7

Amenorrhea and Endometrial Ablation: A Review and New Insights

Immerzeel Peter and Van Eijndhoven Hugo
Isala Klinieken Zwolle
Netherlands

1. Introduction

Amenorrhea and menorrhagia are opposites and not in any way related to each other. However, the main goal of endometrial ablative therapy in menorrhagia is to establish amenorrhea. Therefore, it is obvious that we spend some words on this subject. Menorrhagia is an important problem in premenopausal women visiting their gynaecologist or general practitioner. Treatment of menorrhagia is diverse: oral contraceptives, intra-uterine hormone devices, hysterectomy, or, endometrial ablation. The latter has proved itself as a valuable technique which is fast, minimal invasive and cost-effective without need for hospitalisation. In this chapter we will discuss the history, the different techniques, indications and complications and some special features of endometrial ablation.

2. History

Heavy menstrual bleeding or menorrhagia affects approximately 20% of all healthy premenopausal women aged 30-49 (Vessey, 1992), causing anaemia and/or a decrease in quality of life. It is a widespread problem and approximately 12% of all referrals to a gynaecologist are related to heavy menstrual bleeding.
First step in treatment is medical therapy, that is to say oral contraceptives. The efficiency of this therapy is variable and the best result with an optimal medicamental treatment is about 50% reduction of the amount of blood loss (EHC, 1992). The levonorgestrel-releasing intrauterine system is more effective and reduces heavy menstrual bleeding in 94% (Irvine, 1998). However, many women prefer a non-hormonal treatment when the conservative treatment with oral contraceptives or a levonorgestrel-releasing system is not sufficient. In this group of patients sometimes surgical therapy is indicated. For decades hysterectomy was the only surgical treatment. Although very effective, hysterectomy involves significant physical implications, a high price in both social and economic costs, a high rate of major and minor post-operative complications and a long recovery time.
Targeted endometrial destruction was originally developed and published in 1936 by Bardenheuer (Bardenheuer, 1937), using a radiofrequency electrosurgical probe passing through the cervical canal into the endometrial cavity without endoscopic guidance. Another technique, was developed in 1967 by Cahan and Brockunier (Cahan and

Brockunier, 1967), called cryoendometrial ablation. They used a probe, also without endoscopic guidance, cooling the endometrial lining. Both techniques did not become widely adopted and the use of endometrial ablation was limited until the introduction of hysteroscopy. After 1980, a new less invasive, uterine sparing method, the hysteroscopic endometrial ablation was developed. The first techniques described were the laser ablation, transcervical endometrial resection (TCRE) and rollerball endometrial ablation. The aim of all three techniques was to remove, or destroy the entire thickness of the uterine endometrial lining and the basal endometrial glands present in the superficial myometrium. These techniques were all hysteroscopic, performed under general anaesthesia and requiring good surgical skills for the best therapeutic effect. These techniques, referred as the first generation, are intensively studied and became the gold standard for endometrial ablation in treatment of heavy menstrual bleeding. Compared to medicamental treatment the results of these techniques were much better but obviously less effective than hysterectomy. However, patient satisfaction is high and complication rate is lower compared to hysterectomy (Abbot, 2002).

With ongoing development, a new generation of minimal invasive techniques without the need of the typical surgical skills of the first generation, was born: the so called second generation endometrial ablation. The main difference between the first and second generation techniques is the absence of the hysteroscopy. This makes the technique easier to perform, with a lower risk of complications and without the need for skilled surgeons. Although a whole number of methods are taken together and called the second generation, in reality it is a wide variety of different techniques: the hot liquid balloons, the microwave, bipolar ablation, phototherapy and chemical destruction of the endometrial lining. With the development of the second generation, operation time and hospitalisation became shorter, with a lower need for complimentary surgery following non satisfactory treatment and a higher satisfactory rate (Lethaby, 2009).

3. Endometrial ablation techniques

The development of endometrial destruction techniques starts around 1937 as mentioned before. For long time the idea of endometrial destruction was leaved. During the eighties of previous century, the idea was revived due to new techniques and insights from other medical specialities, especially the urologists.After that period the development of the techniques was a bit faster and is going on till today. Table 1. summarizes the available techniques.

3.1 First generation techniques

3.1.1 Laser

In 1981 Milton Goldrath introduced the first hysteroscopically assisted photo vaporisation of the endometrium (Goldrath, 1981). They used a device that could be introduced through the instrument channel of an operating hysteroscope. The method he used was a Neodymium: Yttrium Alumnum Garnet laser, (Nd:YAG). Because of the high costs and the development of new hysteroscopic techniques, gynaecologists collectively replaced the heavy and expensive technique of laser ablation by the resectoscope. These newer methods, influenced by the resectoscope of the urologist, were adopted worldwide.

Endometrial destruction techniques.
Hysteroscopic: • Nd:YAG laser • Electorsurgical rollerbal • Transcervical resection.

Non hysteroscopic:
• Balloon thermal ablation
  • CavatermTM plus
  • Thermachoice®
  • Thermablate®
  • Menotreat®
• Free fluid thermal ablation
  • Hydro Thermablate®
• Microwave ablation
  • MEA®
• Bipolar radiofrequency ablation
  • Novasure®
• Cryotherapy
  • HerOption®

Other: • Endometrial laser intrauterine thermal therapy: ELITT   • Gynelease® • Chemoablation • Photodynamic ablation

Table 1. Endometrial destruction techniques.

