main Results:** Operative hysteroscopies comprised polypectomies (n = 7125; 82.0%), metroplasty (n = 731; 15.0%), myomectomy (n = 378; 7.8%), and tubal sterilization (n = 194; 4.0%). Twenty-five of the 42,934 patients (0.06%) exhibited symptoms of infection, including 24 patients (96%) with fever, 11 (45.8%) with fever as a single symptom, 7 (29.2%) with fever with pelvic pain, and 10 (41.7%) with fever with dysuria. In 5 patients with fever and pelvic pain, clinical examination and transvaginal ultrasound revealed monolateral or bilateral tubo-ovarian abscess. In these patients, histological examination from surgical specimens revealed the presence of endometriotic lesions.

**Conclusion:** The present study suggests that routine antibiotic prophylaxis is not necessary before hysteroscopy because the prevalence of infections following in-office hysteroscopy is low (0.06%). Journal of Minimally Invasive Gynecology (2019) 26, 733−739. © 2018 AAGL. All rights reserved.

*Keywords:* Antibiotics; Endometrioma; Endometriosis; Hysteroscopy; Infection; Tubo-ovarian abscess

The authors declare that they have no conflicts of interest.

**Precis** The low incidence of infections after diagnostic or operative in-office hysteroscopic procedures suggests that routine administration of prophylactic antibiotics might not be necessary.

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Office hysteroscopy is a well-established technique in gynecologic practice enabling direct visualization of the uterine cavity, allowing for the diagnosis, evaluation, and treatment of various uterine, cervical, and vaginal pathologies in an ambulatory setting with reduced patient discomfort and pain [1−4]. This approach is often beneficial in combining diagnosis and treatment for a particular pathology [1−4].

Whether antibiotic prophylaxis during hysteroscopic procedures should be administered remains unclear, given concerns about the vagina as an area of the body with normal abundant bacterial flora and because the transcervical route may increase the risk of infection [5−9]. Nevertheless, the use of liquid distension fluid that may allow bacteria absorption through the traumatized endometrial surface, together with the potential transfer of vaginal and cervical flora into the uterine cavity by repeated hysteroscope movements (insertion and removal) throughout the cervix, increases the potential for postprocedure infection of the endometrial cavity.

We performed this prospective, multicenter, observational study to evaluate the incidence of infection after both diagnostic and operative hysteroscopic procedures performed in an in-office setting with different distension media.

## Materials and Methods

This study was conducted between November 5, 2015, and October 24, 2017, in the hysteroscopy units of tertiary centers for women's health in Italy (2 different institutions in Bologna and Rome, Foggia, Naples, Palermo, Pistoia, Trento, Negrar). For the study, which was approved by the applicable Institutional Review Boards, premenopausal and postmenopausal women were consecutively recruited to undergo in-office hysteroscopy. All enrolled patients provided informed consent.

Patients were enrolled for diagnostic hysteroscopy with or without targeted endometrial biopsy using saline solution or $CO_2$ as a distension medium, or for operative hysteroscopy for previously diagnosed intrauterine lesions. Patients with clinical signs of infectious disease of the lower genital tract detected before hysteroscopy were not included. Patients with symptoms of infection before hysteroscopy were treated on an outpatient basis with antibiotic therapy and were excluded from the study. Other exclusion criteria were (1) gonadotropin-releasing hormone analogs or other steroid and hormonal therapies (including an intrauterine device) in the previous 8 weeks; (2) cardiovascular, hepatic or renal impairment, or any coexisting disease that would require antibiotic therapy during the study; (3) any condition that would contraindicate the in-office approach (eg, lesion size, intramural development of the pathology); (4) pregnancy, lactation, or abortion in the previous 4 months; (5) known or suspected malignant or premalignant disease; and (6) use of antibiotic therapy during the previous 60 days. Patients with a history of chronic pelvic pain (with no symptoms of infection), anxiety, or evidence of vaginismus were not excluded.

