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REVIEW ARTICLE

A Comparative Study of the use of Different Energy Sources in Laparoscopic Management of Endometriosis-Associated Infertility

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ABSTRACT

Background: Although there is controversy about the mechanism by which endometriosis causes infertility, laparoscopic treatment for endometriosis-associated infertility is becoming popular. However, the optimal modality of energy sources used for dissection and ablation in infertile women remains unexplored.

Objective: To study the best available evidence exploring the use of laparoscopic surgery in infertile women with endometriosis, compare various available energy sources, and their effect on surgical outcome and probability of pregnancy.

Methods: A retrospective review of literature was done to explore the role of laparoscopic surgery and various energy sources in managing endometriosis-associated infertility, using keywords—endometriosis, laparoscopy, infertility, electrosurgery and ultrasonic energy.

Results: Laparoscopic treatment of endometriosis using mechanical or electrical technologies was proposed in the 1980s. Later, use of lasers to vaporize endometriosis and to excise adhesions became popular. The invention of ultrasonic generator and tissue response electrosurgical generator has revolutionized laparoscopic surgery for endometriosis.

Conclusion: No prospective randomized double-blind controlled trial has been conducted to date in this area. Current evidence suggests that laparoscopic excision or ablation, either by electrocautery or laser, improves pregnancy rates. However, the impact of newer energy sources and tissue dissection techniques in this field is yet to be explored.

Keywords: Endometriosis, Infertility, Laparoscopy, Electrosurgery, Ultrasonic energy.

INTRODUCTION

Endometriosis is a severely debilitating condition among women of reproductive age group causing pain and infertility. It was first described in 1860 by von Rokitansky. In 1925, Dr Sampson described endometriosis as, "presence of ectopic tissue which possesses the histological structure and function of uterine mucosa".[1]

In the recent years, there has been a significant increase in the number of infertile patients with endometriosis. It is not clear whether this represents an increase, or simply reflects the more frequent use of laparoscopy. The incidence is 40 to 60% in women with dysmenorrhea and 20 to 30% in women with subfertility.[2-4]

Endometriosis is believed to cause infertility based on a higher prevalence of the disease in subfertile women (up to 50%) compared with women of proven fertility (5-10%).[5] In the current era, endometriosis is known to account for 10 to 15% of the cases of infertility.

The goal of treating pelvic and peritoneal endometriosis is to destroy the implants in the most effective and least traumatic way to minimize the formation of postoperative adhesions. Reproductive pelvic surgery procedures performed by laparotomy are frequently complicated by adhesion reformation and by *de novo* adhesion formation. However, endoscopic surgery fulfils the important microsurgical principles of gentle handling of tissue, constant irrigation, meticulous hemostasis, and precise tissue dissection. Operative techniques in endometriosis are dependent upon the type and extent of the lesions. Various technologies can be used, of which hydrodissection and the CO_2 laser appear to be the most efficient tool.[6,7]

This review explores the available evidence addressing the use of laparoscopic surgery in infertile women with endometriosis, and compares various available energy sources and their effect on surgical outcome and probability of pregnancy.

METHODOLOGY

This study entailed a retrospective review of literature using all available English databases, Cochrane register and Medline articles, which explored the role of laparoscopic surgery and various energy sources in managing endometriosis-associated infertility, using keywords—endometriosis, laparoscopy, infertility, electrosurgery and ultrasonic energy. A hand searching of relevant journals and conference proceedings was also done.

PATHOGENESIS AND THE MECHANISM OF INFERTILITY

Several factors are believed to be involved in the pathogenesis of endometriosis. Retrograde menstruation remains the dominant theory for development of pelvic endometriosis. Failure of immunological mechanisms, angiogenesis and production of antibodies against endometrial cells may also have a role. Endometriotic lesions secrete several pro-inflammatory molecules contributing to development of pain and infertility.[8-10]

The most common site of endometriosis is the ovary. Other common sites are peritoneum, ovarian fossa, uterosacral ligaments, uterovesical fold and Pouch of Douglas. It can present as dysmenorrhea, dyspareunia, chronic pelvic pain, infertility, irregular heavy periods, cyclical rectal bleeding, tenesmus, cyclical hematuria, ureteric obstruction, cyclical pain and swelling in the umbilicus or scars.