3.1.2 Electrosurgical rollerball and transcervical resection of the endometrium

Inspired by the results and knowledge of the urologic resections, new techniques were invented to replace the laser photo vaporisation of the endometrium. The resectoscope that was developed could pass through the instrument channel of an operating hysteroscope. With this loop shaped monopolar electro coagulating assisted resectoscope endometrium can be removed from the entire endometrial cavity (Decherney, 1987). The electrosurgical rollerball is also a hysteroscopic monopolar technique, with the difference that it is not resecting, but only coagulating the endometrial lining. Both methods could be and are often combined in the same session.

3.2 Second generation techniques

The difficulties experienced with the first generation paved the way to develop new techniques without a need for typical surgical skills and without the complications associated with the hysteroscopic technique. Although these newer methods do not require direct visualisation of the endometrium by hysteroscopy, they are mutually different, using either heat or cold, microwave or radiofrequency energy. Compared to the first generation the complication rates are lower, operation time is shorter and some of these techniques can be applied in an outpatient setting. Their effectiveness and safety are intensively studied

and compared to the first generation techniques. These randomised controlled trials are summarized at the end of this paragraph.

3.2.1 Balloon thermal ablation

Balloon thermal ablation basically is a technique in which a balloon catheter attached to a central unit is placed in the uterine cavity. The balloon is then filled with a distension fluid and because of a constant pressure the balloon shapes the endometrial cavity as effective as possible. By heating and circulating the fluid for a specific time, endometrial ablation is accomplished . The balloon techniques differ in cervical dilatation, distension fluid, temperature of fluid, distension pressure and operating time. The main complications are postoperative nausea and uterine cramps, probably related to uterine distension and prostaglandin release. All available techniques are listed below.

3.2.1.1 Cavaterm™ plus

The original Cavaterm™plus unit, consists of a computerised central unit and a single-use silicone balloon. The balloon size can be adjusted according to the size of the uterine cavity. The fluid used is 1.5% glycine, heated from the centre of the catheter to 75 degrees Celsius and constantly circulated throughout the system via a pump. The system monitors the pressure within the circuit and it is maintained between 220-240 mm Hg. The treatment time is 15 minutes and the depth of endometrial ablation is 6-8 mm. Cavaterm plus system uses a 5% dextrose solution and requires cervical dilatation only to 6 mm. The duration of treatment is 10 minutes and there is no need for pre-treatment of the endometrium. The device is portable and has a small diameter probe. To be effective, the intimate contact between the balloon and the endometrium is important. Patient satisfaction rate as recorded is 83% after two years, amenorrhea was achieved in 39% of the patients. (El Thouky, 2004).

3.2.1.2 Thermachoice III

Thermachoice ® comprises a single use balloon catheter, a connecting cable and a dedicated controller unit that is powered from a standard alternating current wall outlet. The outside diameter of the catheter is 5.5 mm and the heating element is incorporated in the balloon itself. After exposure of the cervix and the required dilation, the balloon-tipped catheter is passed through the cervical canal into the endometrial cavity. The surgeon uses a syringe to inflate the balloon with 5% dextrose and water to a predetermined pressure of 160 tot 180 mm Hg. The dedicated controller unit is then activated, therby heating the element and the fluid. The target balloon temperature is 87 degrees Celsius and ablation time is about 8 minutes. The depth of ablation is 4.5 mm. Patient satisfaction rate as registered is 95.9% after one year, amenorrhea is achieved in 15.2% of the patients, complimentory surgery was necessary in 33% of the patients after 5 years (Loffer, 2002).

3.2.1.3 Thermablate®

Thermablate®, an endometrial ablation system (EAS), consists of a light weight, reusable, hand-held treatment control unit with a single-use disposable catheter of 6 mm in diameter. Following insertion of the prelubricated balloon into the endometrial cavity, a glycerine solution is heated to 173 degrees Celsius and the pressure is automatically maintained at 180 mm Hg for a treatment cycle of 2 minutes and 8 seconds. Tissue necrosis to a uniform depth of 4-5 mm. can be accomplished.

3.2.1.4 Menotreat ®

MenoTreat® is a relatively new method, which is mainly used in the Scandinavian countries. The system consists of a disposable silicone catheter with a balloon (two possible sizes) and a control unit. The cervix is dilated to 8 mm for insertion of the 7 mm diameter catheter. The fluid, saline is heated to 85 degrees Celsius in the control unit and circulates from there through the catheter. The pressure is maintained at 200 mm Hg and the treatment time is 11 minutes.