### *Office Diagnostic Hysteroscopy*

All hysteroscopies were performed without the use of single-tooth tenaculum forceps for grasping the cervix, preoperative vaginal antiseptic, or local or general anesthesia. When $CO_2$ was used as the distension medium, a forward-oblique 30° telescope was used (4 mm in diameter, 30 cm long, covered with a single-flow examination sheath of 5.1-mm diameter; Hamou II HysteroMat; Karl Storz, Tüttlingen, Germany), along with a $CO_2$ insufflator (Hamou Hysteroflator; Karl Storz). When saline solution was used as the distension medium, a forward-oblique 30° telescope was used (2.9 mm diameter, 30 cm long; Karl Storz) with a 5.1-mm-diameter continuous-flow sheath (Bettocchi; Karl Storz). Intrauterine pressure was maintained with an electronic system of irrigation and aspiration (Endomat; Karl Storz) and by setting the flow rate at 220 to 350 mmHg, the negative pressure suction at 0.2 bars, and the pressure of irrigation at 100 mmHg. The flow was 80 mL/minute as described previously [10].

When endometrial sampling was indicated, biopsy samples were obtained with a 5-Fr grasper (Karl Storz) when saline solution was the distension medium or with a Mazzon forceps inserted in the single-flow sheath after telescope removal (3 mm diameter, 30 cm long, 1 cm spread; Karl Storz) when $CO_2$ was the distension medium. The telescope was then reinserted into the sheath to verify the accuracy of the biopsy.

### *Office Operative Hysteroscopy*

Office operative hysteroscopy was performed using a 5-mm-diameter continuous-flow hysteroscope with oval profile, a 30° fore-oblique telescope, and a 5-Fr operating channel (Bettocchi Office Continuous-Flow Operative Hysteroscope size 4; Karl Storz). Neither analgesic nor anesthetic drugs were administered for the operative procedures, and the use of a speculum, single-tooth tenaculum forceps for grasping the cervix, and preoperative vaginal antiseptic was avoided. For operative procedures, saline solution (sodium chloride 0.9%) was used as a distension medium, provided through an electronic system of irrigation and aspiration (Endomat; Karl Storz). A stable intrauter'ine pressure was maintained using a flow rate of 220 to 350 mmHg, a negative pressure suction of 0.2 bars, and a pressure of irrigation of 100 mmHg. After panoramic visualization of the uterine cavity, the operative procedures were performed with standard techniques using 5-Fr grasping forceps and scissors (Karl Storz) and bipolar electrodes (Versapoint bipolar Twizzle electrode; Ethicon, Somerville, NJ). Operative time was recorded from the introduction to the extraction of the scope.

Polypectomy of endometrial polyps $\leq 0.5$ cm was performed with 5-Fr grasping forceps and scissors, using a standardized technique as described previously [11]. The procedure was repeated until the polyp was completely detached. Polyps $>0.5$ cm were removed by bending the bipolar electrode. Smaller polyps were sliced from the free edge to the base into 2 or 3 fragments to allow for removal through the uterine cavity using 5-Fr grasping forceps with teeth. To remove the entire base of the polyp without

penetrating too deeply into the myometrium, in some cases the bipolar electrode was bent 25° to 30°, sufficient to obtain a kind of hook electrode [11].

For metroplasty, septum resection was performed starting in the middle portion with the bipolar electrode and refining the base with scissors respecting the 3 diagnostic hysteroscopic criteria established previously [12]. For hysteroscopic removal of grade 0 myomas, a technique similar to polypectomy was applied for submucosal myomas, with the difference that owing to their higher tissue density, they were first divided into 2 half-spheres and then each sliced as described previously [13] using the bipolar electrode [14].

Intrauterine adhesiolysis was performed on intrauterine adhesions, and those that were focal and thin were easily divided in the middle with sharp hysteroscopic scissors [15]. The bipolar electrode was used for both diffuse and firm adhesions.

