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Reproductive Outcome Following Hysteroscopic Treatment of Uterine Septum

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ABSTRACT

Background: Septate uterus is the most common uterine anomaly and a cause for miscarriage and infertility. Existing data suggested a better reproductive outcome of uterine septum following hysteroscopic septum resection. **Objecti**ve: Current study was administered to share our experience in hystroscopic septum resection for reproductive outcome following hysteroscopic treatment of uterine septum and specifically focusing on different treatment protocols after hysteroscopic septum resection. **Methods& materials:** This study was a cross-sectional study based on secondary data that was obtained from medical records of infertile women who had undergone transvaginal hysteroscopy and used different treatment protocols after hysteroscopic correction of uterine septum in Infertility and Reproductive Health Research Center between April 2005 and February 2014. **Results:** The total number of infertile women underwent hysteroscopy uterine septoplasty was 106. The hysteroscopy septoplasty resulted in an overall pregnancy rate of 67% and a live birth 57.5%. Pregnancy rate for patients who had not male infertility was 92.1%. The chi-square test did not reveal any statistically significant difference in side affect, pregnancy, live birth, abortion, preterm deliveries, and term deliveries rate between these patients either with consistent hormone therapy plus IUD insertion or with alternate hormone therapy plus IUD after hysteroscopic metroplasty. **Conclusion:** The findings of the present study indicated hysteroscopic septum resection to remove a uterine septum in women with infertility is safe and may be an efficacious procedure. Treatment following hysteroscopic septum resection, either the consistent or the alternate protocol is both beneficial to improve pregnancy rate.

Key words: Septum resection, Pregnancy rate, Treatment protocols, Reproductive outcome, Hysteroscopy, Uterine septum.

1. INTRODUCTION

Uterine septum is the known type of congenital uterine malformation, approximately with 80–90% of uterine malformations. It can be lead to infertility, miscarriage, abnormal fetal position, and premature birth. Hysteroscopic metroplasty is a simple and safe approach for the removal of the uterine septum (1-5). Many studies represented the progression of spontaneous pregnancy rate after the hysteroscopic removal of septate uterus (6-23). In addition, some investigator suggested different treatment protocol after septum resection to impede asherman syndrome. The postoperative hormone therapy using estrogen and terminal progesterone is controversial because their efficacy has not been demonstrated in well-designed, prospective, randomized studies. They utilized hormone replacement therapy (HRT) and/ or temporary splints such as the intrauterine device (IUD) to maintain the uterine cavity distended to denuding endometrial cavity to prevent septal fusion (24-28). Nonetheless, They also suggested artificial stimulation of endometrial growth postoperatively may assist in the overall healing process by artificially enhancing endometrial growth by use of estrogen and subsequent shedding by use of terminal progesterone, paving the way to normal endometrial growth and subsequent spontaneous ovulation (5, 29, 30).

In spite of the comprehensive study of infertility, little data are available concerning the benefit of different treatment protocols after septum resection on fertility consequence. Our interest was to assess the efficacy of hysteroscopic septum resection on pregnancy rate and benefit of postoperative various methods in infertile women after septum resection.

2. MATERIALS AND METHODS

This study was approved by the ethics committee of Babol University of Medical Sciences. A compilation sheet was developed for the present study after taking permission from the general director of the Center to inspect the information existing in the medical records of infertile women. The research design of this study was a cross-sectional study. The study was based on secondary data from Fatemezahra Infertility and Reproduc-

tive Health Research Center to inspect the information Center that Inclusion criteria for the study were infertile women who received different treatment protocols after hysteroscopic correction of the septet uterus between April 2005 and February 2014. A total of 106 patients was selected and reviewed based on inclusion criteria, 28 of these had male factor. The initial diagnosis of intrauterine septum was done by hysterosalpingography (HSG). Septet uterine and variable lengths (class Va: complete; class Vb: partial) according the American Fertility Society classification of Mullerian duct anomalies, who agreed to undergo hysteroscopic Septoplasty in the infertility center, were included in the study (5, 13, 31-33) .

