Office hysteroscopy study in consecutive miscarriage patients

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Summary

Objective: To assess the prevalence of uterine anatomical abnormalities found by office diagnostic hysteroscopy in a population of patients experiencing more than two consecutive miscarriages and compare the prevalence of uterine abnormalities between patients with two miscarriages and those with three or more consecutive miscarriages. **Methods:** A cross-sectional study of 66 patients with two or more consecutive miscarriages diagnosis was conducted. Patients were divided into two groups: Group A (up to two miscarriages, 23 patients), and Group B (3 miscarriages, 43 patients). They underwent an outpatient diagnostic hysteroscopy study, with either congenital or acquired abnormalities of the uterine cavity being identified. **Results:** Uterine changes were found in 22 (33.3%) patients, with 9 cases of congenital changes [arcuate uterus (4 cases), septate uterus (2 cases), and bicornuate uterus (1 case)], and 13 patients with acquired changes [intrauterine adhesions (7 cases), endometrial polyp (4 cases), and uterine leiomyoma (2 cases)]. No significant differences were found between the groups as regarding both acquired and congenital uterine changes. A positive correlation was found between anatomical changes on hysteroscopy and number of miscarriages ($r = 0.31$; $p = 0.02$). **Conclusion:** Patients with more than two miscarriages have a high prevalence of uterine cavity abnormalities diagnosed by hysteroscopy; however there are no differences in prevalence or distribution of these lesions related to the number of recurrent miscarriages.

Keywords: Abortion, habitual; hysteroscopy; uterine diseases; congenital abnormalities.

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Introduction

Recurring miscarriages are considered when pregnancy is spontaneously interrupted in three consecutive episodes either previously to 20 weeks of gestational age or before the fetus reaches 500 g in weight[1,2]. More recently, there has been a tendency to include into this diagnosis those patients with two early spontaneous pregnancy losses, mainly if they occur later than the age of 35 years[3]. This new approach prevents delays in recognizing the disease in a more critical age group; however, it can contribute to a higher number of studies and invasive procedures ordered in this population, with no benefits necessarily resulting from the case management[3-5]. Repeated miscarriages can occur due to a set of factors, such as: genetic, endocrine, and immune diseases, coagulation system disorders or anatomical factors[3]. Immune changes were more prevalently found in patients with repeated miscarriages, and the frequency of findings was similar when patients with two miscarriages were compared with those with three or more miscarriages[4].

Prevalence of congenital or acquired anatomical changes in patients with repeated miscarriages is high, ranging from 6.3% to 67%[6,7], depending on the type of the study and the study population. Usually, anatomical assessment in these patients is performed through hysterosalpingography, ultrasonography, hysteroscopy, and laparoscopy, with further studies possibly being used, such as tridimensional ultrasonography, hysterosonography, and magnetic resonance[8-10]. Congenital uterine anomalies are correctly diagnosed by ultrasonography, especially when it is combined with a tridimensional resource; on the other hand, diagnostic hysteroscopy allows the diagnosis of acquired anomalies, in addition to congenital anomalies[8,11]. Recently, a reduction in hysteroscopy cost associated with reduced optical diameters has allowed hysteroscopy to be performed in an outpatient basis, with no anesthetics use, minimal discomfort and optimal acceptance by patients[10,12-15]. This study was conducted in order to assess the prevalence of uterine anatomical abnormalities diagnosed by hysteroscopy in a population of patients with more than two consecutive miscarriages. We further looked for a possible difference in prevalence of uterine changes in patients with two miscarriages, compared with those with three or more miscarriages.

Methods

A cross-sectional study was conducted from January 2007 to December 2010 and 74 patients of the Department of Gynecology with consecutive miscarriages were assessed. Only patients with consecutive losses were included, and they were classified according to the number of losses. Miscarriage was considered as a spontaneous gestational loss occurred up to 20 weeks or with a fetal weight lower than 500 g[1,7]. According to the number of miscarriages, patients were divided into two groups: Group A (two miscarriages, n = 23) and Group B (three or more miscarriages, n = 43) for purposes of comparison[1,4]. Patients whose gestational age at the time of the loss was unknown (n = 4), patients with a current pregnancy diagnosed (n = 1), prior uterine surgery other than curettage or C-section (n = 1), patients who refused to participate in the study or patients who did not tolerate the assessment without anesthesia (n = 2) were excluded[16]. Demographics of the sample, such as age, menarche age, cycle characteristics, obstetric history (parousity, gestational age when prior losses occurred), smoking and alcohol consumption were collected at the time the test was ordered. Table 1 shows the distribution of the sample demographics.