Hysteroscopic tubal sterilization was performed by placing the ESSURE insert metal coils (Conceptus, San Carlos, CA) during the proliferative phase of the menstrual cycle without anesthesia, as described previously [16]. In brief, after visualization of the proximal tubal ostia, the surgeon placed the insert in the intramural part of the tube. Optimal placement was achieved when the black stop ring of the insert wire reached the uterine tubal ostia, at which point the wire was removed.

### *Study Endpoint*

Our primary endpoint was the incidence of infection, if 2 or more of the following symptoms were found within the 3 weeks after the in-office diagnostic or operative hysteroscopy: fever (body temperature >38°C or 100.4°F at repeated measurements over a period of ≥48 hours); lower abdominal pain; uterine, adnexal, or cervical motion tenderness; purulent leukorrhea; vaginal discharge or itchiness; and dysuria. These criteria were chosen because they are general signs of infection, and because there is no international consensus on the definition of posthysteroscopy infection [17].

After each procedure, patients were instructed to contact the medical team regarding symptoms suggestive of infection and to record their temperature twice a day for 48 hours after the procedure. Patients were scheduled to return at 4 weeks after the hysteroscopic procedure for follow-up gynecologic examination to discuss postprocedural complications. The duration of the surgical procedure, intraoperative and postoperative complications, and associated side effects were recorded.

### *Statistical Analysis*

All data were analyzed with Prism software (GraphPad Software, La Jolla, CA) and recorded as mean ± standard deviation (range) or as number (%) of patients. The Kolmogorov-Smirnov test was used to evaluate whether values had a Gaussian distribution, to choose between parametric and nonparametric statistical tests. The $\chi^2$ test and independent $t$ test were used to compare proportions and standard deviations, respectively, between groups. Statistical significance was set at $p < .05$.

## Results

Tables 1 to 3 present clinical findings following diagnostic and operative procedures performed by the same surgeon in each center. A total of 42,934 hysteroscopic procedures were evaluated, performed in 26,532 premenopausal patients (61.8%) and 16,402 postmenopausal patients (38.2%). $CO_2$ was used as the distension medium in 17,973 diagnostic procedures (41.9%), all of which were performed as in-office procedures in premenopausal (n = 11,388; 63.4%) and postmenopausal (n = 6585; 36.6%) patients. In contrast, saline solution (n = 24,961) was used in both diagnostic (n = 16,275; 65.2%) and operative (n = 8686; 34.8%) procedures. Use of a vaginoscopic approach was significantly lower and use of a speculum was significantly higher ($p < .001$ for both) when hysteroscopies were performed using $CO_2$ rather than saline solution as the distension medium, in both premenopausal (Table 1) and postmenopausal (Table 2) patients. In diagnostic hysteroscopies, the use of $CO_2$ or saline solution was not associated with differences in terms of procedure duration, independent of the patients' menopausal status (Tables 1 and 2).

Table 3 presents data on operative hysteroscopic procedures. Operative procedures were performed in 8686 patients (premenopausal, n = 4857; postmenopausal, n = 3829). Polypectomy was the most frequently performed operative procedure (n = 7125; 82.0%), in 3729 of 3829 postmenopausal patients (97.3%) and in 3399 of 4857

**Table 1**

Characteristics of premenopausal patients who underwent diagnostic hysteroscopy according to distension medium

| Characteristic | $CO_2$ group (n = 11,388) | Saline solution group (n = 10,287) |
|---|---|---|
| Age, yr, mean ± SD | 40.3 ± 3.9 | 39.6 ± 4.9 |
| Body mass index, kg/m$^2$, mean ± SD | 25.8 ± 2.3 | 26.6 ± 3.5 |
| Parity, n, mean ± SD | 1.6 ± 0.2 | 1.5 ± 0.3 |
| Proliferative phase, n (%) | 9907 (87.0) | 8961 (87.1) |
| Secretory phase, n (%) | 1481 (13.0) | 1326 (12.9) |
| Vaginoscopy, n (%)* | 2722 (23.9) | 10,287 (100) |
| Speculum, n (%)* | 8666 (76.1) | 0 |
| Biopsies, n (%) | 294 (2.6) | 319 (3.1) |
| Duration of procedure, min, mean ± SD | 1.85 ± 2.7 | 1.7 ± 3.8 |

*$p < .001$.

