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TITLE :
HYSTEROSCOPY AND ASSISSTED REPRODUCTIVE TECHNOLOGY

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ABSTRACT

Background: Hysteroscopy is an excellent instrument for evaluating the uterine characteristics in infertile women. It is the gold standard in the assessment of uterine anomalies today.

Aim This review examines the two main applications of hysteroscopy in infertile patients who are candidates for assisted reproductive techniques: (1) In the evaluation the cervix, uterine cavity and rule out any pathology or lesions that could have been missed by hysterosalpingography or sonohysterography. (2). Hysteroscopic surgery as treatment for uterine abnormalities in infertile patient going for assisted reproduction.

Methods: A literature search was conducted using Medline, Pub med, Springer link and Highwire press . the following search terms were used: hysteroscopy, fertility, assisted reproduction, ART, , IVF.. In this review, ART include any form of assisted reproduction, including IVF/ICSI and ovarian stimulation with or without artificial insemination.

Results:
Conclusion: Hysteroscopy is proposed as a necessary investigation prior to IVF cycles and is the mainstay of treatment of uterine anomalies in assisted reproduction.

KEYWORDS
Hysteroscopy, Assisted Reproduction, Infertility

INTRODUCTION

Anomalies within the uterine cavity play an important role in fertility because they are capable of interfering with implantation. Adhesions, septa, polyps, submucous myomas, adenomyosis, endometritis, anomalies of the cervical canal, and lesions of the uterotubal junction are uterine disorders most often observed during investigation of and are implicated in infertility(1). The proper diagnosis and treatment of these anomalies is vital to achieving success in assisted reproduction.

Hysterosalpingography can be used to evaluate tubal patency but provides inadequate information about the uterine cavity (numerous false-positives and false-negatives) and pelvic ultrasound is especially helpful for diagnosing interstitial anomalies in the uterus(1). Hysteroscopy, however, allows direct visualization of the uterine cavity, the endometrial mucus (and the cervical canal). The examination maybe practiced on an out-patient basis, without anesthesia, using appropriate small-caliber instruments and irrigation with physiological saline(2).It may be necessary as a first line investigation because a significant percentage of patients have uterine pathology that may impair the success of fertility treatment. (3,4,5). Hysteroscopic treatment of these anomalies is also possible at the same time.(1,6).

The role of hysteroscopy in assisted reproduction has expanded over the years and the applications are still evolving. There is a growing consensus towards its use in the primary investigation of infertile women prior to In-Vitro Fertilization (2,4,6),as well as in the management of hydrosalpinges in such patients, in place of laparoscopy(7,8,9).

In this review, an attempt is made to examine the various applications of hysteroscopy in assisted reproduction in recent published literature, with particular focus on its use in primary assessment before IVF, assessment after repeat IVF failures as well as the uses of hysteroscopic surgery in assisted reproductive technology.

MATERIALS AND METHODS

A literature search was conducted using Medline, Pubmed , Springer link and Highwire press. The following search term were used: hysteroscopy, fertility, assisted reproduction, ART, IVF. In this review, ART include any form of assisted reproduction, including IVF/ICSI and ovarian stimulation with or without artificial insemination.

Abstracts had to be written in English and if the abstract was pertinent and relevant to the topic, the full article whether in English, German or French was sought. Other sources included Google using the same keywords and the websites of different organizations, such as ESHRE, IFFS, FIGO etc.

There were 1456 citations in total. Selected publications were screened for further references. Criteria for selection of literature included; year of publication(publications more than 10 years old were largely ignored), types of study (preference for systematic reviews and randomized controlled studies), methods of analysis (statistical or non-statistical) and institution where studies were done(specialized fertility and endoscopic units).

FINDINGS AND DISCUSSION

Prevalence of Uterine Anomalies

The prevalence of uterine anomalies in patient undergoing IVF varies widely depending on the study population. A review by Bozdag et al revealed rates of 18-50% in patients undergoing IVF and 40-43% in patients with known IVF failures(5). Hucke and colleagues in a review found 20% anomaly rates among infertile women(6). Four Prospective studies were reviewed with findings of 38% by Hinckley and Milki and 40.6% by Lorusso et al in pre-IVF treatment women while rates of 18% by La Sala et al, and 45% by Olivera et al, in women with recurrent implantation failure(RIF)(3,10,11,12). Endometrial polyps and uterine septum seem to be more frequent in our infertile patients than in the general population (13).

The prevalence figures revealed from this review are quite significant and are a strong argument for a more extensive assessment of the uterine cavity as part of the primary assessment of patients planned for assisted reproduction.

