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Intrauterine adhesions: what is the pregnancy rate after hysteroscopic management?

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Running title: Hysteroscopy for uterine adhesions

Study funding/competing interest: No funding

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Abstract

Objective: To evaluate the rate of pregnancy following hysteroscopic management of intrauterine adhesions

Design: Retrospective study

Setting: From June 2009 to December 2014 in a teaching hospital

Patients: Women treated by operative hysteroscopy for intrauterine adhesions

Intervention: Operative hysteroscopy to manage intrauterine adhesions

Main outcome measure: rate of intrauterine pregnancy after hysteroscopic management of intrauterine adhesions

Results: Out of the 202 women whom benefit from hysteroscopic adhesiolysis, 112(55%) had an effective pregnancy desire. Among them, an intrauterine pregnancy was obtained for 58 women (52%) with a trend to a lower rate for type IV and Vb intrauterine adhesions management (40.5%, $p=0.09$). Pregnancy rates were similar for women undergoing one or more procedures.

Conclusion: Hysteroscopic management of intrauterine adhesions seems useful as it leads to a pregnancy rate of 52%. However, this rate is lower in case of type IV and Vb intrauterine adhesions. Repeated procedures don't seem to lead to less pregnancy; however, a more powerful prospective study should be performed to answer this specific question.

Keywords: Intrauterine adhesions; Operative hysteroscopy; Fertility

Introduction

Intrauterine adhesions were first reported in 1894 (1), with a more elaborated specific description and etiological hypotheses provided later on (2,3). Prevalence estimations range from 2.2% (4, 5) to 40% depending on the type of surgery women previously had (6). A recent increase in the diagnosis has been observed worldwide (7), mostly due to an efficient access to sonography and hysteroscopy. Adhesions often appear after intrauterine procedures, such as aspiration, curettage, uterine compression sutures in case of postpartum hemorrhage, uterine embolization, endometrial or retained products of conception resection techniques and hysteroscopic myomectomy (8-14).

In case of intrauterine adhesions, hysteroscopic adhesiolysis is the gold standard, first described by March (15-21)..Surgical technique involves splitting mechanically intrauterine adhesions using scissors (18, 22, 23). Electro surgery using monopolar or bipolar instrument has also been described (24). Hysteroscopic management of intrauterine adhesions can be difficult if adhesions are severe (25, 26).

After hysteroscopic adhesiolysis, the main goal is to prevent recurrence of adhesions. Recurrence rates range between 3.1 to 23.5% of women, depending on the severity of adhesions at baseline. In severe Asherman syndrome (stage 3 or 4), it can occur in as many as 63% of women.(23, 27-29). The main concern of women who undergo an operative hysteroscopy for intrauterine adhesions is fertility. As published studies about pregnancy rate after adhesiolysis are scarce, we report in this present study pregnancy rate after operative hysteroscopy for intrauterine adhesions.

An increase number of data should allow better information for women who planned this kind of procedure.

Methods

This is a retrospective study of women undergoing operative surgery for intrauterine adhesions in the gynecology department of a teaching hospital between June 2009 and December 2014. Only data providing from women with an effective pregnancy desire after the procedure were finally included in the analysis.

Diagnosis of intrauterine adhesions was performed using hysterosonography or office hysteroscopy. The classification from the European Society of Gynecological Endoscopy (30) was used (Table 1). Hysteroscopic adhesiolysis were performed in the operation room under general or epidural anesthesia.

Diagnostic hysteroscopy was first performed through the cervix. To avoid complications secondary to cervico-isthmic adhesions, intervention begin with small scissors. When the cavity is regained or in the absence of cervico-isthmic adhesions, cervical dilatation is performed carefully with dilators. Pozzi's tenaculums are a good help to introduce hysteroscope in case of cervico-isthmic adhesions and to dilate when it is possible. It helps limit the risk of perforation.