**Table 2**

Characteristics of postmenopausal patients who underwent diagnostic hysteroscopy according to distension medium

| Characteristic | $CO_2$group (n = 6585) | Saline solution group (n = 5988) |
|---|---|---|
| Age, yr, mean ± SD | 59.4 ± 2.9 | 60.3 ± 4.8 |
| Body mass index, kg/m$^2$, mean ± SD | 27.9 ± 4.2 | 28.6 ± 5.3 |
| Parity, n, mean ± SD | 1.6 ± 0.3 | 1.5 ± 0.3 |
| Vaginoscopy, n (%)* | 1333 (20.2) | 5988 (100) |
| Speculum, n (%)* | 5252 (79.8) | 0 |
| Biopsies, n (%) | 1750 (26.6) | 1862 (31.1) |
| Procedure duration, min, mean ± SD | 2.14 ± 1.6 | 2.2 ± 2.8 |

*p < .001.

premenopausal patients (70.0%). In contrast, metroplasty (731 of 4857; 15.0%), myomectomy (378 of 4857; 7.8%), and tubal sterilization (194 of 4857; 4.0%) were typically performed only in premenopausal patients. With respect to the duration of procedures, no significant differences in polypectomy and synechiolysis procedures were noted between premenopausal and postmenopausal patients.

All patients returned for the scheduled follow-up gynecologic examination. Table 4 presents the clinical findings of the 25 patients (0.06%) with complaints suggesting infection. Infectious symptoms were present in 7 of the 17,973 patients who underwent procedures performed with $CO_2$ and in 18 of the 24,961 patients in whom saline solution was used in diagnostic and operative procedures (p = .15). No cases of perforation occurred during diagnostic or operative hysteroscopy.

**Table 3**

Characteristics of premenopausal and postmenopausal patients who underwent operative hysteroscopy

| Characteristic | Premenopausal (n = 4857) | Postmenopausal (n = 3829) |
|---|---|---|
| Age, yr, mean ± SD* | 41.7 ± 4.3 | 58.2 ± 5.1 |
| Body mass index, kg/m$^2$, smean ± SD | 24.8 ± 2.7 | 26.6 ± 4.5 |
| Parity, n, mean ± SD | 1.4 ± 0.2 | 1.5 ± 0.3 |
| Operative procedures, n (%) | | |
| Polypectomy* | 3399 (70.0) | 3729 (97.3) |
| Synechiolysis | 155 (3.2) | 103 (2.7) |
| Metroplasty* | 731 (15.0) | 0 |
| Myomectomy* | 378 (7.8) | 0 |
| Tubal sterilization* | 194 (4.0) | 0 |
| Duration of procedure, min, mean ± SD | | |
| Polypectomy | 6.4 ± 2.7 | 6.6 ± 2.6 |
| Synechiolysis | 7.3 ± 5.2 | 6.2 ± 6.3 |
| Metroplasty | 6.2 ± 2.7 | — |
| Myomectomy | 15.6 ± 5.8 | — |
| Tubal sterilization | 5.4 ± 4.3 | — |
| Vaginoscopy, n (%) | 4857 (100) | 3829 (100) |

*p < .001.