Diagnostic Hysteroscopy: Pre-IVF Treatment and Post-IVF Failures

There is increasing argument that diagnostic hysteroscopy be included as part of routine investigation of infertile couple undergoing IVF (6). The accepted practice in the past had been the review of uterine cavity by Hysterosalpingography with a resort to diagnostic hysteroscopy after recurrent implantation failures (RIF). Economic considerations and lack of expertise is thought to contribute to the reluctance to use hysteroscopy as primary investigative tool (2). A number of prospective studies, 2 RCTs and a systematic review were reviewed under this heading.

A prospective study of 1000 patients undergoing pre-IVF hysteroscopy revealed 62% had a normal uterine cavity. Thirty-two percent had endometrial polyps. Other pathology included submucous fibroids (3%), intrauterine adhesions (3%), polypoid endometrium (0.9%), septum (0.5%) retained products of conception (0.3%), and bi-cornuate uterus (0.3%)(3).

De Placido et al in a prospective series of 950 patients compared mini-hysteroscope (n=602) with 5mm hysteroscope (n=348) in an office setting. There were no difference in cavity finding in the two groups(13). In the prospective series by Lorusso et al, 555 pre-IVF and 311 post IVF failure patients had hysteroscopy followed by IVF cycle. The implantation and pregnancy rates were similar between the groups. Clinical outcomes in patients with repeated IVF failure who had hysteroscopy with no pathology compared with those who had pathology, did not show any statistical differences(10).

Olivera et al and La Sala et al prospectively studied 55 and 100 post IVF patients undergoing diagnostic hysteroscopy respectively. Of the 55 in the Olivera series, 25 (45%) had abnormalities which were treated(12). Eighteen percent of patients in the La Sala series had uterine anomalies (11).

In a randomized controlled study by Rama Raju and colleagues, 520 pre-IVF patients were randomized into a hysteroscopy and a no- hysteroscopy group. Group I (n = 265)

did not have office hysteroscopy. Group II (n = 255) had office hysteroscopy and were further sub-classified into Group II a and Group II b. Group IIa (n = 160) had normal hysteroscopic findings whereas Group IIb (n = 95) had abnormal office hysteroscopy findings, which were corrected at the same time. There was no difference in the mean number of oocytes retrieved, fertilization rate, and number of embryos transferred among the patients in different groups. Statistically significant difference was observed in terms of clinical pregnancy rates between Group I and Group II a (26.2 and 44.44%, $P < 0.05$), and Group I and Group II b (26.2 and 39.55%, $P < 0.05$), respectively (14).

Similarly, a RCT of post IVF failure patients were carried out by Demirol and Gurgan. Four hundred and twenty-one patients who had undergone two or more failed IVF-embryo transfer cycles were prospectively randomized into two groups. Group I (n = 211) did not have office hysteroscopic evaluation, Group II (n = 210) had office hysteroscopy. The patients who had normal hysteroscopic findings were included in Group IIa (n = 154) and patients who had abnormal hysteroscopic findings were included in Group IIb (n = 56). Intrauterine lesions diagnosed were operated during the office procedure. Fifty-six (26%) patients in Group II had intrauterine pathologies and the treatment was performed at the same time. No difference existed in the mean number of oocyte retrieved, fertilization rate, and number of embryos transferred or first trimester abortion rates among the patients in groups. Clinical pregnancy rates in Group I, Group IIa and Group IIb were 21.6%, 32.5% and 30.4% respectively. There was a significant difference in the clinical pregnancy rates between patients in Group I and Group IIa (21.6% and 32.5%, $P = 0.044$, respectively) and Group I and Group IIb (21.6% and 30.4%, $P = 0.044$, respectively). There was no significant difference in the clinical pregnancy rate of patients in Groups IIa and IIb. Patients with normal hysterosalpingography but recurrent IVF-embryo transfer failure should be evaluated prior to commencing IVF-embryo transfer cycle to improve the clinical pregnancy rate(15).

A systematic review of studies evaluating the influence of outpatient (office) hysteroscopy on the outcome of the subsequent IVF cycle was conducted by El Toukhy(16). All trials comparing the outcome of IVF treatment performed in patients who had outpatient hysteroscopy in the cycle preceding their IVF treatment with a control group in which hysteroscopy was not performed were included. The main outcome measure was pregnancy rate. In total, 1691 participants were included in two randomized (n = 941) and three non-randomized controlled studies (n = 750). The quality of the studies was variable. Meta-analyses of the results of five studies showed evidence of benefit from outpatient hysteroscopy in improving the pregnancy rate in the subsequent IVF cycle (pooled relative risk = 1.75, 95% CI 1.51-2.03). The evidence from randomized trials was consistent with that from non-randomized controlled studies (16).