All patients were hospitalized and underwent surgery 2 to 5 days after menstruation period in the early proliferative phase. Patient was placed misoprostol suppository in the posterior vaginal fornix for cervical dilation to facilitate an easier and uncomplicated procedure prior night of surgery.

After performing anesthesia, vaginal speculum placed after cleaning the external uterine ostium with a gauze soaked in iodine solution, surgeon used cervical dilator for dilatation of cervical OS to 10–10.5 cm, a 3.5-mm mini-hysteroscope KARL STORZ, Germany For endoscopy, was administered to preserve hymen integrity; normal saline was used as a factor of distending. An endoscopic vaginal exploration presented the presence of one uterine cervix at the open vaginal side and the uterine distention pressure was set at 150 mm Hg.

An electro resectoscope was inserted to corroborate the size, range of the septum and location. Then the septum by needle electrode was incised, and ultrasonography was applied for monitoring during the operation completely. After hysteroscopy, different regimens were used postoperatively to decrease the formation of intrauterine adhesion in the denuded area of septal incision. Postoperatively, patients totally had an intrauterine device insertion (IUD) to certify the potency of the uterine cavity and to prevent further adhesions. Antibiotic treatment was not taken to the patients. Laparoscopy was done also to rule out bicorn septum. All patients after receiving hormone therapy instruction and consciousness were discharged (26, 29, 33-40).

In 71 women, after septum resection alternate hormone order (first protocol) consist of conjugated estrogens (Premarin; Montreal postoperative Canada ,Wyeth-Ayerst) at a dose of 1.25 mg daily was given for twenty five day after surgery and medroxyprogesterone acetate (Provera; Pharmacia and UpjohnKalamazoo, USA) at a dose of 10 mg twice per day was accomplished from day of sixteen in this time in combination with the conjugated estrogens a dose of 1.25 mg daily till 25th of cycle, after 25 days treatment will stop, then menstruation will occur and after menstruation period again we start this treatment process again for 2 month.

A total of 35 patients were received constant hormone (second protocol) includes; conjugated oestrogen at a dose of 1.25 mg twice daily was given for 50 days. Medroxyprogesterone acetate at a dose of 10 mg twice daily was performed for the last 10 days of this time (i.e. days 54–60) in combination with the conjugated oestrogen. After a withdrawal bleeding, second day of menstruation, the IUD was removed.

Pregnancy and delivery follow-up for 12 months was done. If the pregnancy was not happening spontaneously after 6 month treatment, according to surgeon's idea ART procedure was started (41-47).

Statistical analysis

Data were analyzed using SPSS version 18.0. Comparisons between the type of protocols after septum resection and characteristics of variables were made using t-test. A P value of <0.5 was considered statistically significant. Qualitative data are presented as number and percentage and comparison between groups are estimated by Chi – square and Fisher's exact test.

3. RESULTS

Out of 106 infertile women with septate uterus who undergone hysteroscopy septum resection, 71 (67%) of the patients received first protocol after septum resection and 35(33 %) second protocol. The mean educational of infertility was 4.5±3.3 years. The BMI and menarche age the subjects were 27±4.3 kg/m^2 and 12.9±1.0 years, respectively. Table 1 shows some of the characteristics for different treatment protocols after hysteroscopic septum resection. There was no significant difference between age, menarche age, BMI, job of women, infertility type, and duration infertility types with treatment protocols of patients Table 2 presented reproductive outcome and side effect after septum resection with different treatment protocol, showed a pregnancy rate after hystroscopic septum resection was enhanced. 44(62.0%) of patients had a positive pregnancy rate with first treatment protocol, while 27(77.1%) of patients with Second treatment protocol had a positive pregnancy rate.