Fever occurred in 24 of the 25 patients (96%), including fever alone in 11 (45.8%), fever with pelvic pain in 7 (29.2%), and fever with dysuria in 10 (41.7%) (Table 4). The duration of hysteroscopy was the same for patients with infection and those without infection, with the exception of 2 patients following hysteroscopic synechiolysis (patients 14 and 15, who experienced fever) and 2 patients who underwent myomectomy (patients 24 and 25, who also experienced fever), in whom the duration was longer (Table 4). In the majority of patients (20 of 25; 80.0%), clinical examination and transvaginal ultrasound failed to reveal pelvic disease, and thus the fever that occurred at an average of 24.9 ± 3.09 hours after hysteroscopy was the sole complication noted. In these patients, the administration of amoxicillin-clavulanate potassium (825 mg; Augmentin, GlaxoSmithKline, Verona, Italy) or ciprofloxacin chlorhydrate (500 mg; Ciproxin, Bayer, Milan, Italy) resolved fever after a mean of 33.1 ± 8.5 hours.

Five of the 25 patients (20.0%) presented with pelvic pain and fever of 39°C, suggestive of pelvic inflammatory disease (PID), at 2 days (patient 1), 4 days (patients 2 and 3), and 3 days (patients 4 and 11) days after hysteroscopy. The mean white blood cell count was 15,820 ± 2094 cells/$\mu$L, and the mean C-reactive protein level was 12.2 ± 5.17 mg/dL. These patients had no history of previous PID; however, all 5 patients (100%) had severe endometriosis. Patient 1 was affected by adenomyosis and experienced primary infertility for 3.5 years and bilateral endometrioma (6 cm in the right ovary and 5 cm in the left ovary). Patient 2 underwent repeated surgeries for severe endometriosis (with a 5-cm left endometrioma and a 4-cm rectovaginal endometriotic node), along with a combined laparoscopic segmental bowel resection. Patient 3 had bilateral endometriomas (5 cm in the right ovary and 4 cm in the left ovary), and patient 4 had a right endometrioma (5 cm) and right tubal obstruction (as revealed by hysterosalpingography). Patient 11 had a 3-year history of primary infertility with 3 intracytoplasmic sperm injections and had a left endometrioma (6 cm).

Clinical examination and transvaginal ultrasound revealed a monolateral or bilateral tubo-ovarian abscess in all 5 patients, who subsequently underwent laparoscopy and monolateral or bilateral salpingectomy (Table 4). Vaginal cultures were performed in all cases. Patients who experienced fever with or without dysuria had negative results, whereas bacteria was identified in the 5 patients who experienced monolateral or bilateral tubo-ovarian abscess (*Bacteroides fragilis* in 1 patient, *Escherichia coli* in 2 patients, and *Staphylococcus aureus* in 2 patients).

Histological examination confirmed the presence of endometriotic lesions from surgical specimens and tubo-ovarian abscess, with distal and fimbriae occlusion of the