Thus, these studies along with the prevalence figures provide strong evidence for including diagnostic hysteroscopy as part of the primary investigation of infertile couple planned for assisted conception. Future robust randomized trials comparing outpatient hysteroscopy or mini-hysteroscopy with no intervention before IVF treatment would be a useful addition to further guide clinical practice (16).

Office Hysteroscopy versus Conventional Hysteroscopy

Although diagnostic and operative laparoscopy are well established in gynaecology, diagnostic hysteroscopy is, however, not widely used in the office setting because of the discomfort produced by the procedure. Indeed, conventional hysteroscopy is performed under general anaesthesia with a 4mm optical scope with 5mm external sheath, speculum and tenaculum to grasp and fix the uterus and it sometimes requires cervical dilatation. Since it seems invasive, traumatic and painful it is not very widely acceptable (4). Current evidence seems to weigh heavily in favour of office hysteroscopy.

All of the prospective studies on diagnostic hysteroscopy in this review were done as office procedures in all cases or for most (3,10,11,13,14,15). This implies the pre-eminence of office hysteroscopy in recent practice. Isaacson in a review suggested that under utilization of office diagnostic hysteroscopy denies many women a technique that is likely to keep them from more invasive and less useful procedures, such as diagnostic hysteroscopy and dilatation and curettage performed in the operating room under general anesthesia (2).

The prospective series by De Placido et al concluded that office mini-hysteroscopy is a very effective diagnostic tool in an infertility work-up and is more widely accepted than traditional hysteroscopy (13).

In a multi-centre RCT by Rudi Campo et al, patients were randomly assigned to undergo office diagnostic hysteroscopy either with 5.0mm conventional instruments (n 5 240) or with 3.5mm mini-instruments (n 5 240). Procedures were stratified according to patient parity and surgeon's previous experience. The indications for hysteroscopy were infertility in 219 cases (46%). The pain experienced during the procedure (0–10), the quality of visualization of the uterine cavity (0–3) and the complications were recorded. The examination was considered successful when the pain score was <4, visualization score was >1 and no complication occurred. Less pain, better visualization and higher success rates were observed with mini-hysteroscopy ($P < 0.0001$, $P < 0.0001$ and $P < 0.0001$, respectively), in patients with vaginal deliveries ($P < 0.0001$, $P < 0.0001$ and $P < 0.0001$, respectively) and in procedures performed by experienced surgeons (P 5 0.02, P 5 NS and P 5 NS, respectively). The effects of patient parity and surgeon experience were no longer important when minihysteroscopy was used. They concluded that mini-hysteroscopy can be offered as a first line office diagnostic procedure (4).

Hysteroscopic Surgery in Assisted Reproduction

Operative hysteroscopy has been accepted progressively as the best option for the treatment of intra-uterine pathologies such as polyps, submucous myomas, septum and adhesions (1,4,6). In this respect, hysteroscopic surgery has replaced conventional abdominal surgery. Surgical hysteroscopy is used to treat these anomalies. Patients receive general anesthesia. A high-frequency, low-voltage electric current is used, and glycine for irrigation. This procedure allows resection of submucous myomas and polyps and of septa and adhesions. Some groups use laser beams and irrigation by physiological

saline for these treatments. Coagulation of a superficial focal spot of adenomyosis is not useful in infertility therapy. (1)

There are not many publications addressing surgical hysteroscopy specifically in assisted reproduction, most studies address it in the wider context of managing infertility.

Hysteroscopic Metroplasty for Uterine Septum

The aim of metroplasty is to restore a normal uterine anatomy to improve obstetrical outcomes in some uterine malformations. The hysteroscopic septoplasty cures the septate uterus. It is an effective procedure in the case of recurrent abortion losses. It probably improves the rate of live birth in women without obstetrical antecedent. For some authors, it could be considered at the time of the diagnosis and as first-line treatment in an Assisted Reproductive Techniques (ART) program (17).

Hysteroscopic resection of the septum improves fecundity of women with septate uterus and otherwise unexplained infertility. Patients with septate uterus and no other cause of sterility have a significantly higher probability of conceiving after removal of the septum than patients affected by idiopathic sterility(18).