Variables	First protocol (n=71) N(%)	Second protocol (n=35) (%)	p-Value*
Age(years) mean±SD	30.5±5.1	31.5±4.9	0.295
Menarche age <13 ≥13	 19(26.8) 52(73.2)	 14(40.0) 21(60.0)	0.166
BMI(kg/m2) <25 ≥25	 24(33.8) 47(66.2)	 10(28.6) 25(71.4)	0.587
Job Housewife Work	 62(87.3) 9(12.7)	 31(88.6) 4(11.4)	0.562
Duration infertility <5 =>5	40(56.3) 31(43.7)	25(71.4) 10(28.6)	0.134
Infertility type Primary Secondary	 39(54.9) 32(45.1)	 21(60.0) 14(40.0)	0.620
Male Infertility	21(29.6)	8(22.9)	0.465

*Table 1: Characteristics of women with intrauterine septum according to some characteristics (n=106). *Independent T. Test*

Variables	First protocol (n=71)	Second protocol (n=35)	p-Value*
pregnancy rate	44(62.0)	27(77.1)	0.118
Pregnancy Spontaneously After ART No pregnancy	 27 (38.0) 17(23.9) 27(38.0)	 16(45.7) 11(31.4) 8(22.9)	0.290
Live Birth rate	37(52.1)	24(68.6)	0.107
Abortion rate	3(4.2)	2(5.7)	0.536
Preterm Deliveries	7(9.9)	7(20.0)	0.127
Term Deliveries	34(47.9)	18(51.4)	0.732
Side affect after treatment	20(28.2)	9(25.7)	0.790

*Table 2: Reproductive outcome and side effect after septum resection with different treatment protocol. *Chi. Square Test*

Treatment following hysteroscopic septum resection, either the consistency or the alternate protocol is both adequate to improve rates of pregnancy. There is no meaningful advantage between two adjacent postoperative hormone therapies on pregnancy rate. 27 (28.8%) patient had a spontaneous pregnancy with first treatment protocol after hysteroscopic resection of uterine septum while 16 (45.7%) with second treatment protocol had spontaneous pregnancy. After ART, 17 (23.9%) who had used first treatment protocol had a pregnancy and 11(31.4%) with second treatment protocol had pregnancy after ART while 27(38.0%) patient had not pregnancy after using first treatment protocol and 8(22.9%) patient had not pregnancy after using second treatment protocol. Live Birth rate in patients with first and second treatment protocol was 37(52.1%) and 24(68.6%), respectively. Abortion rate in patients with first and second treatment protocol was 3(4.2%) and 2 (5.7%), respectively. Preterm deliveries in patients with first and second treatment protocol was 7(9.9%) and 7 (20.0%), respectively. Term deliveries in patients with first and second treatment protocol was 34(47.9%) and 18 (51.4%), respectively. Side effect of first and second treatment protocol was 20 (28.2%) and 9 (25.7%), respectively. Chi-square test revealed no statistically significant difference in upper variables and two treatment protocols. 84 (79.2 %) had no side effects during and after both treatments but 1 (9 %) stopped treatment and 21 (19.8 %) needed to add drug. Patients during treatment with first protocol 20 (28.2 %) had a side effect but with second protocol 9 (25.7 %) had side effect.

4. DISCUSSION

Most of the researchers have shown a better reproductive outcome after hysteroscopic resection of uterine septum in woman with septate uterus, however, there is no evidence on the postoperative management of the hysteroscopic septum division (27)(48). Most of authors also reported hysteroscopic metroplasty in patients with uterine septum improved pregnancy rate (10, 42). In this study, pregnancy rate and live birth rate after hystroscopic septum resection in women with septate uterus was high. Two studies found that the pregnancy rate after hysteroscopic metroplasty (around 40%) was lower compared with results (67.0%) (3, 15, 43, 49).Other observational studies also have reported similar findings (50).