**Table 4**

Characteristics of the 25 patients with symptoms of infection

| Patient | Age, yr | BMI, kg/m$^2$ | Clinical findings | Type of hysteroscopy | Distension medium | Duration of hysteroscopy, min | Symptoms | Infectious complications |
|---|---|---|---|---|---|---|---|---|
| 1 | 38 | 22.0 | Infertility, bilateral endometrioma, adenomyosis | Diagnostic | Saline solution | 3 | Pelvic pain | Bilateral tubo-ovarian abscess |
| 2 | 35 | 25.0 | Repeated surgeries for severe endometriosis, intestinal resection | Diagnostic | Saline solution | 2 | Fever, pelvic pain | Left tubo-ovarian abscess |
| 3 | 37 | 25 | Infertility, bilateral endometrioma | Diagnostic | Saline solution | 2 | Fever, pelvic pain | Left tubo-ovarian abscess |
| 4 | 36 | 23 | Right endometrioma | Diagnostic | Saline solution | 1.5 | Fever, pelvic pain | Right tubo-ovarian abscess |
| 5 | 37 | 31.5 | Infertility | Diagnostic | Saline solution | 2 | Fever, pelvic pain | Fever |
| 6 | 45 | 20.1 | Spotting | Diagnostic | Saline solution | 1.5 | Fever | Fever |
| 7 | 57 | 19.8 | Tamoxifen therapy | Diagnostic | Carbon dioxide | 2 | Fever, dysuria | Fever |
| 8 | 36 | 24 | Infertility | Diagnostic | Carbon dioxide | 2 | Fever | Fever |
| 9 | 75 | 28 | Increased endometrial thickness | Diagnostic | Carbon dioxide | 1.5 | Fever, dysuria | Fever |
| 10 | 48 | 28.4 | Tamoxifen therapy | Diagnostic | Carbon dioxide | 1.5 | Fever, dysuria | Fever |
| 11 | 37 | 31.5 | Infertility, 3 ICSI, left endometrioma | Diagnostic | Carbon dioxide | 2 | Fever, pelvic pain | Left tubo-ovarian abscess |
| 12 | 41 | 21 | Resectoscopic myomectomy | Diagnostic | Carbon dioxide | 1.5 | Fever | Fever |
| 13 | 46 | 24.4 | Tamoxifen therapy | Diagnostic | Carbon dioxide | 1.5 | Fever | Fever |
| 14 | 29 | 21.1 | Repeated postpartum curettage | Synechiolysis | Saline solution | 12 | Fever, pelvic pain | Fever |
| 15 | 72 | 26.2 | Uterine cavity distension | Synechiolysis | Saline solution | 11 | Fever | Fever |
| 16 | 34 | 20.7 | Recurrent miscarriage | Metroplasty | Saline solution | 2.5 | Fever | Fever |
| 17 | 29 | 22 | Recurrent miscarriage | Metroplasty | Saline solution | 2 | Fever | Fever |
| 18 | 33 | 18 | Spotting | Polypectomy | Saline solution | 2 | Fever, pelvic pain | Fever |
| 19 | 41 | 29.1 | Spotting | Polypectomy | Saline solution | 2 | Fever | Fever |
| 20 | 66 | 28 | Abnormal uterine bleeding | Polypectomy | Saline solution | 4 | Fever, dysuria | Fever |
| 21 | 62 | 18 | Abnormal uterine bleeding | Polypectomy | Saline solution | 5 | Fever | Fever |
| 22 | 33 | 21 | None | Polypectomy | Saline solution | 2.5 | Fever, pelvic pain | Fever |
| 23 | 45 | 21.5 | Spotting | Polypectomy | Saline solution | 3 | Fever, dysuria | Fever |
| 24 | 48 | 19 | Abnormal uterine bleeding | Myomectomy | Saline solution | 15 | Fever | Fever |
| 25 | 39 | 26 | Abnormal uterine bleeding | Myomectomy | Saline solution | 14 | Fever | Fever |

BMI = body mass index; ICSI = intracytoplasmatic sperm injection.

Fallopian tubes, and the presence of severe tubo-uterine adhesions in all 5 patients.

## Discussion

In the present study, to the best of our knowledge the largest prospective, controlled study to date, we evaluated the incidence of infections after both diagnostic and operative hysteroscopy, as well as associations with the type of distension medium used without prophylactic antibiotic administration. Our data suggest a low prevalence of infections during hysteroscopic procedures, with only 25 patients in our population of 42,934 who underwent a diagnostic or operative hysteroscopy experiencing infection (0.06%), compared with previously reported rates of 0.18% to 11.4% [17−22].

The present study differs from published reports on the same topic in other aspects as well. It was performed using a constant input pressure for both saline solution and $CO_2$; with insertion of the hysteroscope through the vagina, cervical canal, and uterine cavity without use of a speculum, a tenaculum, analgesia, or anesthesia; avoiding preoperative vaginal antiseptic; and evaluating findings derived from both diagnostic and operative hysteroscopic procedures. Therefore, we conclude that our data show that office hysteroscopy is a safe procedure for diagnosing intrauterine disease under direct view (unrelated to the distension medium used), as well as for operatively treating intrauterine disease without increasing side effects.