3.2.2 Free fluid endometrial ablation

Endometrial ablation with HydroThermablator® (HTA) is based on the principle of circulating heated free fluid and is the only technique with hysteroscopic monitoring during the procedure. The device consists of a single use 7.8-mm sheath which is connected to a proprietary controller unit. The controller unit regulates the processes of uterine distension, creation of a closed circuit, fluid heating, and monitoring of temperature and circuit volume. The distending medium is normal saline drawn from a bag mounted on a attached, modified IV pole. After dilatation of the cervix and priming of the circuit, the telescope and sheath are placed transcervical into the endometrial cavity. After confirmation of intracavitary positioning, the microprocessor-controlled automated system is started. The tip of the endoscope and sheath are held at the level of the internal cervical OS. The process takes approximately 3 minutes to heat the fluid to 90 degrees Celsius. The hot fluid is maintained for10 minutes in the uterine cavity, after which it is allowed to cool down in one minute before removal of the device. Necrosis depth is about 3-4 mm. The process can be stopped at any time by the surgeon. If there is a loss of more than 10 mL of the distending medium either through the cervix or the fallopian tubes, the system stops the procedure automatically. To prevent leakage of hot fluid through the fallopian tubes the intra uterine pressure is kept below 55 mm Hg. Specific complications of this technique are perineal, vaginal and thigh burns when the hot fluid leaks from the cervix. The amenorrhea rate reported with the HydroThermablator was 53%, with decrease in menstrual bleeding in 94% of the patients treated. Patient satisfaction rate is high, 98% after 3 years and complementary surgery is necessary in about 11% of the patients (Goldrath, 2003).

3.2.3 Microwave endometrial ablation

There are two versions of the microwave endometrial ablation (MEA) device, one reusable and the other disposable. FemWave® comprises an 8 mm outside diameter probe attached through a reusable cable to a dedicated control module. The microwave frequency is 9.2 GHz, power output 30 W, and the local tissue is heated to about 90 degrees Celsius, achieving a depth of tissue necrosis of about 5-6 mm. The probe also contains an integrated thermal coupling device that transmits information about adjacent tissue temperature to the control module. Activation and control of the device is entirely in the hands of the surgeon. Once the cervix is dilated, hysteroscopic imaging confirms intracavitary placement and after both the canal and cavity are confirmed to be intact, the microwave probe is inserted to the uterine fundus. When the measured temperature of the tissue around the probe reaches 30 degrees Celsius, the device is activated and the surgeon uses sweeping movements in the horizontal plane until a treatment temperature threshold of 80 degrees Celsius is reached. By gradually withdrawing the device the surgeon covers the entire endometrial surface. When the tip of the probe reaches the area

that approximates the location of the cervical channel, the device is deactivated and the probe is removed. Treatment time depends on cavity size and is usually about 2-4 minutes. Endometrial curettage prior to MEA application is not recommended as it increases the risk of unrecognised uterine perforation and subsequent microwave-induced bowel damage. Patient satisfaction after 5 years is about 71%, and amenorrhea is achieved in 84% of patients after 5 years (Sambrook, 2010).

3.2.4 Radiofrequency endometrial ablation

NovaSure® is an ablation technique that uses impedance controlled bipolar radiofrequency (RF) for endometrial ablation. The system is based on a dedicated microprocessor-based control unit and a single use 7.2 outside diameter probe with a bipolar gold mesh electrode array located at the distal end. To detect a perforation of the myometrium, the probe contains a system for determining the integrity of the endometrial cavity based on injection of a fixed volume of CO2. After appropriate cervical dilatation, the electrode assembly is inserted transcervically and the electrode is deployed by retraction of an outer sleeve. The electrodes have a triangular shape that correspond with the surface of the uterine cavity. The surgeon then measures the intercornual distance using an indicator on the probe and enters this value together with the cavity length into the controller unit allowing the system to calculate the amount of power required. Before activation, the dedicated controller unit performs a so called uterine integrity test to exclude a perforation. After this RF energy is applied to the endometrial tissue and at the same time steam and carbonized debris is evacuated from the uterine cavity. This process results in electrosurgical vaporization and underlying desiccation in a relatively short time (90-120 seconds). The depth of vaporization and desiccation varies throughout the uterine cavity, less in the cornual areas and more in the other areas. The process is controlled by increasing tissue impedance of the adjacent desiccated tissue, shutting the system off when it exceeds 50 omega. Patient satisfaction rate of the Novasure® method is 92.8%. After one year, 41% of the patients reported amenorrhea and 88.3% with a satisfactory decrease in monthly menstrual bleeding. Complementary surgery is seen in 9.8% of patients after 5 years (Kleijn, 2008).

3.2.5 Cryotherapy

Cryotherapy was first used in 1967 but enthusiasm was restrained by reports of pelvic abscesses after this procedure. With the development of transcervical uterus sparing techniques for endometrial ablation, the principle of cryotherapy was revitalized resulting in a device called Her Option®. Destruction of the endometrium is achieved by freezing it to -90 degrees Celsius. The device consists of a disposable 4.5 mm outside diameter probe attached to a handle and cable, which is connected to a dedicated controller unit. After exposure of the cervix, cervical dilation is performed if necessary, and the device is inserted into the uterine cavity. The surgeon activates the controller which super cools the tip of the probe to -90 degrees Celsius, resulting in a progressively expanding elliptical frozen zone involving both endometrium and myometrium. The size of this zone depends on the exposure time and can be monitored by the surgeon using transabdominal ultrasound. To cover all the endometrium usually 2 or 3 cycles, with a total treatment time of about 10 minutes, are necessary. The depth of tissue necrosis is about 12 mm. Clinical outcomes shows a reduction in menstrual bleeding of 84.6%, with amenorrhea rates not well documented. Long term follow up shows a hysterectomy rate of about 7% and a reablation rate of 8.1% after 24 months (Townsend, 2003).