In a randomized prospective trial comparing 2 procedures for metroplasty: resectoscopy with monopolar knife was compared with small-diameter hysteroscopy fitted with a Versapoint device. It involved one hundred and sixty patients with septate uterus and a history of recurrent abortion or primary infertility undergoing hysteroscopic metroplasty from 2001 to 2005. Hysteroscopic resection of the uterine septum was performed with either a 26F resectoscope with unipolar knife (80 women, group A) or a 5-mm diameter hysteroscope with Versapoint device (80 women, group B). All patients were managed expectantly, with follow-up lasting 1 year. Operative parameters (operative time, fluid absorption, complications, need for second intervention) and reproductive outcome parameters (pregnancy, abortion, term and preterm delivery, modality of delivery, cervical cerclage) were measured. Operative time and fluid absorption were significantly greater in group A than in group B (23.4 +/- 5.7 vs 16.9 +/- 4.7 minutes and 486.4 +/- 170.0 vs 222.1 +/- 104.9 mL, respectively). The cumulative complication rate was significantly lower in group B than in group A. No difference in any of the reproductive parameters was observed between the 2 groups: pregnancy and delivery rates were 70% and 81.6% in group A vs 76.9% and 84% in group B. Nine women (18.4%) from group B and 8 women (16%) from group B experienced spontaneous abortions. Most patients (54/82) delivered by cesarean section without differences according to the hysteroscopic technique used for metroplasty (65% in group A vs 67.7% in group B) or to the gestational age (65.1% of term and 68.7% of preterm deliveries).
The study concluded that small-diameter hysteroscopy with bipolar electrode for the incision of uterine septum is as effective as resectoscopy with unipolar electrode regarding reproductive outcome and is associated with shorter operating time and lower complication rate(19).

Hysteroscopy for Management of Uterine Synaechiae

Uterine synaechiae precludes success in assisted reproductive techniques and so need to be diagnosed and treated. While sonohysterography and hysterosalpingography are useful as screening tests of intra-uterine adhesions, hysteroscopy remains the mainstay of diagnosis (1).
Hysteroscopy has also become the accepted optimum route of surgery, aimed at restoring the size and shape of the uterine cavity, normal endometrial function and increasing chances at IVF. Treatment options range from simple cervical dilatation in the case of cervical stenosis but an intact uterine cavity, to extensive adhesiolysis of dense intrauterine adhesions using scissors or electro- or laser energy.

Magos in a review concluded that patients in whom the uterine fundus is completely obscured and those with a greatly narrowed, fibrotic cavity present the greatest therapeutic challenge. Several techniques have been described for these difficult cases, but outcome is far worse than in patients with mild, endometrial-type adhesions (20).

The review by Kodaman and Arici concluded that diagnosis and treatment of intra-uterine adhesions are integral to the optimization of fertility outcomes and that favorable result in terms of pregnancy and live birth rates can be expected after hysteroscopic adhesiolysis. Postoperative mechanical distention of the endometrial cavity and hormonal treatment to facilitate endometrial regrowth appear to decrease the high rate of adhesion reformation. Newer anti-adhesive barriers may also prevent the recurrence of intra-uterine adhesions. Endometrial development can remain stunted due to a scant amount of residual functioning endometrium and fibrosis. Potential pregnancy complications, especially placenta accreta, after the treatment of intra-uterine adhesions should be anticipated and discussed with the patient (21).

Hysteroscopic management of Hydrosalpinges

It is well known that the success of assisted reproductive techniques, especially IVF, for patients with tubal pathologies such as hydrosalpinx is reduced by half compared with patients without hydrosalpinx (22).

Theories explaining the mechanisms behind the impaired outcome of in-vitro fertilization still focus on the hydrosalpingeal fluid. The negative effects of hydrosalpinx have generally been attributed largely to: (i) mechanical effects of fluid washing out uterine contents; (ii) embryo and gametotoxicity from toxic hydrosalpinx fluid; (iii) alterations in endometrial receptivity markers; or dwindled cross talk between embryo-endometrium resulting in hindered implantation, and (iv) direct effect on endometrium, leading to intrauterine fluid formation. The underlying mechanism explaining reduced implantation and embryo development awaits further research (23).
The pertinent question is to determine the best mode of treatment. Surgical treatment is generally advocated but a choice has to be made between salpingectomy and proximal tubal occlusion.

A Cochrane systematic review by Johnson and colleagues examined the efficacy of surgical intervention for tubal disease before IVF. Three randomised controlled trials involving 295 (or couples) were included in this review. The odds of ongoing pregnancy and live birth (Peto odds ratio (OR) 2.13, 95% confidence interval (CI) 1.24 to 3.65) were increased with laparoscopic salpingectomy for hydrosalpinges prior to IVF. The odds of pregnancy were also increased (Peto odds ratio (OR)1.75, 95%CI 1.07 to 2.86). There was no significant difference in the odds of ectopic pregnancy (Peto OR 0.42, 95%CI 0.08 to 2.14), miscarriage (Peto OR 0.49, 95%CI 0.16 to 1.52) or treatment complications (Peto OR 5.80, 95%CI 0.35 to 96.79). No data were available concerning the odds of multiple pregnancy.
The reviewers concluded that laparoscopic salpingectomy should be considered for all women with hydrosalpinges prior to IVF treatment (24).