Diagnostic procedure

The patients underwent a diagnostic hysteroscopy at the follicular phase of the menstrual cycle (days 3-15) and all procedures were performed by skilled gynecologists (CAS, JSCF). The examiner did not know the test indication when it was performed. A κ index was calculated among the examiners and no significant difference was found (p = 0.83). In summary, the procedure was performed with 2.6 mm optics with an angle of view of 30º (Karl Storz Endoscopy, Germany). Normal saline was used as a distending medium with a pressure of 20 mmHg to 50 mmHg. Hysteroscopy was performed in an outpatient basis, with neither use of anesthesia nor antibiotic prophylaxis, with cervical grasping by using a Pozzi tenaculum being avoided[17,18]. In case the patient did not tolerate the procedure, it would be discontinued and rescheduled using procedural sedation and anesthesia, and that patient would be excluded from the study.

Classification of findings

Changes found by hysteroscopy were subdivided into congenital or acquired abnormalities. Congenital changes were classified as arcuate uterus, didelphic uterus, bicornuate uterus, unicornuate uterus, and septate uterus. The acquired changes found received the following diagnoses: uterine polyp, leiomyoma, intrauterine adhesions, endometritis, and hyperplasia[8,17].

Statistical analysis

Data was analyzed by the software SPSS 13 (United States of America). Continuous data was described as median and interquartile range. Mann-Whitney and chi-squared test or Fischer's exact test were used to compare groups. Spearman's correlation coefficient was used to correlate variables (number of miscarriages and hysteroscopy findings). Categorical variable (hysteroscopy finding) was turned into a quantitative variable so that the correlation could be made. A p-value < 0.05 was considered significant. The study was approved by the Research and Postgraduation Group at the Clinical Hospital of Porto Alegre.

Table 1 – Distribution of demographics in the sample (median, interquartile range)

	Two miscarriages (n = 23)	Three or more miscarriages (n = 43)	Total n = 66	p
Age (years)	35 (19.7-35.7)	32.7 (29-35)	34 (31-39)	0.64[a]
Menarche age (years)	12.5 (12-16)	11.1 (11-13)	12 (11-13)	0.16[a]
Race				0.49[b]
White	17 (74.0)	36 (83.7)	53 (80.3)	
Afrodescendant	3 (13.0)	5 (11.6)	8 (12.1)	
Mixed	3 (13.0)	2 (4.7)	5 (7.6)	
Regular cycles	18 (78.3)	38 (88.4)	56 (84.8)	0.27[b]
Pregnancies	2 (2.0-3.0)	3 (3.0-4.0)	3 (3-4)	0.0001[a]
Deliveries	0.5 (0.5-1.0)	0.5 (0.5-1.0)	0.5 (0.5-1)	0.86[a]
C-sections	0.1 (0.1-0.5)	0.2 (0.1-0.5)	0.1 (0.1-0.5)	0.17[a]
Miscarriage	2 (2.0-2.0)	3 (3.0-4.0)	3.0 (2.0-3.2)	0.0001[a]
GA at the miscarriage (weeks)	11 (9.0-12.0)	11 (9.5-13)	11 (9.0-12.0)	0.7[a]
Weight (kg)	55 (53.5-64.7)	60 (56.5-64.7)	60 (55.0-67.5)	0.43[a]
Height (m)	1.57 (1.56-1.68)	1.61 (1.57-1.65)	1.58 (1.57-1.65)	0.41[a]
BMI (kg/m^2)	22.6 (20.1-24.2)	23.04 (22.3-23.9)	23.1 (22.3-26.4)	0.83[a]
Smoking	18 (78.3)	38 (88.4)	12 (18.2)	0.27[b]
Alcohol consumption	5 (21.7)	7 (16.3)	2 (3.0)	0.7[b]

[a] Mann-Whitney; [b] Chi-squared.
GA, gestational age.

Results

Twenty-two (33.3%) patients in the sample were found to have uterine cavity changes, with 9 of them being congenital and 13 acquired anomalies. By evaluating the congenital changes in the uterine cavity, the following diagnoses were found: arcuate uterus (n = 4), bicornuate uterus (n = 3) and septate uterus (n = 2). By considering the acquired anomalies, the most frequent diagnoses were: intrauterine adhesion (n = 7), polyp (n = 4), leiomyoma (n = 2) (Table 2).

When groups with two miscarriage episodes were compared with groups with three or more miscarriages, the sample characteristics found had a similar distribution between the groups. Regarding hysteroscopy findings, both congenital and acquired changes had no significant differences between the groups (Table 2). Hysteroscopy anomalies in patients in Group A were no different from anomalies in Group B (10 vs. 12, respectively, p = 0.2, chi-squared). When the number of miscarriages was correlated with hysteroscopy findings, a correlation coefficient r = 0.31 (p = 0.02 – Spearman's) was found, the correlation of the number of miscarriages with the number of patients having intrauterine adhesions was r = 0.11 (p = 0.39 – Spearman's).