3.2.6 Endometrial laser intrauterine thermal therapy (ELITT)

The ELITT diode laser system (Gynelase®) is a system that produces 830nm diode laser light through a flexible quartz fibre to an intrauterine device., This device is composed of three fibres that ensure circumferential diffusion of the active laser light inside the uterine cavity. The fibres adhere to the uterine walls and uniformly distribute the laser beam over the endometrium from the fundus to the isthmus of the uterine cavity. This procedure exploits the thermic and coagulative properties of the laser beam in a way that the poorly accessible cornual endometrium also can be ablated. The cervical canal is first dilated up to 7 mm, and the closed diffuser device is then introduced into the uterine cavity. When it reaches the fundus, the surgeon opens the lateral fibres, giving the system an inverted triangular shape that adapts to the uterine cavity. The laser is activated for 7 minutes in a continuous tissue exposure mode in three consecutive steps; distension fluid is not required for this procedure. Results of ELITT show an amenorrhea rate of 61% after 36 months and an overall patient satisfactory rate of 89%, re-intervention by hysterectomy is reported in 5% of the patients (Perino, 2004).

3.2.7 Photodynamic therapy

Photodynamic therapy for endometrial ablation (PEA), provides a photo oxidation-based, selective endometrial destruction, tested mainly in animal studies. There is only one human feasibility study executed (Degen, 2004). PEA was performed by injecting 5-aminolevulinic acid (ALA) into the uterine cavity. After three to six hours a light dose of 160J/cm3 at a wavelength of 635 nm was applied to the endometrial lining using a balloon-light diffuser. The light was fractionated in sequences of 5 minutes of illumination followed by gaps of 2 minutes. Bleeding patterns were significantly reduced 1-3 months after treatment, but this reduction was not significant after long term follow up. This technique is still in an experimental stage.

3.2.8 Chemoablation

With so called chemo ablation 95% trichloroacetate (TCA) is used to destroy the endometrium. This compound is also used in the treatment of papilloma warts. Before the procedure, patients receive non-steroidal anti-inflammatory drugs orally. Under local anaesthesia, with a paracervical block, a 3mm cannula must be inserted into the cervix. Through this cannula the volume of TCA needed is instilled into the uterine cavity. Leakage from the cervix is collected in a sponge. The treatment results were recorded both with and without pre-treatment with a GnRH analogue one month before surgery. Patient satisfactory after 1 year is 93.3% and 95.6%, respectively in the group without and with pre-treatment. Amenorrhea is accomplished in 31.1% and 26.7% in these groups and reduction of bleeding is reported in 68.9 and 66.7%, respectively (Kucuk, 2005).

4. Randomized controlled trials

Many studies have been performed over the last years, involving both first and second generation techniques. We have selected the most relevant randomized controlled trials with long term follow-up. The results are summarized in table with regard to patients satisfactory, amenorrhea rates, reintervention surgery rates and the main conclusions of the authors.

Study	Satisfactory	Amenorrhea Rate	Reintervention surgery	Conclusion
Studies comparing 1st generation techniques with 2nd generation techniques.				
Sambrook, 2009 10 year follow up: - MEA - TCRE	 60% 52%	 83% 88%	 17% 28%	Both techniques achieve significant and comparable improvement in menstrual symptoms, health-related quality of life and high rates of satisfaction. With the known operative advantages, lower costs and fewer hysterectomies, it is clear that MEA is a more effective and efficient treatment for heavy menstrual loss than TCRE.
Goldrath, 2003 - HTA - Rollerball ablation	 98% 97%	 53% 46%		Endometrial ablation with the HTA is a safe, effective, and durable treatment of menorrhagia in a broad patient population. It offers advantages over RB by reducing anaesthesia requirements, reducing operating time, and eliminating risks of excessive fluid absorption, and is more easily learned.
Studies comparing 2nd generation with 2nd generation techniques				
Kleijn, 2008 5 year follow up. - Bipolar radiofrequency. - Thermal balloon		 48% 32%	 9.8% 12.6%	At 5 years follow up, bipolar thermal ablation was superior over balloon ablation in the treatment of menorrhagia.
Sambrook, 2009, - MEA - Thermal balloon	 76% 77%	 41% 38%		Both treatments are acceptable to women, with high levels of satisfaction. Microwave is quicker to perform with faster hospital discharge.

Table 2. Randomized controlled trials performed last years.

A large Cochrane Database review intensively studied and combined the studies comparing first and second generation techniques (Lethaby, 2009). The authors conclude that endometrial ablation offer a less invasive surgical alternative to hysterectomy. The conclusions of this review slightly favour the second generation techniques. Advantages were a shorter surgery time (15minutes), the use of local anaesthesia, and fewer complications like fluid overload, uterine perforation, cervical lacerations and haematometra. However, the second generation was associated with more equipment failure and patients were more likely to suffer from nausea, vomiting and uterine cramping postoperatively.

4.1 Conclusion

Main problem in comparing the first and second generation techniques is the heterogeneity of all studies. Especially, in the first generation, experience and skills of the surgeon are important cofounding factors. No significant differences are found in amenorrhoea rates and requirement for any additional surgery or hysterectomy between both generations. In general, one can say that with the introduction of the second generation the operation time is shorter, complications like fluid overload and perforation are reduced and the skills and experience of the surgeon has become less important.

5. Factors affecting outcome of endometrial ablation

The outcome of endometrial ablation regarding patients' satisfaction , amenorrhea rates and side effects, is intensively studied. In this paragraph we will discuss the factors that possibly affect the outcome of endometrial ablation.