Although there is substantial evidence confirming an association between endometriosis and infertility, a causal relationship has not yet been established.[11] Nevertheless, the fecundity rate of infertile patients with minimal or mild endometriosis is not significantly lower than that of women with unexplained infertility.[12,13] Endometriosis may thus play a determinant role in infertility in more advanced forms only. In a series of 123 women with endometriosis-associated infertility undergoing expectant management, Olive et al[14] observed a pregnancy rate of 45% in patients with mild disease and 19.5% in those with moderate disease. No conception was achieved in patients with severe lesions.

Moderate-severe endometriosis is likely to result in infertility because of adhesions disrupting the anatomical relationships between fallopian tube and ovary. Severe dyspareunia preventing regular sexual intercourse could also affect fertility. Distal occlusion of the fallopian tube may result in hydrosalpinx, leading to a direct effect on embryos as well as an alteration in uterine implantation.[15]

Other mechanisms by which endometriosis may contribute to infertility include disorders of folliculogenesis or endocrine abnormality, inflammatory or immunological abnormality and increased miscarriage rate.[15] The presence of endometriosis affects multiple aspects of the reproductive cycle, including oocyte quality, embryogenesis, and receptivity of the endometrium. Further evidence of poor oocyte quality and reduced implanting ability of embryos is provided by studies showing no adverse effect on implantation rates in women with endometriosis using donated oocytes. Recipients of oocytes from donors with endometriosis have lower implantation rates.[16-18]

Thus, even though laparoscopic surgery has become the preferred treatment modality, it may not overcome the bio-molecular alterations associated with chronic inflammation and causing infertility. Furthermore, the anatomical insults to reproductive function due to endometriosis, such as tubal damage and severe adnexal adhesions, might be irreversible.

STAGING OF ENDOMETRIOSIS

The American Fertility Society (AFS) proposed its revised staging in 1996.[19] This remains the most widely used classification. This classification considers the size, site and depth of the lesions. Point scores were given depending upon severity. Four stages of the disease were suggested: Stage I (minimal), stage II (mild), stage III (moderate) and stage IV (severe).

The revised AFS score enables easy and clear communication through standardized reporting, but has a number of significant drawbacks:[20]

i. It does not help in comparison of different treatments
ii. It is unable to predict disease progression, impact on future fertility and disease recurrence rate
iii. It is prone to observational variation which impairs reproducibility
iv. It is also a poor indicator of severity as it does not consider bowel adhesions or multifocal nodular disease.

ROLE OF SURGICAL MANAGEMENT

Endometriosis can be treated medically or surgically by laparoscopy or laparotomy. Medical hormonal treatment has no role in the treatment of endometriosis-associated infertility in the absence of pain. This is because any hormonal treatment used to suppress endometriosis is contraceptive and does not improve pregnancy rates. In fact, postoperative hormone therapy in patients with endometriosis prevents pregnancy during what may be the optimal time for conception to occur following surgery.

The advantages of laparoscopic surgery are quicker recovery, shorter hospital stay, effective treatment of ovarian endometriomata and relief of pain. It also improves fertility without increasing the risk of multiple pregnancies associated with assisted conception treatment. The limitation of laparoscopy is the intraoperative risk of injury to adjacent structures. Appropriate surgical skill and availability of appropriate equipment is required. There is a 6.3% conversion rate to laparotomy associated with gynecological laparoscopy.[21] Otherwise laparotomy is indicated only in cases of severe endometriosis with extensive dense adhesions along with deeply infiltrating endometriosis.

Based on the results of a meta-analysis of cohort studies, 15 years ago surgical treatment of endometriosis was estimated to produce overall crude pregnancy rates 38% higher than non-surgical treatment.[22] Moreover, surgical techniques have evolved and instrumentation has improved tremendously.

More convincing evidence emerged from a randomized clinical trial comparing diagnostic laparoscopy alone or resection or ablation of visible lesions that included 341 infertile patients with minimal or mild endometriosis,[23] in whom surgery enhanced fertility.