Kontoravdis et al in a Prospective randomized study to evaluate and compare the clinical impact of proximal tubal occlusion and salpingectomy when performed before IVF in patients with hydrosalpinges, concluded that proximal tubal occlusion, when performed in women with unilateral or bilateral hydrosalpinges before their IVF treatment, represents a potentially beneficial surgical procedure, increasing significantly the chances for successful implantation and for clinical and ongoing pregnancy. Proximal tubal occlusion may be viewed as a valid alternative when salpingectomy is technically difficult or not feasible. One hundred fifteen patients with unilateral or bilateral hydrosalpinges, who were candidates for IVF treatment had laparoscopic proximal tubal occlusion or laparoscopic salpingectomy, controlled ovarian stimulation, IVF, and embryo transfer. Patients who underwent proximal tubal occlusion before IVF demonstrated significantly increased implantation, clinical-pregnancy, and ongoing-pregnancy rates compared with those with no surgical intervention and demonstrated implantation, clinical-pregnancy, and ongoing-pregnancy rates comparable to those who underwent salpingectomy(25).

There is now a preference for achieving proximal tubal occlusion via hysteroscopy. Darish and El Saman carried out a prospective comparative study to determine whether hysteroscopic tubal occlusion will produce the same efficacy as laparoscopic tubal occlusion of functionless hydrosalpinx prior to IVF/ICSI. The study phase included 27 patients with uni- or bilateral functionless hydrosalpinges, who were randomly divided into 2 groups. Group A comprised 14 patients who were randomly allocated for laparoscopic occlusion. Group B included 13 patients scheduled for a hysteroscopic approach. Laparoscopic occlusion of the isthmic part of the fallopian tube was carried out using bipolar diathermy in 9 (64%) cases or clips in 3 (21.4%) cases in Group A. Roller ball electrode of the resectoscope was utilized for occlusion of the tubal ostium under local, spinal, or general anesthesia in Group B. Second-look office hysteroscopy was performed in Group B whenever possible. In both groups, hysterosalpingography or sonohysterography was carried out 1 month later to confirm tubal occlusion. The mean number of abdominal scars/patient was 1.4 and 1.5 in both groups, respectively. Unilateral functionless hydrosalpinx was encountered in 7 (50%) and 5 (38%) cases in both groups, respectively. In Group A, the procedure was possible and successful in 10 cases (76.9%), while in Group B, hysteroscopic access and occlusion were achieved in 12

(85.7%) and 9 (64.2%) cases, respectively. In Group B, diagnostic hysteroscopy showed fine marginal adhesions in 2 cases (15%), and a small polyp in 1 case (7.7%). Hysteroscopic tubal occlusion showed shorter operative time (9+/-2.8 versus 24+/-4.8 min, p=0.0001) and hospital stay (2+/-1.8 versus 5+/-1.1h, p=0.0001). Second-look office hysteroscopy was performed in 8 cases in Group B and revealed no significant cornual lesions at the site of hysteroscopic occlusion(7).
This preliminary study demonstrates the feasibility of hysteroscopic tubal occlusion of functionless hydrosalpinx in all cases with acceptable efficacy. It has the advantage of adding a valuable evaluation of the endometrial cavity prior to IVF/ICSI. It should be an option for treatment protocol in cases of functionless hydrosalpinges (7).

The recent introduction of the Essure microinsert has added impetus to the drive for hysteroscopic management of hydrosalpinges.
Hiktari et al in a prospective case series of 5 women with unilateral or bilateral hydrosalpinges on transvaginal ultrasound, laparoscopy, or hysterosalpingogram who were planning further fertility therapy, concluded that hysteroscopic placement of the Essure microinsert is a minimally invasive option for proximal tubal occlusion in patients requiring occlusion of hydrosalpinges before IVF and with contraindications to abdominal surgery. This technique may offer a safer alternative (8).

Mijaytovic et al conducted a prospective, single-arm, clinical study to investigate the success rate of proximal tubal occlusion with Essure devices in subfertile women with hydrosalpinges, and to observe the results of subsequent treatment with IVF. Ten women with uni- or bilateral hydrosalpinges prior to IVF were involved. In all patients laparoscopy was felt to be contraindicated. Hysteroscopic placement of Essure devices was carried out in an office setting. All patients had successful placement of the Essure devices without any complications. Proximal tubal occlusion was confirmed by hysterosalpingography in 9 out of 10 patients. A 40% ongoing pregnancy rate was achieved with 20% life births after one IVF cycle and/or frozen embryo transfer. They concluded that proximal occlusion of hydrosalpinges with Essure devices before IVF is a successful treatment for patients with a contraindication for salpingectomy (9).