There may be concerns owing to the fact that the vagina is an area of the body with normal abundant bacterial flora [5,6], the endocervix is not sterile [7−9], and the transfer of vaginal and cervical flora into the uterine cavity and fallopian tubes may increase the risk of PID. These concerns are logical, given that the distension medium could spread endometrial cells or vaginal and cervical flora or bacteria into the peritoneal cavity through the tubes. However, it may be hypothesized that the minimal amount of fluid rinsed into the pelvic cavity is insufficient to trigger an inflammatory response. On the other hand, our findings suggest that in the presence of damaged tubes owing to pelvic adhesions or endometriosis, fluid related to the distension medium may remain in the tubes and trigger or reactivate a latent infection. It has been previously demonstrated that the presence of endometrioma is a risk factor for the development of tubo-ovarian abscess, as has been reported after oocyte retrieval and cyst aspiration after hysteroscopy [23]. We hypothesize that the presence of old blood in the endometrioma may provide a culture for the growth of bacteria residing in the vagina and be introduced into the tubes by the distension medium, thereby predisposing patients to pelvic abscess. In addition, the presence of damaged fallopian tubes may predispose patients to pelvic infection. In a retrospective study, McCausland et al [24] found 3 cases (1.5%) of tubal abscesses after operative hysteroscopy in 200 patients with a history of PID, further supporting the possible role of preexisting tubal disease in the genesis of infection after office hysteroscopy.

Nevertheless, the complications observed after synechiolysis may be related to the fact that hysteroscopy may potentially reactivate a latent infection, a hypothesis supported by the evidence supporting the role of infection in intrauterine adhesions [25]. However, the low incidence of complications after hysteroscopy in our cohort led us to believe that there is no reason to avoid hysteroscopy in patients with known adhesions.

Finally, with respect to the patients in whom fever was present with or without dysuria and promptly resolved after antibiotic administration, we ascribe such this complication to a subclinical urinary tract infection or a reaction of the upper genital tract owing to the distension medium used.

In conclusion, data from the present study suggest that incidence of infection after both diagnostic and operative in-office hysteroscopic procedures are low, and thus prophylactic antibiotics may be unnecessary.

## References


1. la Chapelle CF, Veersema S, Brölmann HA, Jansen FW. Effectiveness and feasibility of hysteroscopic sterilization techniques: a systematic review and meta-analysis. *Fertil Steril*. 2015;103:1516–1525. .e1−e3.
2. Craciunas L, Sajid MS, Howell R. Carbon dioxide versus normal saline as distension medium for diagnostic hysteroscopy: a systematic review and meta-analysis of randomized controlled trials. *Fertil Steril*. 2013;100:1709–1714. .e1−e4.
3. Di Spiezio Sardo A, Bettocchi S, Spinelli M, et al. Review of new office-based hysteroscopic procedures 2003-2009. *J Minim Invasive Gynecol*. 2010;17:436–448.
4. Clark TJ. Outpatient hysteroscopy and ultrasonography in the management of endometrial disease. *Curr Opin Obstet Gynecol*. 2004;16:305–311.
5. Sirota I, Zarek SM, Segars JH. Potential influence of the microbiome on infertility and assisted reproductive technology. *Semin Reprod Med*. 2014;32:35–42.
6. Martin DH. The microbiota of the vagina and its influence on women's health and disease. *Am J Med Sci*. 2012;343:2–9.
7. Thinkhamrop J, Laopaiboon M, Lumbiganon P. Prophylactic antibiotics for transcervical intrauterine procedures. *Cochrane Database Syst Rev*. 2013;5:CD005637.
8. Osborne NG, Wright RC. Effect of preoperative scrub on the bacterial flora of the endocervix and vagina. *Obstet Gynecol*. 1977;50:148–151.
9. Jr Mishell DR, JH Bell, Good RG, Moyer DL. The intrauterine device: a bacteriologic study of the endometrial cavity. *Am J Obstet Gynecol*. 1966;96:119–126.
10. Raimondo G, Raimondo D, D'Aniello G, et al. A randomized controlled study comparing carbon dioxide versus normal saline as distension media in diagnostic office hysteroscopy: is the distension with carbon dioxide a problem. *Fertil Steril*. 2010;94:2319–2322.
11. Litta P, Cosmi E, Saccardi C, Esposito C, Rui R, Ambrosini G. Outpatient operative polypectomy using a 5-mm hysteroscope without anaesthesia and/or analgesia: advantages and limits. *Eur J Obstet Gynecol Reprod Biol*. 2008;139:210–214.
12. Bettocchi S, Ceci O, Nappi L, Pontrelli G, Pinto L, Vicino M. Office hysteroscopic metroplasty: three "diagnostic criteria" to differentiate between septate and bicornuate uteri. *J Minim Invasive Gynecol*. 2007;14:324–328.