In a retrospective, matched, controlled study, the role of septet uterus in the reproductive performance of patients requiring in vitro fertilization (IVF) was evaluated. The pregnancy rate before metroplasty was lower than after metroplasty, and the abortion rate was higher. They suggest that the presence of septate uterus may be decreased the pregnancy rate and increased the abortion rate after the embryo transfers for IVF/ICSI (51). In the present study, in 63 patients who had hysteroscopic resection of uterine septum and did not conceive naturally pregnant, of these 28 (44.5%) became pregnant by ART.

Many authors studied on pregnancy outcome after hystroscopic septum resection but they did not use hormonal postoperative therapy and concluded improved pregnancy rate after hystroscopic septum resection (9, 11, 15, 18, 20, 21, 38, 52-60). Nouri et al also agreed with these results and they represented an overall pregnancy rate of 60.1% and a live-birth rate of 45% after hysteroscopic metroplasty (20). Other studies also have shown that neither IUD placement, nor estrogen treatment, nor both prevent intrauterine adhesions or facilitate pregnancy after hysteroscopic uterine septum resection (29). Another study also was agreed that a postoperative 3-month estrogen plus IUD insertion or estrogen alone after hysteroscopic metroplasty are not necessary (61). This result showed that after hysteroscopic metroplasty without using postoperative therapy also we had improved reproductive outcome. Versus other authors also studied on pregnancy outcome after hystroscopic septum resection but they used hormonal postoperative therapy and concluded improved pregnancy rate after hystroscopic septum resection (13, 62-70).

While some authors were used only estrogen after hystroscopic metroplasty but reproductive performance significantly improved (26, 45, 71-73). We found that both intrauterine device and estrogen plus progesterone (HRT) was same for effect on reproductive outcome and the was no significant difference between two protocols on pregnancy rate (41).

In our infertility center we used two treatment protocols that mentioned upper and this was according to our surgeon's idea. We were able to show that the different treatment after septum resection was elected according to surgeon's idea and the postoperative reproductive outcome was similar in both method and there were no significant differences on delivery rates. The presenting findings showed that hysteroscopy for resection of uterine septa will increase the odds of clinical pregnancy in infertile women, but the evidence is not conclusive at present. Therefore, it is suggested that in women with septate uterus and a history of infertility, hysteroscopic septoplasty is a confident and efficient procedure resulting in a higher pregnancy rate. But more randomized controlled trials and prospective studies with enough samples with no intervention and consistent follow-up data are needed to, which could provide the highest level of evidence and substantiate the effectiveness of the hysteroscopic removal of uterine septum in infertile women and various postoperative treatments. Further research studies should focus on specific populations with clear indications, to draw reasonable and meaningful conclusions about the outcomes of hysteroscopic metroplasty. Adequate time after the procedure should be allowed so that subjects have ample time to attempt conception and also to give birth, to allow for accurate live-birth rate calculations.

Limitation: Because of some limitations, we don't have access to all surgical reports and therefore lacked detailed data on the diameter of cervical dilatation and intraoperative findings in some cases; we were also not able to calculate the exact time interval between the hysteroscopic intervention and the beginning of the pregnancies. A short interval between hysteroscopic intervention and conception might be an additional risk factor for preterm birth. Second, some of the infertile patients who underwent hysteroscopic septum resection in the course of infertility assessment at our clinic may have conceived naturally after the procedure, but were lost to follow-up or turned to another clinic for ART.

5. CONCLUSION

Treatment following hysteroscopic septum resection, either the consistent or the alternate protocol is both beneficial to improve pregnancy rate. There is no meaningful advantage between two adjacent postoperative hormone therapies on pregnancy rate. We have shown that hysteroscopic septum resection to remove a uterine septum in women with infertility is safe and

may be an efficacious procedure. However, the need remains for larger randomized controlled trials and prospective studies with enough samples with no intervention and consistent follow-up data to address the effectiveness and safety of adjunct therapy with hysteroscopic septum resection.

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CONFLICT OF INTEREST: NONE DECLARED.

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