5.1 Patient factors

Patient characteristics are important to decide whether a treatment modality is suitable for an individual patient. There are not many studies reporting pre operative factors influencing the outcome of global endometrial ablation. Patient factors that could predict amenorrhea after endometrial ablation are: an age older than 45 years, uterine length less than nine centimetres and endometrial thickness less than four millimetres (El-Nashar, 2009). Patient factors found to be prognostic for treatment failure are an age younger than 45 years, parity of five or greater, prior tubal ligation and history of dysmenorrhoea (El-Nashar, 2009). The role of leiomyomas in the outcome of endometrial ablation has not been established. Submucous leiomyomas increase the volume of menstrual bleeding by mechanisms that are, to date, not well understood. One of these mechanisms is probably the larger cross sectional area of endometrium of the uterine cavity. As a result, endometrial ablation is assumed to be successful in the treatment of women with myomas, but on the other hand, leiomyomas are also considered an important reason for treatment failure. Literature on this subject is not conclusive, and the presences of myomas has often been reason for exclusion. With the development of different new techniques it is expected that the presence of leiomyomas will not always be an exclusion factor for endometrial ablation, e.g. no evidence is found that the presence of leiomyomas is a predictive value for post operative amenorrhea rate or treatment failure (El-Nashar, 2009).

5.2 Preoperative thinning of the endometrium

Complete endometrial destruction is one of the most important determinants of treatment success. During the menstrual cycle endometrial thickness varies from as little as 1mm in the immediate postmenstrual phase to 10 mm or more in the late secretory phase. The techniques described have an ablation depth, ranging mostly from 4-6 mm. It is obvious that an endometrial thickness of 10 mm with a technique infiltration depth of 6 mm, is less effective. Therefore, thinning of the endometrium and planning of the surgery could contribute to a successful outcome. On the other hand, does pre-treatment with agents like GnRH analogues or Danazol add additional side effects and costs to any endometrial ablation procedure? A large Cochrane review was published in 2009. In this study the effect of pre-operative endometrial thinning before endometrial ablation was investigated. (Sowter, 2009).

5.2.1 Gonadotrophin-releasing hormones analogues

Down regulation of the receptors by Gonadotrophin- Releasing Hormones (GnRH) analogues results in a hypoestrogenic state leading to atrophic endometrium. Side effects of the treatment may be hot flushes, vaginal dryness, mood swings, headache, libido loss, difficulties in sleeping and weight changes. The use of GnRH analogues preoperatively showed a significant reduction in endometrial thickness on ultrasound and atrophic endometrial glands on histological examination (Donnez, 1997), This effect of GnRH analogues is larger compared to the effect of Danazol or preoperative admission of progestagens. Comparing hysteroscopic resection of the endometrium with or without GnRH, pre-treatment favours shorter duration of surgery, the surgery was easier to perform and a higher rate of amenorrhea 12 months postoperatively. There is no evidence that these results may be the same in patients treated with the second generation endometrial ablation techniques. Overall, the long-term effects of GnRH analogues as pre-treatment are unclear. (Sowter, 2009).

5.2.2 Danazol

Danazol is a testosterone analogue, with anti-hormonal effect, resulting in a secondary decrease of LH and FSH with ovarian failure. Side effects are acne, greasy skin, stem changes, weight gain, libido loss. Danazol is more effective than no treatment in inducing atrophy in endometrial glands and reducing endometrial thickness as measured with ultrasound. Pre-treatment with Danazol does not lead to higher rate of amenorrhea, patient satisfaction or less women requiring further surgery, under patients undergoing first generation endometrial ablation or resection. Compared to the GnRH analogues, the effect of Danazol on thinning the endometrial lining is inferior. (Sowter, 2009).

5.2.3 Progestagens

Pre-treatment with progestagens does not lead to an adequate reduction of endometrial thickness or atrophy of the endometrial glands (Rich, 1995). The use of progestagens is not recommended at all pre-operatively except in case of a trial (Sowter, 2009).

5.3 Surgical skills

One of the reasons for the development of the second generation techniques are the long learning curve and advanced surgical skills necessary for an adequate hysteroscopic

resection of the endometrium. It is demonstrated that complication risk and treatment failure of the first generation techniques are much higher when the experience of the surgeon is limited to less than 100 procedures. (Overton, 1997). With the introduction of the second generation, the advanced operating skills have become less important without impairing treatment results or patients satisfaction (Lethaby, 2009).

5.4 Conclusion

Although pre-treatment with both GnRH analogues and Danazol results in thinning of the endometrial layer, they do not seem to offer any benefit regarding to treatment outcome, patients satisfaction or number of complications. The experience and surgical skills of the surgeon are important factors in the first generation hysteroscopic techniques. Specially, the presence of large myomas, the size of the uterus and the endometrial thickness seem to be a limitation for the use of the second generation techniques

6. Complications

With the development of first and second generation endometrial ablative techniques for treating heavy menstrual bleeding, its use expanded really fast during the last decades. Advantages of these therapy compared to hysterectomy are the shorter operation time, the shorter post operative period, the cost effectiveness and the lower morbidity and mortality compared to hysterectomy . However, both peri- and postoperative complications related to endometrial ablation are described.