Another tool often used to limit the risk of perforation was sonographic guidance. Its use was only based on the surgeon's choice.

An operative hysteroscope is then introduced through the cervix, and intrauterine adhesions were removed using a bipolar knife. Systematic second look office hysteroscopy was performed four to six weeks after operative hysteroscopy.

Demographic data, risk factors, preoperative symptoms, and types of intrauterine adhesions were recorded. Data about operative hysteroscopy were also recorded. A phone questionnaire was carried out to collect subsequent fertility, pregnancy issues and complications. Data from the maternities were then collected.

A descriptive statistical analysis was performed using Stata software STATA/SE version 14.2 (4905 Lakeway Drive. College station. Texas 77845. USA). Categorical variables are described as percentages, and continuous variables are described as means [CI95%]. Comparisons were performed using a chi square test for categorical variables and a Student T test for continuous variables.

Ethical committee approval was obtained (CEROG 2015-GYN-0701).

Results

During the study period, 202 women who had undergone operative hysteroscopy for intrauterine adhesions were included. Flow chart of inclusion is in Figure 1.

We then analyzed data of 112 women (55%) with an effective pregnancy desire after operative hysteroscopy. Mean age was 34.3 [CI95% 33.3-35.3]. The mean number of previous pregnancies was 2.3 [CI95% 1.9-2.6], and the mean number of previous term pregnancy was 0.8 [CI95% 0.6-1.0]. Fifty-two women (46%) had a previous term delivery.

Excluded women were significantly older than included ones and had a higher number of previous deliveries. A significant difference was also found in the rate of infertility. These results were expected as excluded women are the ones with no pregnancy desire (older with more previous delivery and less infertility). These results are shown in Table 2.

Forty-four women (84%) had at least one known risk factor for intrauterine adhesion, such as previous aspiration/curettage, previous hysteroscopy, previous myomectomy, or previous embolization for postpartum hemorrhage. These results are detailed in Table 2.

A diagnosis of intrauterine adhesions was suspected because of symptoms in 87% of women (infertility in 52.7% of women, amenorrhea in 23.2% mainly). For asymptomatic women the diagnosis could be made after a systematic second look hysteroscopy after hysteroscopic myomectomy or retained product of conception resection.

According to European classification, 2 women had type I adhesions, 17 had type II (without the IIa), 29 had type IIa, 20 had type III, 14 had type IV, and 7 had type Va and 23 had type Vb, as reported in Table 3.

All women were operated in day care surgery and 102 (91%) had second look office hysteroscopy planned 4 to 6 weeks after surgery. A sonographic guidance was used in 29 cases out of 112 (25.9%), mainly in type IV and Vb adhesions (46.0%) ($p < 0.01$). There was no significant difference in the number of procedure achieved whether or not ultrasound guidance was employed ($p = 0.51$). The only intraoperative complication reported (0.9%) was a posterior perforation leading to an interruption of the procedure.

Results of second look office hysteroscopy were available for 106 women. A normal uterine cavity was obtained after one procedure in 85 out of 106 women (80%), after two procedures in 8 out of 106 women (7.6%), and after more than two procedures in 13 out of 106 women (12.4%).

An intrauterine pregnancy was obtained for 58 out of 112 women with a pregnancy desire (52%) in a mean time of 10.6 months [7.9-13.5] after their last procedure. It was a spontaneous pregnancy for 50 women (86%) and after IVF for 8 women (14%). These pregnancies resulted in 46 births (79.3%) (27 by vaginal delivery and 19 by cesarean section), 10 miscarriages (17.2%) and 2 ectopic pregnancies.

There was no significant statistical difference ($p = 0.15$) between the rate of pregnancy for women with no previous pregnancy (36.8%) and that for women with at least one previous pregnancy (54.8%).

There was no statistical difference in pregnancy for women requiring one procedure (47/84; 56%) compared with women who had more than one procedure (8/21; 38%)

($p=.14$). It also has to be noticed that women with severe adhesions (type IV or Vb) more often required more than one procedure (43.2 versus 16.0%, $p<0.01$).