Hysteroscopic Myomectomy for Submucous Fibroid

Uterine fibroids occur in 30% of women and are associated with a degree of subfertilityand they interfere with infertility(). But, the effect of fibroids on the outcome of assisted reproductive techniques specifically, has not been investigated much.

However in a study by Hart et al, data were prospectively collected on 434 women undergoing IVF/ICSI in the assisted conception unit of an inner London teaching hospital. During the study period, 112 women with (study), and 322 women without (controls), intramural fibroids were treated. Patients were similar regarding the cause and duration of their infertility, number of previous treatments, and basal serum FSH concentration. Women in the study group were on average 2 years older (36.4 versus 34.6 years; $P < 0.01$). There was no significant difference in the duration of ovarian stimulation or gonadotrophin requirement, number of follicles developed, oocytes

collected, embryos available for transfer or replaced. When analyzing only women with intramural fibroids of ≤5 cm in size (n = 106) pregnancy, implantation and ongoing pregnancy rates were significantly reduced: 23.3, 11.9 and 15.1 respectively compared with 34.1, 20.2 and 28.3% in the control group (P = 0.016, P = 0.018 and P = 0.003). The mean size of the largest fibroids was 2.3 cm (90% range 2.1–2.5 cm). Logistic regression analysis demonstrated that the presence of intramural fibroids was one of the significant variables affecting the chance of an ongoing pregnancy, even after controlling for the number of embryos available for replacement and increasing age, particularly age 40 years, odds ratio 0.46 (95% CI 0.24–0.88; P = 0.019). This study demonstrated that an intramural fibroid halves the chances of an ongoing pregnancy following assisted conception.(26)

Racknow and Arici, in a review in 2005 concluded that fibroid location, followed by size, is the most important factor determining the impact of fibroids on IVF outcomes. Any distortion of the endometrial cavity seriously affects IVF outcomes, and myomectomy is indicated in this situation. Myomectomy should also be considered for patients with large fibroids, and for patients with unexplained unsuccessful IVF cycles (27)

Somigliana et al in their analysis concluded that available evidence also suggests that submucosal, intramural and subserosal fibroids interfere with fertility in decreasing order of importance. Physicians are advised to pursue a comprehensive and personalized approach clearly exposing the pros and cons of myomectomy to the patient, including the risks associated with fibroids during pregnancy on one hand, and those associated with surgery(28).

Surrey and colleagues, in a prospective case-controlled study evaluated the impact of myomectomy on in vitro fertilization-embryo transfer (IVF-ET) and oocyte donation cycle outcome. Patients were grouped with submucosal leiomyomata resected hysteroscopically (group A: 15 oocyte donor recipients; group 1 = 31 IVF-ET patients) and those with intramural components or strictly intramural leiomyomata that distorted or impinged upon the endometrial cavity resected at laparotomy (group B = 26 oocyte donor recipients; group 2 = 29 IVF-ET patients). Precycle hysteroscopic or abdominal myomectomy were performed with subsequent fresh IVF-ET or oocyte donation. Results of controlled ovarian hyperstimulation as well as ongoing pregnancy and implantation rates were evaluated in comparison with contemporaneous patient groups without such lesions (group C = 552 oocyte donor recipients; group 3: 896 IVF-ET patients). The mean number and size of leiomyomata were significantly larger in patients who underwent abdominal myomectomy. However, neither ongoing pregnancy nor implantation rates were significantly different in comparison with controls among either oocyte donor recipients (group A: 86.7%, 57.8%; group B: 84.6%, 55.2%; group C 77%, 49.1%). The findings were similar for those undergoing IVF-ET in comparison with controls (group 1: 61%, 24%; group 2: 52%, 26%; group 3: 53%, 23%). This study showed that precycle resection of appropriately selected clinically significant leiomyomata results in IVF-ET or oocyte donation cycle outcomes that are similar to controls.(29)

Kolankaya and Arici concluded in their review that myomas that compress the uterine cavity with an intramural portion and submucous myomas significantly reduce pregnancy rates, and should be removed before assisted reproductive techniques are used and that hysteroscopic myomectomy is the gold standard for the treatment of submucous myomas (30).