13. Di Spiezio Sardo A, Mazzon I, Bramante S, et al. Hysteroscopic myomectomy: a comprehensive review of surgical techniques. *Hum Reprod Update*. 2008;14:101–119.
14. Bettocchi S, Di Spiezio Sardo A, Ceci O, et al. A new hysteroscopic technique for the preparation of partially intramural myomas in office setting (OPPIuM technique): a pilot study. *J Minim Invasive Gynecol*. 2009;16:748–754.
15. Fernandez H, Peyrelevade S, Legendre G, Faivre E, Deffieux X, Nazac A. Total adhesions treated by hysteroscopy: must we stop at two procedures? *Fertil Steril*. 2012;98:980–985.
16. Franchini M, Boeri C, Calzolari S, et al. Essure transcervical tubal sterilization: a 5-year X-ray follow up. *Fertil Steril*. 2011;95:2114–2115.
17. Nappi L, Di Spiezio Sardo A, Spinelli M, et al. A multicenter, double-blind, randomized, placebo-controlled study to assess whether antibiotic administration should be recommended during office operative hysteroscopy. *Reprod Sci*. 2013;20:755–761.
18. Munro MG. Complications of hysteroscopic and uterine resectoscopic surgery. *Obstet Gynecol Clin North Am*. 2010;37:399–425.
19. Kasius JC, Broekmans FJ, Fauser BC, Devroey P, Fatemi HM. Antibiotic prophylaxis for hysteroscopy evaluation of the uterine cavity. *Fertil Steril*. 2011;95:792–794.
20. Agostini A, Cravello L, Shojai R, Ronda I, Roger V, Blanc B. Postoperative infection and surgical hysteroscopy. *Fertil Steril*. 2002;77:766–768.
21. Morrill MY, Schimpf MO, Abed H, et al. Antibiotic prophylaxis for selected gynecologic surgeries. *Int J Gynaecol Obstet*. 2013;120:10–15.
22. Gregoriou O, Bakas P, Grigoriadis C, Creatsa M, Sofoudis C, Creatsas G. Antibiotic prophylaxis in diagnostic hysteroscopy: is it necessary or not? *Eur J Obstet Gynecol Reprod Biol*. 2012;163:190–192.
23. Lin YH, Hwang JL, Seow KM, Chong KM, Huang LW. Tubo-ovarian abscess with septic shock in a case of endometrioma following diagnostic hysteroscopy. *Taiwan J Obstet Gynecol*. 2010;49:359–360.
24. McCausland VM, Fields GA, McCausland AM, Townsend DE. Tubo-ovarian abscesses after operative hysteroscopy. *J Reprod Med*. 1993;38:198–200.
25. Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome: one century later. *Fertil Steril*. 2008;89:759–779.