Finally, the rate of pregnancy following management of type IV or Vb synechiae (40.5%) was lower than in other type (57.3%) without a significant difference ($p=0.09$) (Table 3).

Discussion

In this study, after hysteroscopic adhesiolysis the rate of intrauterine pregnancy is 52%. The latest did not significantly differ depending on number of procedures performed.

The European Society of Gynecological Endoscopy (ESGE) classification used in this study (30) is the most recent European classification and provides more details than March's classification (22). However, a universal classification would be more useful, as it is currently difficult to compare data from studies using different classifications.

In this study, rate of type I adhesions is low because most of them are treated during office hysteroscopy. The only woman included did not tolerate the office procedure. The rate of complication is low in this study (0.9%), which is comparable to similar previous studies. Mainly represented by perforations, the published complication rate ranges between 0.79% to 4.5% (28, 31-34).

Data on fertility rate after hysteroscopic management of intrauterine adhesions are scarce, with the published rate being anywhere from 30% to 66% depending on the type of adhesions (23, 33-37). For this reason, this study's data may be useful.

This study also reveals more than one operative time more frequently in type Iv and Vb adhesions and trend to a lower rate of pregnancy in this group compared to other types. These results are consistent with previous published data that also reveals a relatively worse prognosis for pregnancy in women presenting type 4 adhesions. Roy et al. found a lower rate of pregnancy after severe adhesions (33.3% versus 58%) such as Yu et al. in their literature review. (33), (38)

Mean time between surgery and pregnancy in this study is 10.6 months. This delay is consistent with published data (mean time around 12 months) (33, 34).

Recurrences of intrauterine adhesions are frequent and sometimes lead to repeated procedures (23, 27-29). Although this study does not report any significant difference in the pregnancy rates between women requiring one procedure and those requiring many procedures, it should be noticed that these rates of pregnancy are still different. The power might be insufficient to conclude. Published data on prognosis of repeat procedures are scarce. Fernandez et al. determined a 40.9% rate of pregnancy after repeated procedures (16), and our results are consistent with this previous study whereas these two studies did not include the same women as these two studies didn't take place in the same hospital. However, another study did not report any pregnancy after repeated procedures (33).

In many published studies, the rate of ART after hysteroscopic management of intrauterine adhesions is from 24% to 35% (36, 37). In the present study, this rate is very low (14%), revealing that spontaneous pregnancies are possible after hysteroscopic management of intrauterine adhesions.

In the AAGL practice report, the rate of pregnancy is reported to be higher in women with a previous pregnancy (39) even if it resulted in a miscarriage. Although our study did not find such a significant result, the recorded rate of pregnancy in women with no previous pregnancy is lower (36.8% versus 54.8%). The absence of a significant difference may be due to an insufficient statistical power.

The main weakness of this study remains in its retrospective nature, as this does not allow access to information that may be relevant. Its main strength is its large number of participants.

A multicenter prospective study should be performed but it will need a prolonged inclusion period. Information for women about the rate of pregnancy after hysteroscopic management of intrauterine adhesions should then be enhanced.