In reviewing surgical technique employed at hysteroscopy, 2 publications were examined:

Attilio et al in a review of surgical techniques, confirmed that myomas that compress the uterine cavity with an intramural portion and submucous myomas significantly reduce pregnancy rates, and should be removed before assisted reproductive techniques are used and that hysteroscopic myomectomy is the gold standard for the treatment of submucous myomas. The choice of the technique mostly depends on the intramural extension of the fibroid, as well as on personal experience and available equipment. 'Resectoscopic slicing' still represents the 'gold standard' technique for treating fibroids, even if several other effective techniques including ablation by neodymium-yttrium-aluminum-garnet laser, morcellation and office myomectomy have been proposed. At present, the 'cold loop' technique seems to represent the best option as it allows a safe and complete removal of such fibroids in just one surgical procedure, while respecting the surrounding healthy myometrium(31).

Touboul and colleagues tried to determine the rate of uterine synechiae after bipolar hysteroscopic myomectomy in patients suffering from infertility(32). In a retrospective case series study, a group of 53 patients with primary (n = 30) and secondary (n = 23) infertility who underwent bipolar hysteroscopic resection of myomas between 2001 and 2006, and an outpatient hysteroscopy was performed 2 months after the fibroid resection. The formation of uterine synechiae and pregnancy rates were collected from the patients' clinical notes. The submucosal myomas were intracavitary class 0 (n = 12), intramural class 1 (n = 19), and intramural class 2 (n = 22). The mean age of the women was 35.0 +/- 4.8 years. The mean myoma size was 25 +/- 11 mm. Postoperative office hysteroscopies revealed synechiae in four (7.5%) of 53 patients. Sixteen (32.7%) of the 49 patients not lost to follow-up conceived, and 12 (24.5%) of them delivered at term. Myoma size >/=3.5 cm and age <35 years were associated with a significantly higher pregnancy rate in univariate and multivariate analysis. They concluded that the incidence of uterine synechiae after bipolar hysteroscopic resection of fibroids was 7.5%. This appears to be lower than that reported in previous studies using monopolar energy(32).

Thus, bipolar hysteroscopic myomectomy may be a better option for infertile women.It must be said ,however, that drawing clear guidelines for the management of fibroids in infertile women is difficult due to the lack of large randomized trials aimed at elucidating which patients may benefit from surgery(32).

Hysteroscopic management of Endometrial polyps

There were very few studies addressing hysteroscopic polypectomy in assisted reproduction and there is no consensus about the management of patients diagnosed with endometrial polyp in IVF cycles.

Lass and colleagues at Bourn Hall Clinic Cambridge, investigated the effect of endometrial polyps on pregnancy outcome in an in vitro fertilization (IVF) program. Endometrial polyps less than 2 cm in diameter were suspected by transvaginal ultrasound before oocyte recovery in 83 patients. Forty-nine women (Group I) had standard IVF-embryo transfer, while in 34 women (Group II) hysteroscopy and polypectomy were performed immediately following oocyte retrieval, the suitable embryos were all frozen, and the replacement cycle took place a few months later. Of the 32 hysteroscopies, a polyp was diagnosed in 24 cases (75%) and polypoid endometrium in another 5 patients (15.6%). An endometrial polyp was confirmed by histopathological examination in 14 women (58.3%). The pregnancy rate in group I was similar to the general pregnancy rate of the unit over the same period (22.4 vs 23.4%) but the miscarriage rate was higher (27.3 vs 10.7%, P = 0.08). In Group II, the pregnancy and miscarriage rates were similar to those of the frozen embryo cycles at Bourn Hall (30.4 and 14.3 vs 22.3 and 12.1%, respectively).Their conclusion was that small endometrial polyps, less than 2 cm, do not decrease the pregnancy rate, but there is a trend toward increased pregnancy loss. A policy of oocyte retrieval, polypectomy, freezing the embryos, and replacing them in the future might increase the "take-home baby" rate(33).

Batioglu and Kavmak in a prospective series reported 6 patients with endometrial polyp (measuring <2 cm) diagnosed by transvaginal ultrasonography performed on days 7 and 9 of the cycle in patients who underwent IVF. These six patients were treated by hysteroscopic polypectomy preceding oocyte retrieval under general anaesthesia after informed consent was obtained. The cause of infertility was male factor in three patients, tubal factor in one, and two cases were unexplained. All patients had undergone ovulation induction and luteal support according to the long luteal protocol. As a result, in three cases pregnancy was achieved (one multiple and two singleton) and three cases were unsuccessful. One of the pregnant women gave birth at term, while the other two pregnancies are still ongoing. They concluded that, with no consensus regarding the management of patients diagnosed with endometrial polyp in IVF cycles. Cryopreservation, cycle cancellation and embryo transfer preceding polypectomy is the current management choice(34).