Endoscopic surgery is precise enough that adhesions can be excised without destroying surrounding tissue or damaging vital structures, such as the ureters, bladder and bowel. Removal of all adhesions and restoration of the normal anatomic relationship of the pelvic organs enhances the fertility.

OPERATIVE TECHNIQUES

A variety of mechanisms, involving some form of physical energy, can be used to divide tissue and enable hemostasis.[24] The available modalities for dissection in minimal access surgery include:

- *Blunt dissection:* Can be done with a closed scissors tip, grasper, inactive suction cannula, heel of inactive electrosurgery hook or a pledget. Blunt dissection is used to open planes and expose structures, especially when the anatomy is obscured by adhesions. Insignificant hemostatic capability is the main disadvantage.
- *Sharp scissors dissection:* Implants are grasped and removed by precise dissection with scissors. This allows histological confirmation and avoids destruction of peripheral tissue. The main disadvantage is the risk of hemorrhage which can usually be controlled by bipolar cauterization.
- *High frequency radio wave electrosurgery:* This is the most convenient and most risky method of dissection in minimal access surgery. Most of the complications in laparoscopic surgery are due to use of energized instrument (1-2%).
  - *HF monopolar electrosurgery:* Monopolar electrosurgery has become the most widely used cutting and coagulating technique in minimal access surgery. This permits complete and deep coagulation of the nodules. Its main advantage is its efficiency and the absence of hemorrhage. Associated complications include thermal injury to nontargeted organs due to insulation failure, direct coupling or capacitive coupling, absence of biopsies and extensive destruction of the surrounding tissue. Other problems encountered include effect on pacemakers, return electrode burns and toxic smoke.
  - *Bipolar diathermy:* A bipolar system is safer as the current does not pass through the patient but instead returns to the generator via the receiving electrode after passage through the grasped tissue. Its main advantages are absence of hemorrhage and restriction of thermal injury to the surrounding tissue. The main disadvantages are superficial coagulation and, therefore, a potentially incomplete treatment of deeper implants. The primary electrothermal tissue effect is limited to desiccation, not cutting. It requires slightly more time than monopolar coagulation because of lower power settings and bipolar generator output characteristics. Hemostasis over a large area is not possible. Grasping dense tissue between both the active and return electrodes is difficult.
- *Ultrasonic surgical dissection (Harmonic scalpel):* This uses mechanical energy at 55,500 vibrations/sec, thus disrupting hydrogen bonds and forming a coagulum. It is ideal for dividing and simultaneously sealing small and medium vessels with less instrument traffic, reduction in operating time, less smoke and no electrical current.
- *High velocity and high pressure water-jet dissection:* This produces clean cutting of reproducible depth. Other advantages are the cleansing of the operating field by the turbulent flow zone. Problems encountered with the use of this modality include the 'hail storm' effect causing excessive misting which obscures vision, lack of hemostasis, difficulty in gauging distance and poor control of depth of the cut.
- *Hydrodissection:* Hydrodissection uses the force of pulsatile irrigation with crystalloid solutions to separate tissue planes. The operating field is kept clear. However, no hemostasis is achievable.
- *Argon beam coagulator:* The argon beamer is used in conjunction with monopolar electrosurgery to produce fulguration or superficial coagulation. Less smoke is produced because there is lesser depth of tissue damage. However, a significant drawback of this modality is an increase in intra-abdominal pressure to potentially dangerous levels due to high-flow infusion of argon gas.
- *Laser dissection:* The degree and extent of thermal damage produced by laser depends on the structure, water content, pigmentation, optical and thermal properties, and perfusion of the tissue.

  Each of the various types of laser available has a specific clinical application.
  - The argon laser coagulator is the ideal method of treating small red endometriotic deposits.
  - *CO_2 laser vaporization:* This is the most efficient technique for superficial ablation permitting a complete, precise, controlled and bloodless destruction of the implants. It can be used on multiple and widespread disease even if the diagnosis of some lesions is doubtful, with minimal risk to adjacent organs, such as the ureter and bowel. Its major drawback is production of smoke. It is relatively inexpensive (compared to other lasers).
  - *CO_2 laser excision:* This method is preferred for large nodules as vaporization is a slow procedure. CO_2 laser excision is equivalent to sharp excision but avoids the problems of hemorrhage and is therefore faster. It is mainly useful for removing rectovaginal nodules.
  - *Other laser procedures:* Nd: YAG laser, KTP laser and holmium laser have also been used to treat endometriotic implants. These lasers are mainly coagulating, and therefore the destruction is less precise than with the CO_2 laser. They are more ergonomic as they can be

used with flexible fibers. However, they are more expensive.

The best therapy is performed with the CO_2 laser vaporization in association with an accurate dissection technique.[7]

- *Tissue response electrosurgical generator* (Ligasure™): This has unique vessel sealing ability. It can be used on vessels up to 7 mm. It precisely confines its effects to the target tissue with virtually no charring, and with minimal thermal spread to adjacent tissue. It senses body's collagen to actually change the nature of the vessel walls by obliterating the lumen.

ENDOSCOPIC SURGERY IN ENDOMETRIOSIS-ASSOCIATED INFERTILITY

Endometriotic Implants

The destruction of implants can be achieved using numerous techniques: Precise excision, bipolar coagulation, monopolar coagulation, CO_2 laser vaporization or excision, and different methods of coagulation using other types of laser. Superficial peritoneal endometriosis is vaporized with the laser, coagulated with monopolar or bipolar current or excised. Implants less than 2 mm can be coagulated, vaporized or excised. When lesion is greater than 3 mm, vaporization or excision is needed. Lesions greater than 5 mm must be excised or deeply vaporized[15] (Fig. 1).

Current guidelines for the treatment of stages I and II endometriosis-associated infertility recommend ablation of endometriosis lesions plus adhesiolysis to improve fertility.[25,26] The beneficial effect of surgical removal of the lesions in mild endometriosis is small and may be short-lived.[27] This may be due to the fact that a number of occult lesions may be left behind after removal of the visible lesions. These may develop into minimal endometriosis and grow further.

Thus, the optimal time for conception is within the first 18 months following surgical resection.[28] However, even after surgery, the monthly fecundity rate remains lower than that in fertile women. This suggests that the destruction of visible endometriotic implants does not affect all factors by which endometriosis contributes to infertility.[23]

Adamson[29] in 1997 proposed that surgery for endometriosis-associated infertility is more effective for severe than mild endometriosis.

Adhesions

Adhesiolysis is difficult in cases of endometriosis. Adhesions are thick and vascular, and often involve bowel, broad ligament, tubes, etc. Different techniques can be employed individually or in association. The best method involves dissection with forceps and/or dissectors, and aquadissection in conjunction with a CO_2 laser (in place of scissors) (Figs 2 and 3).

Endometriomas

There are two different surgical techniques to treat the endometrioma:

i. Cystectomy with excision of the endometriotic cyst (Fig. 4)
ii. Drainage/aspiration of the cyst content and ablation of the cyst capsule with laser or electrocoagulation (Figs 5 and 6).

Cystectomy

Any periovarian adhesions must be removed prior to cystectomy. An entry site is made in the endometrioma on the opposite side of the ovarian hilus. The endometrioma is evacuated and repeatedly washed. A 'cystoscopy' is then performed by introducing the laparoscope into the endometriotic cavity. The inner lining of the cyst is examined to confirm the diagnosis and to eliminate the presence of a malignant cyst. A forceps is used to grasp the ovary at the edge of the incision. A second pair of grasping forceps holds the lining of the cyst. Then, by applying countertraction to the two forceps, cleavage is performed. Generally, the best approach is to pull the cyst away from the ovary.

When the cyst has been completely cleaved, it must be removed from the abdomen using an 'endoscopy bag' or through a suprapubic trocar or the umbilical trocar. A thorough

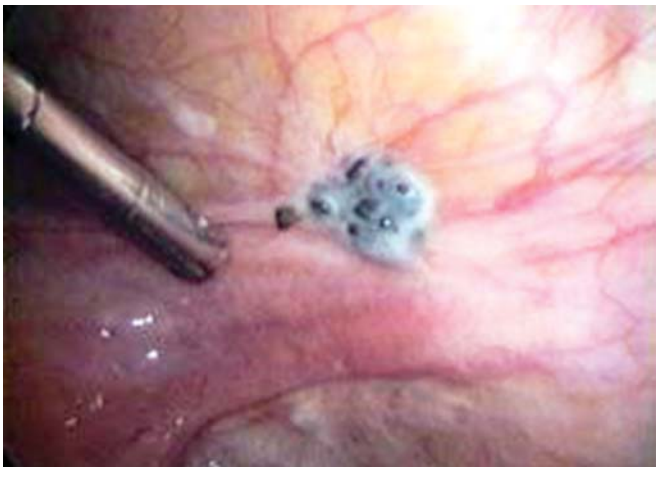

Fig. 1: Endometriotic implants can be excised with scissors or deeply vaporized with bipolar or harmonic scalpel

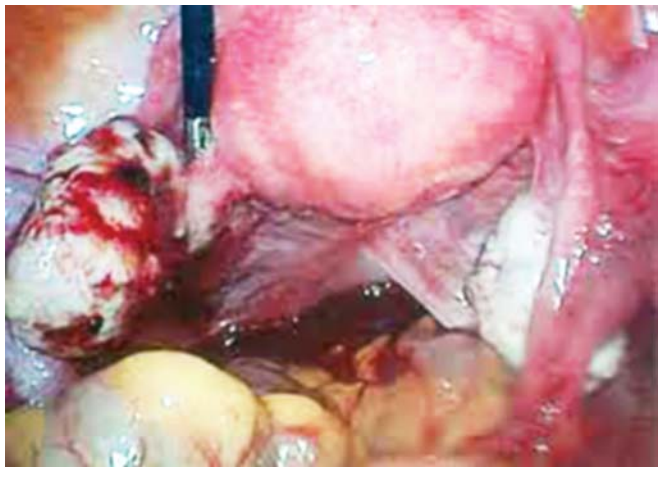

Fig. 2: Dense adhesions may be vascular and are coagulated with bipolar electrocautery before cutting

peritoneal washing is given and hemostasis achieved. The ovary is left unsutured since sutures can cause adhesion formation. However, when necessary, suture is placed within ovarian stroma and the knot is tied inside the ovary to minimize adhesion formation. Alternatively, biological glue can be applied and edges of the incision brought together.

Draining the endometrioma or partially removing its wall is inadequate because the cyst lining remains functional leading to reoccurrence of the symptoms. Two randomized controlled trials reported that laparoscopic ovarian cystectomy for endometriomata results in a better pregnancy rate than drainage alone.[30,31]

Another advantage of excision over ablation is that the cyst can be examined histologically and a diagnosis of ovarian cancer excluded.

Hemorrhage: Any bleeding from the intraovarian vasculature is minimal and is self-controlled within a few minutes. Hemorrhage from the hilus may occur during the dissection of the inferior pole of the cyst. This can be difficult to locate. The immediate solution is to evert the entire ovary in order to localize it and then control hemostasis using bipolar electrocoagulation. Monopolar electrocoagulation must be avoided because of the risks of accidents and complete coagulation of the ovarian vascularization.

Laser Vaporization of Endometrioma

The endometrioma is opened, aspirated and washed. It is then largely incised to evert the internal layer which is destroyed by vaporization with a CO_2 laser, introduced through the laparoscope. The results are apparently equivalent with different types of lasers, but Argon or KTP lasers induce less bleeding and are easier to use since they can travel through flexible fibers. This is easily done with small cysts (< 3 cm), but in cases of larger cysts it is impossible to be sure that all the internal layer has been destroyed.

Rectovaginal Septum and Uterosacral Ligaments Endometriosis

Deep endometriosis exists when the lesions penetrate 5 mm or more.[32] In addition to pain, most of these patients suffer from associated infertility. Operative laparoscopy for these lesions

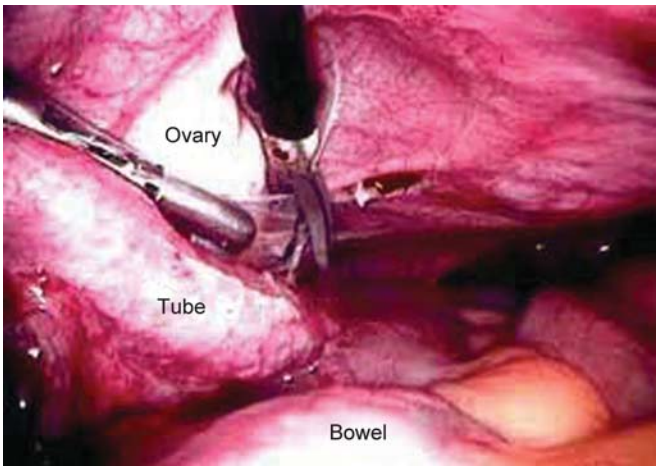

Fig. 3. Flimsy adhesions can be directly cut by sharp dissection with scissors

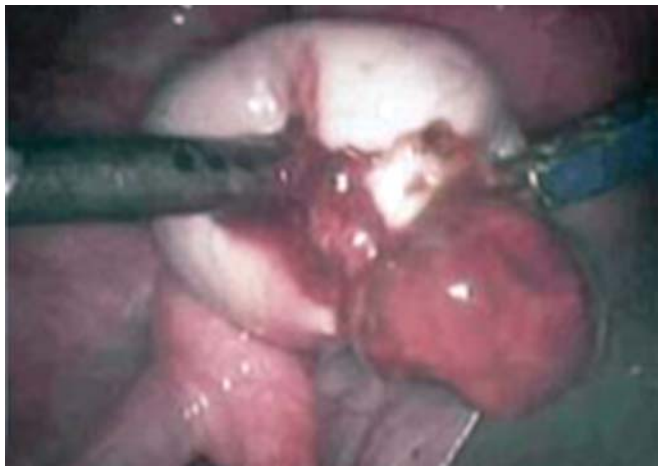

Fig. 5: Puncture of endometriotic cyst using monopolar with tritome for drainage and aspiration of the cyst contents

Fig. 4. Excision of the endometriotic cyst wall can be done with monopolar current using electrosurgical hook, or the vibrating jaw of the harmonic scalpel or bipolar coagulation, followed by sharp dissection with scissors

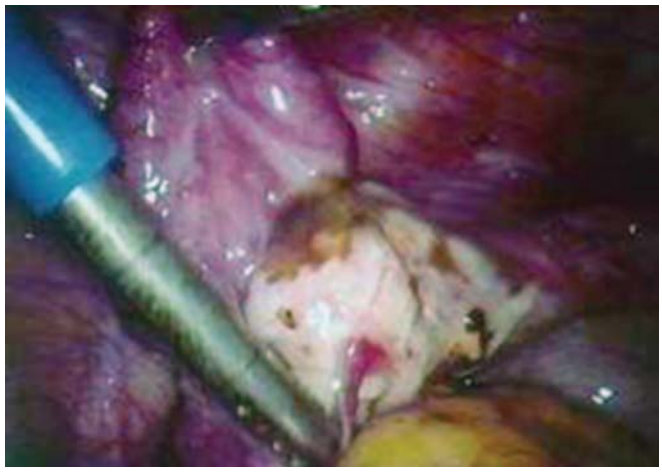

Fig. 6: Stripping of the cyst capsule from ovarian cortex

often involves considerable dissection. It is, thus, necessary to establish precisely the impact on fertility of this type of surgery (Fig. 7).

Either laser or aqua dissection can be used, separately or combined. Dissection must be performed with care to avoid any injury to organs, such as the rectum or ureters. In some cases it may be safer to catheterize the ureter in order to facilitate this dissection.

POSTSURGICAL FERTILITY OUTCOMES

A 50% pregnancy rate was obtained after laparoscopic management in a series of 814 women with endometriomas.[33] The removal or destruction of endometriomas may provide more benefit than simply restoring the normal anatomy and ovarian structure.

In another study, CO_2 laser was used laparoscopically for removal of endometriotic implants.[34] Of 102 infertile patients, 60.7% conceived within 24 months after laparoscopy. The rates of conception after surgery were: 75% for patients with mild endometriosis, 62% for moderate endometriosis, and 42.1% for patients with severe endometriosis.

However, it has been suggested that ovarian surgery for endometriomas could be deleterious for the residual normal ovarian tissue, either by removing ovarian stroma with oocytes together with the capsule or by thermal damage provoked by coagulation.[15] However, a recent histological analysis revealed that the ovarian tissue surrounding the cyst wall in endometriomas is morphologically altered and possibly not functional. Thus, a functional disruption may already be present before surgery.[35] Therefore, the decreased ovarian response observed in patients previously treated for a large ovarian endometrioma, may also be a consequence of the disease.

EFFECT OF ENDOSCOPIC SURGERY ON IVF CYCLES

With advances in IVF, a number of patients opt for IVF without undergoing adequate surgical treatment of endometriosis. The success rate of IVF in women with endometriosis is lower compared with that of women undergoing IVF for other indications. Laparoscopic excision of endometrioma before IVF reduces the risk of worsening endometriosis during ovarian stimulation, reduces the risk of infection during oocyte retrieval and allows histological diagnosis avoiding occult malignancy.

Thus, laparoscopic diagnosis and treatment of endometriosis is believed to be useful in increasing the probability of conception either spontaneously or with IVF treatment.

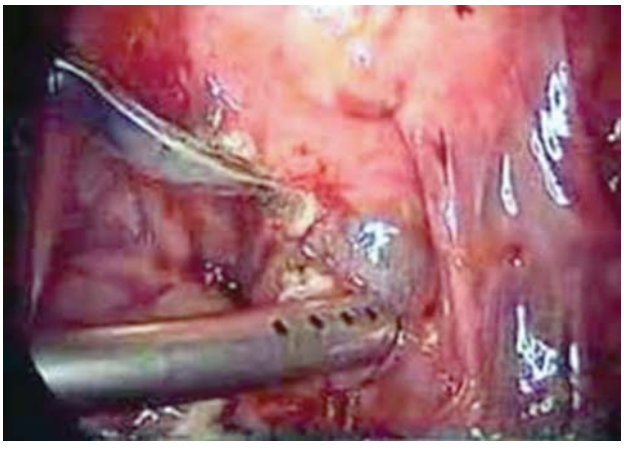

Fig. 7: Excision of deep rectovaginal endometriosis with bipolar electrocautery and scissors. Harmonic scalpel or CO_2 laser may be used alternatively

STRATEGY OF MANAGEMENT IN INFERTILITY

Three different situations may be encountered:[24]

i. Clinical diagnosis of endometriosis is suspected. Diagnostic laparoscopy, staging and treatment are performed in the same operative sitting.
ii. Clinical diagnosis of endometriosis is suspected. Diagnostic laparoscopy reveals extensive endometriosis for which laparoscopic treatment appears extremely difficult. Medical treatment may be administered for 3 to 6 months, followed by laparoscopic surgery performed as a second step.
iii. When severe endometriosis can be diagnosed without laparoscopy according to clinical findings or ultrasound scan, medical therapy is given before laparoscopic treatment. In the last two situations, GnRH analogs are prescribed for 3 to 6 months prior to laparoscopic treatment.

In women with stage I/II endometriosis-associated infertility, expectant management or superovulation/IUI after laparoscopic excision or ablation of all visible disease can be considered for younger patients. Women, 35 years of age or older, should be treated with superovulation/IUI or IVF-ET. In women with stage III/IV endometriosis-associated infertility, conservative surgical therapy with laparoscopy and possible laparotomy are indicated.[11]

Based on a literature review, the most realistic intrauterine pregnancy rate achieved is ~ 40%.

There is no advantage of repeating surgery within a short interval as this may reduce ovarian reserve and increase the risk of a poor response to ovarian hyperstimulation for IVF.

CONCLUSION

Current evidence suggests that laparoscopic excision or ablation, either by electrocautery or laser improves pregnancy rates. The dissection technique and energy source required depends on the type and constituency of the tissue and the extent of the lesions. The ideal dissection technique requires a modality that can accomplish meticulous hemostasis and will be tissue selective without causing inadvertent tissue damage. In actual practice, a combination of energy forms is applied with selection of the most appropriate one at each particular phase of the operation.

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