ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Eva-Skuk/142

URF PUBLISHERS
connect with research world

Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 2 & Iss: 4

Original Research

Reproductive Outcomes after Hysteroscopic Management of Asherman's Syndrome: A Single-Center Retrospective Analysis

Eva Skuk[1,2*], Dzhamilyat Abdulkhalikova[1], Nina Jančar[1,2], Vesna Šalamun[1,2], Sara Korošec[1,2] and Helena Ban Frangež[1,2]

[1]Department of Human Reproduction, Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana, Šlajmerjeva 3, 1000 Ljubljana, Slovenia

[2]Faculty of Medicine, University of Ljubljana, Vrazov trg 2, 1000 Ljubljana, Slovenia

Citation: Skuk E, Abdulkhalikova D, Jancar N, Šalamun V, Korošec S, Frangež HB. Reproductive Outcomes after Hysteroscopic Management of Asherman's Syndrome: A Single-Center Retrospective Analysis. *Medi Clin Case Rep J* 2024;2(4):533-537. DOI: doi.org/10.51219/MCCRJ/Eva-Skuk/142

Received: 26 October, 2024; **Accepted:** 01 November, 2024; **Published:** 04 November, 2024

***Corresponding author:** Dr. Eva Skuk, MD, Department of Human Reproduction, Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana Šlajmerjeva 3, 1000 Ljubljana, Slovenia, Tel No: +38641933521, E-Mail: eva.skuk@ukclj.si

ABSTRACT

Background: The injury of basal endometrium due to surgical interventions or inflammation can cause intrauterine adhesions, socalled Ashermann's syndrome. The main complications are infertility and spontaneous abortions.

Methods: In our retrospective observational study, performed at the tertiary teaching hospital in the period between 2012 and 2018, treatment of secondary infertility and following pregnancy outcomes of 7 women diagnosed with Asherman's syndrome was observed. Intrauterine adhesions were resected under general anesthesia using hysteroscopy until the normal size of the cavity was achieved. Afterward, hyaluronic gel and intrauterine device were applied to the uterine cavity for 8 to 10 days. The patients were followed up for at least three years after the surgery.

Results: During this period, all women experienced stronger menstrual bleeding, 4 of 7 conceived and three delivered at term.

Conclusion: By using this approach in different cases of Aschermann's syndrome, satisfactory results can be obtained in otherwise infertile women in a relatively short period.

Keywords: Asherman syndrome; Implantation; Hysteroscopy; Endometrial injury; Infertility

Introduction

Intrauterine adhesions or intrauterine synechiae is an acquired, gynecological disorder of the uterus, characterized by fibrous tissue bands that develop within the uterine cavity, often in response to a uterine procedure. Asherman's syndrome is a condition when intrauterine adhesions are accompanied by specific symptoms (for example, amenorrhea, dysmenorrhea, infertility)[1]. The first case of intrauterine adhesion was published back in 1894 by Heinrich Fritsch. However, Israeli gyne-cologist Joseph Asherman was the first to publish a complete description of Asherman syndrome in 1948 when he investigated 29 women with amenorrhea due to stenosis of the cervical ostium and suggested the pathology could be caused by trauma to the endometrium[2,3].

The uterine cavity is lined by an epithelial layer called endometrium, consisting of functional and basal layers. The

functional layer is adjacent to the uterine cavity; it is built up in the first phase of the menstrual cycle and is completely shed during menstruation. The basal layer is below the functional layer, adjacent to the myometrium and is stable anytime during the menstrual cycle. It contains stem cells. Therefore, it is the source from which regeneration and formation of the functional layer of the endometrium occur. Basal layer trauma plays a crucial role in the formation of intrauterine adhesions. Injury to the basal layer causes the formation of fibrous tissue in the areas where there is damage or loss of stroma. Sometimes, these fibrin strings create tissue bridges between the walls of the uterine cavity, resulting in adhesion formation[1,2,4]. Disease severity can vary greatly, depending on the extent of adhesions. The degree of formed adhesions and the impact of these adhesions on the uterine cavity anatomy can cause a different presentation. Minimal disease presentation is characterized by thin strings of tissue across the uterine cavity. However, severe disease is characterized by complete obliteration of the cavity, potentially with the anterior uterine wall adherent to the posterior wall. In addition, vascularization may be compromised due to endometrial damage and scarring[5].