Madani et al in a similar series studied, nine patients who underwent assisted reproduction treatment cycles and were diagnosed with endometrial polyps less than 1.5 cm by transvaginal ultrasonography. Eight patients were treated by long protocol and one patient was the recipient of an egg donation cycle. In all patients, polyp resection was performed through hysteroscopic polypectomy. Polypectomy was done during ovarian stimulation in the standard treatment cycles, and during hormone replacement therapy in

the recipient of the egg donation cycle. The interval between polyp resection and embryo transfer was 2-16 days. Four patients achieved pregnancy (two twins, two singletons), four patients were unsuccessful, and one pregnancy was a blighted ovum. All of the successful pregnancies were still ongoing.They concluded that if polypectomy before embryo transfer in an IVF cycle is proven to be safe, then embryos will be transferred without cycle cancellation. And that since this study included nine patients; further studies with more patients are required to confirm these findings(35).

In a different scenario, Perez-Medina and colleagues carried out a prospective randomized study to determine whether hysteroscopic polypectomy before intrauterine insemination (IUI) achieved better pregnancy outcomes than no intervention. A total of 215 infertile women from the infertility unit of a university tertiary hospital with ultrasonographically diagnosed endometrial polyps (EP) undergoing IUI were randomly allocated to one of two pretreatment groups using an opaque envelope technique with assignment determined by a random number table. Hysteroscopic polypectomy was performed in the study group. Diagnostic hysteroscopy and polyp biopsy was performed in the control group. Total pregnancy rates and time for success in both groups after four IUI cycles were compared by means of contingency tables and life-table analysis. A total of 93 pregnancies occurred, 64 in the study group and 29 in the control group. Women in the study group had a better possibility of becoming pregnant after polypectomy, with a relative risk of 2.1 (95% confidence interval 1.5–2.9). Pregnancies in the study group were obtained before the first IUI in 65% of cases. Their conclusion was that hysteroscopic polypectomy before IUI is an effective measure(36).

Implications for Sub-Saharan Africa

Diagnostic and operative hysteroscopy are not used equally worldwide, neither is the practice of assisted reproductive techniques. There were no studies accessed on hysteroscopy in assisted reproduction from SubSaharan Africa. However,infertility is a worldwide issue in reproductive health, more so in Africa. Negative consequences of childlessness are experienced to a greater degree in developing countries when compared with Western societies(37). Bilateral tubal occlusion due to sexually transmitted diseases and pregnancy-related infections is the most common cause of infertility in developing countries, a condition that is potentially treatable with assisted reproductive technologies (37).

In view of the World Health Organization's definition of health, the psychological and social consequences of infertility simply cannot be ignored. Prevention of infertility is difficult and does not help the couple seeking medical advice for infertility, whereas efficient treatment for infertility is time consuming, expensive and often unsuccessful (38). New reproductive technologies are either unavailable or very costly in developing countries(37). It is sadly obvious that, as in all developmental issues, Sub-Saharan Africa is being left behind.

Strategies to tackle these short-comings would include optimizing the use of modern gynaecological endoscopy where possible. Exhaustive infertility investigation can be conducted within the span of two couple-physician contacts, thereby responding to the

couple's concern, avoiding loss of time and energy due to inappropriate therapies, and directing the subfertility treatment correctly from the start(38).

Trained gynaecologists can easily conduct this investigation even in developing countries with proper planning and allocation of resources. The investigation can be employed either with an emphasis on diagnosis alone (and then even under local anaesthesia) or, if the necessary infrastructure is available, in combination with operative endoscopy under general anaesthesia where indicated(38).

Implementation of infertility care in low-resource settings include simplification of diagnostic and ART procedures, minimizing the complication rate of interventions, providing training-courses for health-care workers and incorporating infertility treatment into sexual and reproductive health-care programmes(37). The use of office hysteroscopy will also help to reduce cost and is more convenient for patients(2,4). There is also a need to stimulate and encourage research in Endoscopy and ART in Sub-Saharan Africa.

For the reasons of social justice, infertility treatment in developing countries requires greater attention at national and international levels (37).

CONCLUSION

Hysteroscopy is efficacious as primary assessment in couples planned for ART. It is also the gold standard in the management of detected uterine anomalies. Office hysteroscopy is a safe and viable alternative to conventional hysteroscopy and should be encouraged even more so in low-resource settings in order to optimize patient preparation.

The applications of hysteroscopy in assisted reproduction is rapidly evolving. There are, however many areas of hysteroscopy which require more research to enable the adoption of best practices in assisted reproduction.

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