6.1 Perioperative complications

Perioperative complications are strongly related to the experience of the surgeon and the technique used. In general, second generation techniques have a lower complication rate due to shorter operating time and compared to the hysteroscopic assisted methods relatively easy procedures. In the Mistletoe study (Overton, 1997), complications of more than 10000 patients treated in the United Kingdom between 1993 and 1994 with endometrial resection, endometrial ablation by rollerball and laser, cryotherapy and radiofrequency ablation were registered. Most common complications with the first generation techniques are peri- or postoperative haemorrhage and uterine perforation. Haemorrhage was reported in 2.38% of the cases, ranging from 0.97% in case of roller ball alone to 3.53% with the combination of endometrial dissection and rollerball. Uterine perforation was reported in 1.48% of the cases. The experience of the surgeon with the technique used is the most important factor influencing the complication rate (Overton, 1997).

6.2 Postoperative complications

Post operative complications diagnosed after treatment or after discharge from the hospital include heavy bleeding, abdominal pain, urinary retention, hypotension, nausea, vomiting, bradycardia, chest pain, urinary tract infection, haematurie, hyponatraemia, pyrexia, deep venous thrombosis and fluid overload syndrome. These complications are rare and only small numbers are recorded. Overall percentages reported range from 0.77%-2.86% of the cases, depending on the technique used (Overton, 1997). The fluid overload syndrome is a well known and possible fatal complication. Absorption of distension fluid could cause

hyponatremia with mild symptoms like nausea, but also serious consequencess like seizures and even death due to cerebral oedema. The incidence of fluid overload syndrome is associated with the duration of surgery. In general, the complications as registered in the Mistletoe study are more likely to occur after the first generation techniques. Complications as nausea, vomiting and uterine cramping are more related to the second generation techniques (Lethaby, 2009).

6.3 Late onset complications

Complications diagnosed more than six weeks postoperatively are endometritis, septicaemia, pneumonia, peritonitis, pulmonary embolism and surgery for bowel repair. This group of complications are recorded in 1.25% of the cases (Overton, 1997). A cervical or lower uterine segment stenosis after endometrial ablation can cause a secondary to bleeding in the uterine cavity. Symptoms are amenorrhea in concert with cyclic lower abdominal or pelvic pain. The complaints usually start months and sometimes years after the procedure. Treatment modalities are cervical dilatation, hysteroscopic drainage or hysterectomy. Tubal sterilisation is a risk factor for hysterectomy after endometrial ablation. Abdominal pain is caused by bleeding from persistent or regenerating cornual endometrium causing a focal cornual hematometra with retrograde bleeding into an occluded fallopian tube. This syndrome is called post ablation tubal sterilisation syndrome (PATSS). The exact incidence of central hematometra and PATSS is unknown but it is estimated around 10% of the patients . (McCausland, 2007).

7. Endometrial ablation and pregnancy

Approximately, one in every five premenopausal women refers to a health care professional because of heavy menstrual bleeding. Because endometrial ablation is not reliable as contraceptive, all these women are at risk to become pregnant after the treatment. In two large studies including more than nine thousand patients the pregnancy rate after ablation was 0.68% (Pugh, 2000; Roy and Mattox, 2002). Obviously, when none of the patients had used contraceptives this percentage should have been higher. Pregnancy after endometrial ablation is associated with a number of complications and is therefore considered to be a contraindication.

The literature on complications during pregnancy is limited to case reports. Miscarriage is reported in 21% of the pregnancies after ablation (Hare, 2005). Although ectopic pregnancies are described it is unclear whether the number is increased after endometrial ablation. With an ongoing pregnancy the risk for pre term delivery (31%), pre term labour (21%), pre term rupture of membranes (17%), intra uterine growth restriction (12%) malpresentations (39%), and pathological placentation (17%) are all increased. The latter is notorious, leading to a wrong implantation of the placenta in the uterine wall with a high rate of hysterectomy after caesarean section (Hare, 2005). Moreover, the diagnosis in these cases is difficult because classical ultrasonsgraphic appearances of this abnormality may not be present after ablation. Therefore, patients should be counselled carefully, an active wish for children must be excluded and additional contraceptive methods are necessary after the endometrial ablation. If a patient becomes pregnant, close follow up is advised with monitoring of growth and placentation.

Because many patients do not prefer oral contraceptives or a levonorgestrel device after endometrial ablation, the procedure is frequently combined with laparoscopic sterilisation. Recently, the first reports of the combined approach of endometrial ablation and hysteroscopic sterilisation are published. These studies demonstrate that hysteroscopic essure® sterilisaton after both radiofrequency and balloon endometrial ablation is feasible and safe. Although it is attractive to combine these minimal invasive procedures a serious concern is the reliability of the hysterosalpingography (HSG) as confirmation of the sterilisation. In about 26% tubal occlusion can not be determined by HSG because of severe uterine synechiae, probably caused by the endometrial ablation (Detollenaere, 2011). Whether or not endometrial ablation can safely be performed after an earlier hysteroscopic sterilisation remains to be established.