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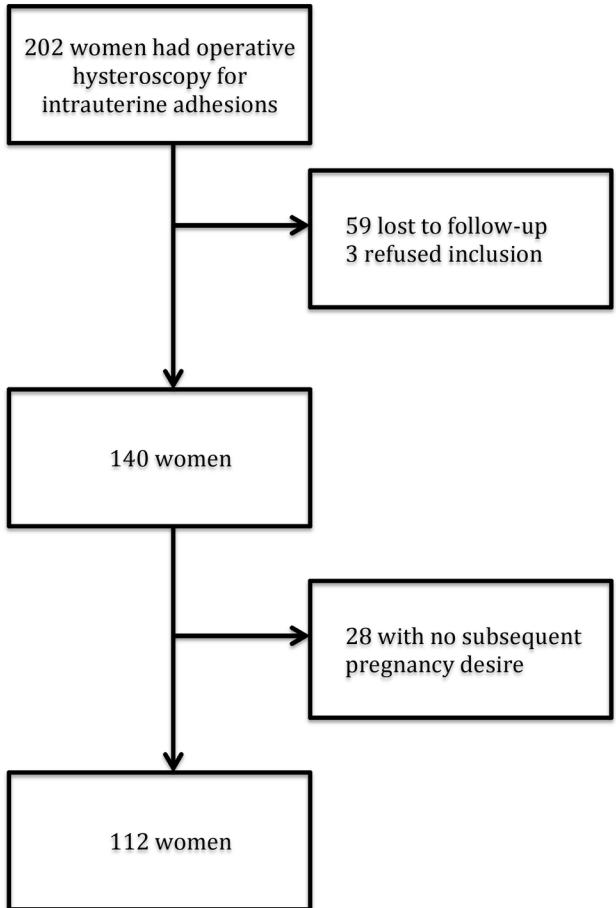


Table 1: European Society of Gynecological Endoscopy (ESGE) classification of intrauterine adhesions (Wamsteker and De Block 1998).

Grade	Extent of intrauterine adhesions
I	Thin or filmy adhesions Easily ruptured by hysteroscopic sheath alone. Cornual areas normal
II	Singular dense adhesion Connecting separate area of the uterine cavity. Visualization of both ostia possible. Cannot be ruptured by hysteroscopic sheath alone.
Ila	Adhesions affect just the cervico-isthmic area. Furthermore, cavity is normal with visualization of both ostia.
III	Multiple dense adhesions Connecting separate areas of the uterine cavity. Unilateral obliteration of ostial area of the tubes
IV	Extensive dense adhesions with (partial) occlusion of the uterine cavity. Both tubal ostial areas (partially) occluded
Va	Adhesions grade I or II with amenorrhea or hypomenorrhea
Vb	Dense or extensive adhesions grade III or IV with amenorrhea

Table 2: Description of included women

	Included women (n=112)				Excluded women (n=90)				p
	Mean	CI 95%	N	%	Mean	CI 95%	N	%	
Age	34.3	33.3-35.3			38.5	36.4-40.6			<0.01
Number of previous pregnancy	2.3	1.9-2.6			2.4	2.1-2.8			NS
Number of previous delivery	0.8	0.6-1.0			1.3	1.1-1.6			<0.01
Previous delivery			52	46			61	68	<0.01
Previous aspiration or curettage			58	52			34	38	0.05
Previous hysteroscopy			40	36			32	36	NS
Previous open myomectomy			19	17			18	20	NS
Previous embolization for postpartum hemorrhage			7	6			5	6	NS
Previous endometritis			8	7			3	3	NS
At least one known risk factor			95	85			67	74	NS
Symptomatic intrauterine adhesions			97	87			72	80	NS
Amenorrhea			26	23			21	23	NS

Hypomenorrhea			9	8			5	6	NS
Dysmenorrhea			8	7			9	10	NS
Irregular bleeding			7	6			7	8	NS
Infertility			60	54			25	28	<0.01
Post-partum control (after late fetal loss, premature delivery, post-partum hemorrhage)			5	4			5	6	NS
Post-operative control (after open myomectomy, operative hysteroscopy)			10	9			14	16	NS

Table 3: Type of intrauterine adhesions and rate of pregnancy

	N	%	N pregnancies	%
Type I	2	1.8	1/2	50.0
Type II (except IIa)	17	15.2	8/17	47.1
Type IIa	29	25.9	16/29	55.2
Type III	20	17.9	14/20	70.0
Type IV	14	12.5	6/14	42.9
Type Va	7	6.3	4/7	57.1
Type Vb	23	20.5	9/23	39.1