Risk factors for the condition include all processes that can potentially damage the endometrial basal layer. Intrauterine operating procedures (such as curettage or myomectomy) are most commonly associated with developing intrauterine adhesions[6,7]. Intrauterine adhesion formation may also occur without preceding uterine surgical procedures; the condition has been recognized in cases of uterine infections. Literature suggests the connection between chronic endometritis and intrauterine adhesions. The adhesions are believed to form secondary to chronic inflammation of the endometrium[1,2]. Genital tuberculosis is known to be associated with intrauterine adhesions, which are often severe, with complete obliteration of the uterine cavity[8]. Uterine compression sutures (B-Lynch sutures) used to treat severe postpartum hemorrhage have been associated with the development of intrauterine adhesions[9]. In addition, some studies suggest a higher chance of forming intrauterine adhesions in hypoxia or reduced uterine perfusion that occurs with uterine artery embolization[10]. Pregnancy appears to be an independent risk factor involved in intrauterine adhesion formation. During the immediate postpartum or postabortion period, the endometrium is thought to be more vulnerable to atrophy due to the decline in estrogen levels[11]. Furthermore, curettage following pregnancy loss also increases the risk of developing adhesions. Still, it is unclear how much of the risk is related to the gravid state itself and the operative intrauterine trauma[12].

Intrauterine adhesions can be asymptomatic and may be an incidental finding in these cases. Typical symptoms associated with Asherman's syndrome include abnormal or changed menstrual bleeding patterns, amenorrhea (usually secondary), infertility (can be due to blockage of sperm or changes in the endometrium that prevents implantation of the blastocyst), chronic pelvic pain (due to hematometra), recurrent pregnancy loss (due to abnormalities in endometrium)[1,2,13]. Physical examination in patients with intrauterine adhesions is typically normal. In some cases, transvaginal ultrasound examination may show a thin endometrial lining, which can only indicate such a condition. However, while ultrasound findings can be suggestive of intrauterine adhesions, their results do not confirm the diagnosis. Hysterosalpingography (HSG) can also detect adhesions; the sensitivity is lower than hysteroscopy. Direct visualization of intrauterine adhesions with hysteroscopy is the gold standard for the diagnosis. On the one hand, hysteroscopy helps us to evaluate the presence, stage and morphologic characteristics of intrauterine adhesions; on the other hand, it also enables simultaneous treatment of the condition. Resolving the adhesions with hysteroscopy can be performed in an office or operating room setting, which allows diagnosis confirmation and treatment in a single procedure[2,14,15].

Materials And Methods

This retrospective observational study was carried out at the Department of Human Reproduction, Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana, between 2012 and 2018. In our research, we included cases of 7 women who presented in our department with Asherman's syndrome and were then operated on and followed up for at least three years. All women were between 29 and 41 years old, the average age being 33.1 years. All women were treated for secondary infertility and were evaluated for possible etiology of the condition. They all underwent the standard protocol of our department, which includes the patient's history, hormonal analysis, a transvaginal ultrasound and the partner's semen analysis.

History showed that four of them had previous vaginal deliveries (either one or two vaginal deliveries) and three of them had previous spontaneous abortions (up to 4 abortions). The deliveries before surgery were uneventful; however, 2 out of 4 women had endometritis after the delivery. The other two women had regular postdelivery courses without complications. All three women with previous spontaneous abortions had curettage following the abortion and no known complications afterward.

All of them tried to conceive for more than one year before the surgery. Their periods were regular, but the bleeding was scarce or absent in one case. We evaluated the stage of Asherman's syndrome in these patients according to the American Fertility Society classification4. Classification of intrauterine adhesions may be helpful because the patient prognosis and reproductive outcome are usually related to the degree of disease. American Fertility Society classification is a scoring system of mild, moderate and severe intrauterine adhesions based on the extent of obliteration of the endometrial cavity, appearance of adhesions and patient menstrual characteristics assessed with hysteroscopy or hysterosalpingography. The first category, the degree of the obliterated cavity, is scored with "1" if less than 1/3 of the cavity is obliterated with synechiae, score "2" if more than 1/3 but less than 2/3 of the cavity is involved and score "3" if more than 2/3 of the cavity is obliterated. The second category, type of adhesions, is scored with "1" (if the adhesions are filmy), "2" (if the adhesions are filmy and dense) or "3" (if adhesions are dense). The last category is a menstrual pattern and is scored with "0" (if the menstrual pattern is completely normal), "2" (if the patient reports hypomenorrhea) or "4" (if the patient reports amenorrhea). The overall sum of scores then classifies intrauterine adhesions into stages. Scores 1-4 describe stage I (also called mild), scores 5-8 represent stage II (moderate) and scores 9-12 stage III (severe)4. In our case, three women had Asherman's syndrome stage 1, two women had stage 2 and two had stage 3, according to the American Fertility Society classification.

The diagnosis of Asherman's syndrome was made by ultrasound and hysteroscopy. Hysteroscopy was used for diagnosis and treatment, so we simultaneously confirmed and resolved the intrauterine adhesions. Patient information was provided to all women before the procedure and we obtained their written consent. Because the treatment procedure was operative hysteroscopy, all patients underwent the treatment in general anesthesia in the formal operating theatre setting. All performing physicians had the necessary skills and expertise to carry out hysteroscopy. Hysteroscopy was performed with sterile normal saline or glucose solution as the distending medium in all procedures. The Storz 22 Fr monopolar hysteroscope was used in 6 cases and in one case, the office hysteroscope was needed to enable the introduction of a wider hysteroscope through the uterine cervix. In 3 cases, ultrasound was used to help identify and follow the resection plane of the uterine cavity.

In all 7 cases, intrauterine adhesions were resected to the degree that the normal size of the uterine cavity was achieved. Both tubal Ostia were reached and visualized during the procedure in 4 out of 7 cases. In 2 cases, more than one hysteroscopic procedure was needed to resect all adhesions and to reform the uterine cavity.

After hysteroscopic resection, the hyaluronic gel was applied to the uterine cavity and an additional intrauterine device was placed into the uterine cavity (we used a copper intrauterine device from which copper was removed before the procedure and only form plastic remained). The intrauterine device was removed after 8-10 days. A single dose of preventive antibiotic was administered to all seven patients during the operative procedure. No hormonal therapy was administered after the operative procedure.

All seven patients were followed for a period of time (approximately three years). We obtained information on changes in menstrual flow and pattern, spontaneous conception and reproductive outcomes at regular checkup's.

Results

After the procedure, all seven women experienced stronger period bleeding. We performed a transvaginal ultrasound in the periovulatory phase; endometrium was measured between 3 and 9 mm. In three years of follow-up, 4 out of 7 women conceived. Three women conceived naturally and one after in vitro fertilization (IVF). Two women failed to conceive after 2 or 3 IVF attempts despite good quality embryos (blastocysts) being transferred into the uterus. These two women had the thinnest endometrium in the periovulatory phase (3 and 4 mm). One woman did not decide to undergo IVF. Three women delivered at term and one had a spontaneous abortion at seven weeks. Deliveries, including the delivery of the placenta, were normal in two cases and in one woman, there were missing cotyledons in the delivered placenta that needed manual removal.

Discussion

The overall incidence of intrauterine adhesions is challenging to assess because the condition can be asymptomatic and a definite diagnosis is based on invasive procedures only1. However, the incidence has been reportedly increasing over the last few decades; firstly, due to an increase in operating procedures that cause iatrogenic trauma to the endometrium; secondly, due to improvement of hysteroscopic diagnostic techniques; and lastly, as one of the main symptoms of the condition is infertility, these patients go through a diagnostic procedure that enables us to find intrauterine adhesions[1,16]. In our department, we studied seven women who primarily presented with secondary infertility and were diagnosed with Asherman's syndrome.

In our group, 4 out of 7 women reached pregnancy and delivered at term. On the one hand, restoration of menstrual blood flow was achieved in high ratios in our group of women as well, as in previous reports[17-20]. On the other hand, pregnancy and delivery rates are quite low. In our group, the pregnancy rate was 4/7 (57%) and the delivery rate was 3/7 (43%), similar to previous reports[21-24].

Patients were treated with hysteroscopic adhesiolysis, which is, in literature, currently the standard treatment for Asherman's syndrome[15,18]. Hysteroscopy has rapidly grown in use in the last decades, becoming the standard procedure for evaluating the uterine cavity. It enables us to have simultaneous direct visualization of the uterine cavity and the treatment of intrauterine pathologies during the same process. However, the specific operative approach for intrauterine adhesions is still debated to define optimal management to achieve the best possible results. Over the past few years, different techniques of hysteroscopic adhesiolysis have been described and suggested. Hysteroscopic scissors are used to resolve adhesions[13,25]. Hysteroscopic resection with a monopolar probe was also found to be efficient. However, cold instruments are preferred since the use of electricity could damage them even more, the endometrium[26,27]. Our study used the Storz 22 Fr monopolar hysteroscope in 6 cases. In one case, the office hysteroscope was needed to introduce a wider hysteroscope through the uterine cervix.

The reoccurrence of adhesions is estimated to be between 21 and 42 %, depending on the grade of the operated adhesions[17]. However, no established approaches to further preventing intrauterine adhesions exist and long term data are limited. Approaches that have been associated with reduced postoperative adhesion formation are postoperative hormone therapy, semisolids (gel), intrauterine contraception devices (IUD), Foley catheters and intrauterine balloons[26]. In our study, several approaches were used. Second look hysteroscopy that was performed two weeks months after the first surgery and resection of newly formed adhesions seemed to improve pregnancy rates as well as delivery rates[27]. Another method is the application of estrogen after the procedure to enhance endometrial growth, although there are no evidence based recommendations on the optimal formulation or duration of estrogen regimens. Estrogen is used alone or in combination with an intrauterine device or Foley catheter to prevent contact between uterine walls. According to the literature, pregnancy rates are higher if estrogen is used with some mechanical barrier between uterine walls[28]. Another investigated method was a hyaluronic gel, which significantly reduces the reformation of adhesions according to a randomized controlled trial[29]. However, later studies could not confirm that hyaluronic gel was more effective than no prevention[30]. We decided to use the combination of an intrauterine device and hyaluronic gel. In addition, we decided to use a classic intrauterine device without copper instead of a Foley catheter since the balloon causes compression of the endometrium and, in our opinion, this would lower the perfusion of the tissue that needs to be well perfused for the endometrium

to grow. An inflated balloon in the uterine cavity also causes discomfort in women.

However, our analysis has some limitations. First, the analyzed group of 7 patients; therefore, our study is unable to detect the difference in reproductive results due to the relatively small sample size. Second, we could not assess the impact on the mode of delivery due to a small number of overall deliveries. Moreover, we did not include a control group in this study as there is no standard treatment for intrauterine adhesions.

Conclusion

In conclusion, intrauterine adhesions may be a high risk factor for infertility and pregnancy loss. The extent of the cavity involved is one of the main factors for the prognosis of reproductive outcomes. Hysteroscopic adhesiolysis for Asherman's syndrome is a relatively safe and effective choice for resolving issues in menstrual bleeding patterns and treating infertility. A combination of hyaluronic gel and intrauterine device after hysteroscopic resection of intrauterine adhesions was well tolerated, resulting in restored uterine cavities and satisfactory reproductive and obstetric outcomes in our case series.

Acknowledgment

The authors would like to thank the specialists, the interns and the nurses at the Department of Human Reproduction at the University Medical Centre Ljubljana for completing and checking the databases and the obstetricians in Slovenia for reporting to the National Perinatal Information System regularly.

Author Contributions

Helena Ban Frangež designed the research, performed the study and revised the manuscript. Vesna Šalamun, Jančar Nina, Dzhamilyat Abdulkhalikova and Sara Korošec provided research data. Eva Skuk analyzed the data and wrote the manuscript.

Ethics Approval And Consent To Participate

The study on women after reproductive surgery was approved by the National Medical Ethics Committee at the Ministry of Health of the Republic of Slovenia (No. 0120-174/2018/6) and was conducted following the WMA Declaration of Helsinki. Collection and analysis of anonymized data of deliveries from the National Perinatal Information System are allowed by the Personal Data Protection Act (Article 17, Official Gazette of the Republic of Slovenia No 94/07, 2004) and by the Healthcare Databases Act (Official Gazette of the Republic of Slovenia No 65/00, 2000; No 47/15, 2015; 31/18, 2018). Before inclusion to surgical procedures, each patient signs an informed consent for the procedure and anonymized data collection and analysis for research purposes. The present research was performed by relevant guidelines and regulations. The patients/participants provided written informed consent to participate in this study.

Conflict Of Interest

The authors declare no conflict of interest.

Funding

This research received no external funding.

References

1. Deans R, Abbott J. Review of intrauterine adhesions. J Minim Invasive Gynecol 2010;17(5):555-569.
2. Salazar CA, Isaacson K, Morris S. A comprehensive review of Asherman's syndrome: causes, symptoms and treatment options. Curr Opin Obstet Gynecol 2017;29(4):249-256.
3. Asherman JG. Amenorrhoea traumatica (atretica). J Obstet Gynaecol Br Emp 1948;55(1):23-30.
4. The American Fertility Society classifications adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, müllerian anomalies and intrauterine adhesions. Fertil Steril 1988;49(6):944-955.
5. Chen Y, Chang Y, Yao S. Role of angiogenesis in endometrial repair of patients with severe intrauterine adhesion. Int J Clin Exp Pathol 2013;6(7):1343-1350.
6. Al-Inany H. Intrauterine adhesions. An update. Acta Obstet Gynecol Scand 2001;80(11):986-993.
7. Taskin O, Sadik S, Onoglu A, et al. Role of endometrial suppression on the frequency of intrauterine adhesions after resectoscopic surgery. J Am Assoc Gynecol Laparosc 2000;7(3):351-354.
8. Sharma JB, Sharma E, Sharma S, Dharmendra S. Female genital tuberculosis: Revisited. Indian J Med Res 2018;148(8):71-83.
9. Poujade O, Grossetti A, Mougel L, et al. Risk of synechiae following uterine compression sutures in the management of major postpartum hemorrhage. BJOG 2011;118(4):433-439.
10. Song D, Liu Y, Xiao Y, et al. A matched cohort study comparing the outcome of intrauterine adhesiolysis for Asherman's syndrome after uterine artery embolization or surgical trauma. J Minim Invasive Gynecol 2014;21(6):1022-1028.
11. Yu D, Li TC, Xia E, et al. Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. Fertil Steril 2008;89(3):715-722.
12. Vitale SG, Parry JP, Carugno J, et al. Surgical and Reproductive Outcomes after Hysteroscopic Removal of Retained Products of Conception: A Systematic Review and Meta-analysis. J Minim Invasive Gynecol 2021;28(2):204-217.
13. Yu D, Wong YM, Cheong Y, Xia E, Tin-Chiu L. Asherman syndrome--one century later. Fertil Steril 2008;89(4):759-779.
14. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 2000;73(2):406-411.
15. AAGL Elevating Gynecologic Surgery. AAGL Practice Report: Practice Guidelines on Intrauterine Adhesions Developed in Collaboration with the European Society of Gynaecological Endoscopy (ESGE). J Minim Invasive Gynecol 2017;24(5):695-705.
16. Hooker AB, Lemmers M, Thurkow AL, et al. A systematic review and meta-analysis of intrauterine adhesions after miscarriage: prevalence, risk factors and long-term reproductive outcome. Hum Reprod Update 2014;20(2):262-278.
17. Hanstede MM, van der Meij E, Goedemans L, et al. Results of centralized Asherman surgery, 2003-2013. Fertil Steril 2015;104(6):1561-1568.
18. Yamamoto N, Takeuchi R, Izuchi D, et al. Hysteroscopic adhesiolysis for patients with Asherman's syndrome: menstrual and fertility outcomes. Reprod Med Biol 2013;12(4):159-166.
19. Pabuçcu R, Atay V orhon E, Urman B, Ergün A. Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. Fertil Steril 1997;68(6):1141-1143.
20. Capella-Allouc S, Morsad F, Rongières-Bertrand C, et al. Hysteroscopic treatment of severe Asherman's syndrome and subsequent fertility. Hum Reprod 1999;14(5):1230-1233.

21. Fedele L, Vercellini P, Viezzoli T, Ricciardiello O, Zamberletti D. Intrauterine adhesions: current diagnostic and therapeutic trends. Acta Eur Fertil 1986;17(1):31-37.

22. Feng Z, Yang B, Shao J, Liu S. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions after induced abortions: Clinical analysis of 365 cases. Gynaecological Endoscopy 2001;8:95-98.

23. Zikopoulos KA, Kolibianakis EM, Platteau P, et al. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the Versapoint system. Reprod Biomed Online 2004;8(6):720-725.

24. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment and reproductive outcome. Am J Obstet Gynecol 1988;158(6):1459-1470.

25. Huang X, Li TC, Xia E. Hysteroscopic adhesiolysis using the "ploughing technique". Annals of Translational Medicine 2020;8(13):811.

26. Di Spiezio Sardo A, Calagna G, Scognamiglio M, O'Donovan P, Campo R, De Wilde RL. Prevention of intrauterine post-surgical adhesions in hysteroscopy. A systematic review. Eur J Obstet Gynecol Reprod Biol 2016;203:182-192.

27. March CM. Management of Asherman's syndrome. Reprod Biomed Online 2011;23(1):63-76.

28. Xu W, Zhang Y, Yang Y, Zhang S, Lin X. Effect of early second-look hysteroscopy on reproductive outcomes after hysteroscopic adhesiolysis in patients with intrauterine adhesion, a retrospective study in China. Int J Surg 2018;50:49-54.

29. Acunzo G, Guida M, Pellicano M, et al. Effectiveness of auto-cross-linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic adhesiolysis: a prospective, randomized, controlled study. Hum Reprod 2003;18(9):1918-1921.

30. Lin XN, Zhou F, Wei ML, et al. Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis. Fertil Steril 2015;104(1):235-240.