8. Endometrial ablation and endometrial cancer

Endometrial carcinoma is the most common gynaecologic malignant disease with a prevalence worldwide of 1/1000. Because an endometrial carcinoma is mostly diagnosed in an early stage , FIGO stage 1 (73%) or stage II (10%) the five year survival rates are high, for both stages 91%. The risk for endometrial carcinoma increases between 50-70 years and is 8- fold higher in postmenopausal women. Approximately 50% of the endometrial cancers occur in women with associated risk factors like unopposed estrogen stimulation, obesity, diabetes mellitus, chronic anovulation, hypertension and histological complex atypical endometrial hyperplasia or adenomatous hyperplasia (Bakarat, 2009). The most frequent first symptom of endometrial cancer is post- menopausal loss of blood. As endometrial ablation is a relatively new therapy with a variety of techniques, data on the incidence of endometrial cancer after endometrial ablation are lacking. Most cases are reported after a first generation technique. It is suggested that the incidence of endometrial cancer after ablation is reduced in case of maximal destruction of the endometrium. However, some evidence suggests that incidence of endometrial cancer is unchanged, after EA with first generation techniques (Neuwrith, 2004). It is unclear whether endometrial cancer originates from islands of regenerated endometrium below the basal layer or from adenomyosis. The diagnosis of this type of malignancy may be delayed after ablation because adhesions or scars could mask the symptoms of the disease. In case of post-menstrual bleeding after ablation ultrasound and hysteroscopy can be difficult to perform because of the anatomical distortion of the uterine cavity. (Jarvela, 2002; Luo, 1999) Theoretically, in patients at risk for standard operative therapy, endometrial ablation could play a role in the treatment of endometrial neoplasia or cancer. Whether this treatment modality is a serious option requires further study.

9. Conclusion

In this chapter we discussed the most commonly used methods for endometrial ablation and gave a historic overview of these techniques. For today the “gold standard” is still transcervical endometrial resection with rollerball ablation throughout the world. However, the second generation techniques are developing fast and it is likely that they will replace the first generation. It is important to continue research to establish optimal endometrial ablative therapy to improve amenorrhoea rates, patients satisfaction and reduce the need for hysterectomy.

10. References

Abbott, J. & Garry, R. The surgical management of menorrhagia. *Human Reproduction Update,* Vol. 8, No. 1, (February, 2002), pp. 68–78, ISSN 13554786.

Barakat, R., Markman, M. & Randall, M.. Principles and Practice of Gynecologic Oncology. 5th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2009.

Bardenheuer FH. Elektrokoagulation der Uterusschleimhaut zur Behandlung klimakterischer blutungen. *Zentralblatt fur Gynakologie*, Vol. 4, 1937, pp. 209–211.

Cahan, W. & Brockunier, A. Cryosurgery of the uterine cavity. *American Journal of Obstetrics and Gynaecology*. Vol. 99, No. 1, September 1967, pp. 38–153.

DeCherney, A., Diamond, M. & Lavy, G. Endometrial ablation for intractable uterine bleeding: hysteroscopic resection. *Obstetrics and Gynaecology*. Vol. 70, No 4, October 1987, pp. 668–670.

Degen, A,. Gabrech, T., Mosimann, L., Fehr, M., Hornung, R., Schwarz, V., Tadir, Y., Steiner, R., Wagnières, G. & Wyss, P. Photodynamic Endometrial Ablation for the Treatment of Dysfunctional Uterine Bleeding: A Preliminary Report. *Lasers in Surgery and Medicine,* Vol. 34, No.1,, 2004, pp. 1–4.

Detollenaere, R., Vleugels, M. & Van Eijndhoven, H. Combining Novasure endometrium ablation and Essure hysteroscopic sterilization: a feasibility study to evaluate the confirmation tests. *Gynecological Surgery*. Vol. 8, No. 1, February 2011, pp. 59-63, ISSN 16132076.

Effective Healthcare. What are effective ways of treating excessive regular menstrual blood loss in primary and secondary care?. *Effective Health Care Bulletin*. Vol. 9, August 1995, pp.1–14.

Goldrath, M. Evaluation of Hydro-ThermAblator and rollerball endometrial ablation for menorrhagia 3 years after treatment. *Journal of the American Association of Gynecologic Laparoscopists* . Vol. 10, No. 4, November 2003, pp. 505–511.

Goldrath, M., Fuller, T. & Segal, S. Laser photovaporization of endometrium for the treatment of menorrhagia. *American Journal of Obstetrics and Gynaecology*. Vol. 140, No. 1, May 1981, pp. 14–19.

Hare, A. & Olah, S. Pregnanacy following endometrial ablation: a review article. *Journal of obstetrics and gynaecology*. Vol. 25, No. 2, February 2005, pp. 108-114.

Irvine, G.,Campbell-Brown, M., Lumsden, M., Heikkila, A., Walker, J. & Cameron, I.. Randomised comparative trial of the levonorgestrel intrauterine systemand norethisterone for the treatment of idiopathic menorrhagia. *British Journal of Obstetrics & Gynaecology*. Vol. 105, No. 6, June 1998, pp. 592–598.

Jarvela, I., Tekay, A. & Santala, M. Ultrasonographic features following thermal balloon endometrial ablation therapy. *Gynecologic and Obstetric Investigations*. Vol. 54, No. 1, 2002, pp.11–16.

Kleijn, J., Engels, R., Bourdrez, P., Mol, B. & Bongers, M. Five-year follow up of a randomised controlled trial comparing NovaSure and ThermaChoice endometrial ablation. *British Journal of Obstetrics & Gynaecology.* Vol. 115, No. 2, January 2008, pp. 193-198.