Table 2 – Distribution of hysteroscopy findings between the groups (median, interquartile range)

	Two miscarriages (n = 23)	Three or more miscarriages (n = 43)	Total (n = 66)	P
Hysteroscopy				
Normal (reference)	13 (56.6)	31 (72.1)	44 (66.7)	
Congenital changes	4 (17.3)	5 (11.6)	9 (13.6)	0.44[c]
Acquired changes	6 (26.1)	7 (16.2)	13 (19.7)	0.32[c]
Type of hysteroscopy change				
Arcuate uterus	1 (4.3)	3 (7.0)	4 (6.1)	0.9[a]
Bicornuate uterus	2 (8.7)	1 (2.3)	3 (4.5)	0.23[a]
Septate uterus	1 (4.3)	1 (2.3)	2 (3.0)	0.52[a]
Polyp	2 (8.7)	2 (4.7)	4 (6.1)	0.57[a]
Leiomyoma	2 (8.7)	0 (0)	2 (3.0)	0.11[a]
Intrauterine adhesion	2 (8.7)	5 (11.6)	7 (10.6)	0.9[a]

[a] Fischer's exact test.

Discussion

In our study, we demonstrated consecutive miscarriages are associated with uterine cavity anomalies, as about one-third of the sample had congenital or acquired changes on hysteroscopy. We further demonstrated changes are equally distributed in patients with two miscarriages compared with those with three or more consecutive miscarriages.

Studies have sought to analyze if the traditional definition for repeated miscarriage, considering three consecutive episodes, should be reviewed; however, findings are still incipient[1-5]. Our study is in accordance with previous studies demonstrating that although there is a high incidence of anatomical changes in the population of patients with repeated miscarriages[1,3,19], there is no difference in incidence of findings regarding patients with two miscarriages compared with those with three or more events[1,2]. Jaslow et al.[4], by evaluating a large series of repeated miscarriage cases demonstrated immune changes were similarly distributed, regardless the number of miscarriages. This set of findings indicates the assessment of patients with repeated miscarriages can be reviewed, by trying to identify the patients earlier and in a more particular way.

Over the last years, hysteroscopy has been shown as an excellent diagnostic and therapeutic tool in gynecology[2,15,20]. We have found a high prevalence of acquired anatomical abnormalities, particularly intrauterine adhesions. This fact is likely associated with these patients having usually undergone uterine emptying procedures. Uterine curettage is known to produce intrauterine adhesions[20,21]. Although the intrauterine manual vacuum aspiration procedure is increasingly prevalent here in Porto Alegre, a large number of patients still undergo standard uterine curettage procedures[20]. In our study, a correlation between hysteroscopy anomalies and number of miscarriages was present ($r = 0.31$); thus, we can assume there is an association between anatomical changes and increased miscarriage incidence. Unfortunately, the correlation is not sustained in cases of intrauterine adhesions ($r = 0.11$).

Our study has several points to be highlighted. We could show a homogeneous series of repeated miscarriage cases. The data collect was appropriate, controlling the methodology employed to carry out the tests and interexaminer variability. As our practice is a reference center in endoscopy, with studies being performed for various indications, the examiners were unaware of the test indication as it was performed; however, the patient's obstetric and surgical history was informed, preventing the examiner's total blinding.

Despite we were careful about methodology, our study has limitations. Our incidence of repeated miscarriage cases, as well as the hysteroscopy abnormal findings, is supposedly higher than that found in the general population. Moreover, endoscopy availability likely allowed uterine anomalies which otherwise could go undetected or be diagnosed later to be diagnosed earlier. Another noticeable point in our study was a higher number of patients with more than three miscarriages over the group with only two miscarriages[16]. In our sample, we do not have the patients' hysterosalpingography data. This is an easily available, non-invasive, and low-cost study showing a correlation with findings in other tests, such as ultrasonography and hysteroscopy. However, hysterosalpingography has a high false-positive and false-negative rates as a disadvantage, in addition to being a more painful test for most patients[22,23].

Conclusion

Thus, repeated miscarriage cases have an increased prevalence of acquired and congenital uterine anomalies diagnosed by outpatient diagnostic hysteroscopy. It is shown as an applicable and easily performed test for that population. Changes in the uterine cavity have already been present from two miscarriages; thus, starting earlier the anatomical investigation in repeated miscarriages can be suitable as managing these cases. Prospective studies with a higher number of patients are still required so that changes in management of repeated miscarriages can be defined.

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