Kucuk, M. & Okman, T. Intrauterine instillation of trichloroacetic acid is effective for the treatment of dysfunctional uterine bleeding. *Fertility and Sterility* Vol. 83, No. 1, 2005, pp. 189-194

Lethaby, A. Hickey, M. & Garry, R. Enodmetrial destruction techniques for heavy menstrual bleeding. *Cochrane Database Systematic Review* Vol. 7, No. 4, October 2009, CD001501

Loffer, F. & Grainger D. Five-year follow-up of patients participating in a randomized trial of uterine balloon therapy versus rollerball ablation for treatment of menorrhagia. *Journal of the American Association of Gynaecologic Laparoscopy.* Vol. 9, No. 4, November 2002, pp. 429–435.

Luo, X. Lim, C. & Li, L. Hysteroscopic appearance of the endometrial cavity after microwave endometrial ablation. *Journal of Minimal Invasive Gynaecology*. Vol. 17, No. 1, January - February1999, pp. 30–36.

Neuwirth, R., Loffer, F. & Trenhaile, T. The incidence of endometrial cancer after endometrial ablation in a low-risk population. *Journal of the American Association of Gynaecologic Laparoscopists*. Vol. 11, No. 4, November 2004, pp. 492–494.

Overton, C., Hargreaves, J. & Maresh, M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. *British Journal of Obstetrics and Gynaecology.* Vol 104, No. 12, December 1997, pp. 1351-1359.

Perino, A., Castelli, A., Cucinella, G., Biondo, A., Pane, A. & Venezia, R. A randomized comparison of endometrial laser intrauterine thermotherapy and hysteroscopic endometrial resection. *Fertility and sterilitiy*. Vol. 82, No. 3, September 2004, pp. 731-734.

Pugh, C., Crane, J. & Hogan, T. Successful intrauterine pregnancy after endometrial ablation. *Journal of the American Association of Gynecologic Laparoscopists* Vol. 7, No. 3, August 2000, pp. 391 – 394.

Rich, A., Manyonda I., Patel, R. & Amias, A. A comparison of the efficacy of danazol, norethisterone, cyproterone acetate and medroxyprogesterone acetate in endometrial thinning prior to ablation: a pilot study. *Gynaecological Endoscopy.* Vol. 4, No. 1, 1995, pp. 59–61, ISSN: 09621091.

Roy, K. & Mattox, J. Advances in endometrial ablation. *Obstetrical & Gynaecological Survey,* Vol. 57, No. 12, December 2002, pp. 789 – 802.

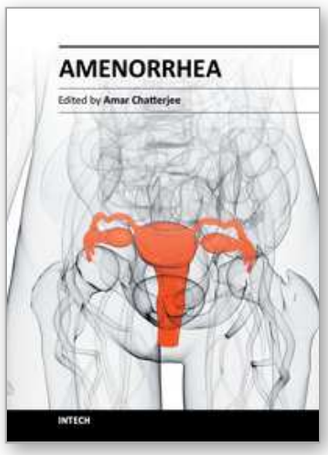
Sambrook, A., Bain, C., Parkin, D. & Cooper, K. A rondomised comparison of microwave endometrial ablation with transcervical resection of the endometrium: follow up at a minimum of 10 years. *British Journal of Obstetrics & Gynaecology.* Vol. 116, No. 8, July 2009, pp. 1033-1037.

Sambrook, A., Jack, S. & Cooper, K. Outpatient microwave endometrial ablation: 5-year follow-up of a randomised controlled trial without endometrial preparation versus standard day surgery with endometrial preparation. *British Journal of Obstetrics & Gynaecology*. Vol.117, No. 4, March 2010, pp.493–496.

Sowter. Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding (Review) *Cochrane database systematicreview,* Vol 3, 2009, CD 001124.

Townsend, D., Duleba, A. & Wilkes, M. Durability of treatment effects after endometrial cryoablation versus rollerball electroablation for abnormal uterine bleeding: two-year results of a multicenter randomized trial. *American Journal of Obstetrics and Gynaecology*. Vol. 188, No. 3, March 2003, pp. 699–701.

Vessey, M., Villard-Mackintosh, L., McPherson, K., Coulter, A. & Yeates, D. The epidemiology of hysterectomy: findings in a large cohort study. *British Journal of Obstetrics & Gynaecology.* Vol. 99, No. 5, May 1992, pp.402–407.



Amenorrhea

Edited by Prof. Amar Chatterjee

ISBN 978-953-307-988-2

Hard cover, 148 pages

Publisher InTech

Published online 09, December, 2011

Published in print edition December, 2011

This book on "Amenorrhea" is a wonderful collection of updated reviews dealing mostly with the aphysiological aspects of secondary amenorrhea. The book represents a collection of eight chapters, each chapter in the book is written by the international experts with extensive experience in the areas covered. We hope that readers will find this book interesting, helpful and inspiring.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Immerzeel Peter and Van Eijndhoven Hugo (2011). Amenorrhea and Endometrial Ablation: A Review and New Insights, Amenorrhea, Prof. Amar Chatterjee (Ed.), ISBN: 978-953-307-988-2, InTech, Available from: http://www.intechopen.com/books/amenorrhea/amenorrhea-and-endometrial-ablation-a-review-and-new-insights

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen