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REVIEW ARTICLE

Treatment options for dysfunctional uterine bleeding: evaluation of clinical results

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Abstract Abnormal uterine bleeding is one of the most common problems in women of reproductive age, and dysfunctional uterine bleeding (DUB) accounts for about half the cases. The aim of this review is to present all treatment options for women suffering from DUB and to evaluate their effectiveness. A detailed search strategy on electronic databases was carried out to identify trials and reviews on management of abnormal uterine bleeding. Tranexamic acid is the most effective medical treatment. A levonorgestrel-releasing intrauterine device is a low-cost, simple, and effective medical method, comparable to hysterectomy in terms of quality of life. In cases of DUB resistant to medical treatment, surgical treatment should be offered. First-generation ablation techniques are effective, but have a long learning curve. Second-generation ablation devices are highly effective and safe alternatives, thoroughly compared to first-generation techniques. Hysterectomy is the only method that guarantees treatment of dysfunctional uterine bleeding, but is a major operation associated with higher morbidity and mortality rates. Proper counseling of each woman with DUB regarding all treatment modalities can provide the best choice for each patient. More prospective randomized trials are needed to establish the effectiveness of these methods

Keywords Dysfunctional uterine bleeding · Ablation · Menorrhagia · Hysteroscopy

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Background

Abnormal uterine bleeding (AUB) is one of the most common problems in women of reproductive age, with a prevalence of more than 5% in this age group [1]. Women who seek for help from their gynecologists complain of cyclical (menorrhagia) or irregular noncyclic bleeding (metrorrhagia) that may have physical, emotional, and social impacts in their life. It is estimated that AUB affects 10–30% of menstruating women at any time [2], and about 20% of referrals of women to their gynecologists are due to menstrual disorders [3].

Menorrhagia is defined as excessive menstrual loss more than 80 ml per cycle in a cyclical pattern over consecutive cycles [4]. The duration of abnormal menstruation also varies greatly with an average of 7 days, and the heaviest blood loss on the first 2 days. However, an accurate measurement is quite difficult, and studies have shown that up to 60% of women presenting with a complaint of dysfunctional uterine bleeding (DUB), have objectively measured blood loss above the normal range [5, 6], while conversely there is a proportion of women with definite measured excessive blood loss who paradoxically do not seek for help [7].

In clinical studies, objective methods should be used to estimate the menstrual blood loss. However, in clinical practice the discomfort of the patient and the assessment of the hematological status are the basis for considering an appropriate treatment. Since subjective and objective estimates of menstrual loss do not correlate well, the severity of bleeding must be quantified. The gold standard method of measuring blood loss is Hallberg's alkaline hematin technique [8]. Tampons and towels are collected. Hemoglobin is extracted by a 5% NaOH solution and related back to actual blood loss. Although this method has

been modified by other researchers to simplify and quicken the procedure [9], all versions require women to collect their used sanitary wear. In order to create a simpler method of estimation of blood loss, Higham [10] developed a semiquantitative measurement using a pictorial blood loss assessment chart. This chart consists of a simple scoring system of the used pads and tampons and the degree of staining of each item in a way that results in a score. According to Higham, a score above 100 correlates with menstrual loss of more than 80 ml, while Janssen [11] slightly modified the chart and recommended a cutoff score of 185 for menorrhagia. Although the technique is semiquantitative and there is poor correlation between actual loss and chart score [12], Higham's pictorial chart flow is nowadays the most widely used method of assessing menstrual blood loss, although efforts are done from time to time to make the chart more accurate [13].

AUB may be due to anatomical, endocrine, hematological, and iatrogenic factors, though there are cases without any obvious pathology. The latter is usually referred under the name of DUB. It is a diagnosis of exclusion, wrongly used synonymously from time to time as menorrhagia. Dysfunctional uterine bleeding accounts for about half the cases of excessive menstrual loss [14]. It is recommended that women with AUB should be examined in total by ultrasound scan, or preferably hysteroscopy and blood tests (platelets, coagulation parameters), in order to exclude causes of bleeding that can be treated successfully [15, 16].

Methods and findings

The aim of this review is to present the treatment options and the data on their clinical outcomes for women suffering from DUB.

Medical treatment for dysfunctional uterine bleeding

Medical treatment options for DUB include tranexamic acid, nonsteroidal anti-inflammatory drugs (NSAIDs), combined oral contraception pill, progestogen, danazol and gonadotropin-releasing hormone analogues (GnRH-a). The effectiveness of the reported medical therapy for DUB has been evaluated and reviewed in systematic reviews in the Cochrane Library.

Tranexamic acid

Antifibrinolytic tranexamic acid has proven to be more effective than placebo, NSAIDs, progestogen in the luteal phase of menstrual cycle, or ethamsylate when subscribed to women with DUB, without any serious adverse effects [17]. A reduction in menstrual flow by 34–59% has been reported by Wellington and Wagstaff [18], which is quite impressive. However, this drug is mainly indicated for acute or short-term use and not as a definite treatment for DUB.

The main problem with the administration of tranexamic acid for the treatment of DUB is the potential risk of thromboembolic disease due to its antifibrinolytic effect. Although this is always an issue, especially in cases of severe anemia, it seems that the risk does not reach a statistical significance [19].

Nonsteroidal anti-inflammatory drugs

Prostaglandins are found in high concentrations in the endometrial shedding. Nonsteroidal anti-inflammatory drugs inhibit prostaglandin synthesis and decrease menstrual blood loss. NSAIDs are quite effective in cases of DUB compared to placebo, but they are less effective than either tranexamic acid, danazol, or levonorgestrel intrauterine system [20].

Combined oral contraceptive pill

The combined oral contraceptive pill is another effective alternative treatment for DUB, offering at the same time contraception to women. It reduces menstrual blood loss, but there are not enough data to determine its value in comparison to other drugs [21, 22]. So it seems reasonable to offer a combined oral contraceptive pill (COC) in young women suffering from DUB who also seek for contraception at the same time.

Progestogens

The administration of progestogens for the treatment of anovulatory DUB was always a tempting alternative for physicians, in order to restore the natural cycle of endometrial growth and shedding. The oral luteal phase progestogens do not seem to be more advantageous over other hormonal medical treatments or levonorgestrel-releasing intrauterine device [23, 24]. A long-term administration of progestogen is sometimes followed by severe side effects, such as water retention and hirsutism, depending on the type and dose of progestagen.

Danazol–gonadotropin-releasing hormone analogues

Danazol and the GnRH analogues were found as highly effective agents for DUB compared to other medical treatments [25, 26]. However, the administration of danazol or GnRH-a is limited due to their strong side effects. Long-term administration of danazol may cause hirsutism while GnRH-a is associated with irreversible bone loss when used

for more than 6 months. Thus, their utility is restricted mainly for short-term use, especially in cases of severe anemia, until further treatment is decided.

Levonorgestrel-releasing intrauterine device

Another medical method for the treatment of DUB is the levonorgestrel-releasing intrauterine system (Mirena®). It was originally developed as a contraceptive method [27], but it has been proven quite effective in the treatment of DUB, so the device acquired approval for that indication too.

Its efficacy is based on the continuous local release of the progestogen (levonorgestrel) within the uterine cavity, which suppresses endometrial growth. Studies report reduction of blood loss in menstrual cycles up to 97%, with its maximum efficacy 1 year after insertion [24, 28-31]. The majority of women with Mirena® bleed only for 1 day or experience just spotting during their period, while 15% of them become amenorrheic [31].

There are two trials comparing levonorgestrel intrauterine device (IUD) with medical treatment, two trials to transcervical resection of the endometrium and three trials comparing Mirena® with balloon ablation [24]. Mirena® was found superior to cyclical progestogens and mefenamic acid, but is significantly less effective than endometrial ablation in reducing blood loss. Interestingly, levonorgestrel IUD was found more cost effective than hysterectomy in Hurskainen et al.'s trial. [32].

Surgical treatment for dysfunctional uterine bleeding

In cases of DUB resistant to medical treatment, physicians should offer to women an alternative surgical treatment. In such patients, one could choose between endometrial ablation techniques and hysterectomy, taking into consideration patient's age, physical condition, and will.

Dilatation and curettage, which is offered as an alternative treatment option in women with excessive blood loss during menstrual periods, results in a temporary reduction of blood loss for the first month after the procedure, therefore it should not be proposed and performed in women suffering from DUB [33].

Endometrial ablation techniques

Since Ashermann in 1948 [34] described for the first time the association between amenorrhea and dilatation and curettage for termination of pregnancies, several investigators have studied the possibility of a controlled destruction of the basal layer of the endometrium in order to treat abnormal uterine bleeding.

Several methods have been developed from the early 1980s for the ablation of the endometrium and have been studied in cohort studies and randomized controlled trials. Basically, all these methods are divided in two large groups with a criterion, the need of direct visualization of the endometrial cavity.

First-generation endometrial ablation techniques

First-generation endometrial ablation techniques are based on direct visualization of the endometrial cavity with a hysteroscope. Three methods were developed since the late 1980s, and their efficacy were studied and compared to other techniques by many investigators. Before the application of each technique, endometrial thinning was necessary by using GnRH-a or danazol.

Hysteroscopic laser ablation The first laser method was a neodymium-YAG laser, which destroyed the endometrium through a hysteroscope [35]. Observational studies have reported a satisfaction rate up to 97% and amenorrhea rates ranging between 25% and 60% after hysteroscopic laser ablation (HLA) (Table 1) [36-40]. Failure rates varied between 7% and 21% in the same studies. There is only one prospective randomized trial comparing laser ablation with transcervical resection of the endometrium reporting 23% amenorrhea rate and 90% satisfaction rate [41]. Despite the promising results of its use, the equipment's high cost and extended learning curve remain obstacles for its wide application.

Table 1 Results of hysteroscopic laser ablation

Study	Study	No. of patients	Follow-up	Satisfaction rate	Amenorrhea rate	Failure rate
Garry et al., 1991 [36]	Observational	859	6 months	97%	60%	Not reported
Erian, 1994 [37]	Observational	2,342	>12 months	93%	56%	7%
Garry et al., 1995 [38]	Observational	524	6-42 months	Not reported	28.9%	14.3%
Bhattacharya et al., 1997 [41]	RCT	372 (188)	1 year	90%	45%	16%
Philips et al., 1998 [40]	Observational	746	6.5 years	89%	37%	Not reported
Shankar et al., 2003 [39]	Observational	174	1.5–9 years	Not reported	24.7%	20.7%

randomized controlled trials

Transcervical endometrial resection The wide use of a resectoscope in gynecological operations allowed its application as a method for treatment of DUB [42]. Transcervical endometrial resection (TCRE) has been shown to be an effective and safe method for treating DUB [43]. TCRE was tested in nonrandomized prospective studies, which reported a satisfaction rate between 85% and 87% and an amenorrhea rate varying up to 46% (Table 2) [44, 45]. TCRE is comparable to other hysteroscopic endometrial ablation techniques in terms of amenorrhea and satisfaction rates [46, 47]. Direct visualization of the endometrial cavity and the possibility of treating concomitant endometrial pathology at the time of endometrial ablation remain the major advantages of the method.

Rollerball endometrial ablation The technique was developed in 1989 in Australia by Vancaillie [48] and soon became quite popular due to its relative simplicity and excellent results [49] (Table 3). Studies report comparable results from its application to the other two first-generation ablation techniques (satisfaction rate up to 94% and amenorrhea rate varying between 29% and 35%) [46, 47]. Rollerball endometrial ablation requires less operative time and shorter learning curve compared to TCRE and HLA [47].

Studies evaluating first-generation ablation techniques revealed quite impressive results regarding their effectiveness, treating three fourths of the women suffering from DUB, who would otherwise proceed to hysterectomy in terms of definite treatment. They are acknowledged to be the "gold standard" by which other, newer procedures are judged [47].

A large retrospective study, though, that was carried out in United Kingdom, caused great skepticism in the medical community. The Mistletoe study [50] reports on the complications of the application of first-generation endometrial ablation techniques and showed that all three methods are safe procedures for the treatment of DUB, with a complication rate of 4.4%. HLA and rollerball ablation are considered safer methods than TCRE, while resection of the endometrium caused more of the serious and possibly fatal complications, which include uterine perforation and bleeding, bowel injury, visceral burn, and hyponatremic encephalopathy with cerebral edema. In cases of performing any of these techniques by inadequate trained gynecologists, the failure rate rose significantly, while serious complication rates increased dramatically [51, 52].

All these issues reported in the Mistletoe study triggered researchers and companies to offer new methods for the treatment of DUB.

Second-generation endometrial ablation techniques

Many endometrial ablation devices have been developed in the early 1990s for the treatment of DUB and categorized as second-generation ablation techniques. Their application did not require the use of a hysteroscope, so the advantage of a direct visualization of the endometrial cavity no longer existed. Therefore, endometrial biopsy prior to ablation is a mandatory prerequisite.

Every method consists of a different device which, by different means (hot liquid, laser, bipolar energy, ultrasound, microwaves, heating balloons, or cryoablation), causes selective destruction of the endometrial layer. These devices require less skills of the surgeon, as they are very simple to use, so the learning curve is smaller. The operation time is shorter, the anesthesia/analgesia can become minimal, and the complication rate is reduced, as all the devices have a self-control mechanism [53].

In some of these techniques, a preoperative thinning of the endometrium with GnRH-a or danazol is not necessary, in contrast to all first-generation ablation techniques [54].

Table 2 Results of TCRE

Study	Study	No of patients	Follow-up	Satisfaction rate	Amenorrhea Rate	Failure rate
O'Connor and Magos, 1996 [44]	Observational	525	5 years	87%	40%	Not reported
O'Connor et al., 1997 [45]	RCT	172 (116)	1 year	87%	46%	Not reported
			2 years	86%	Not reported	Not reported
			3 years	85%	21%	Not reported
Bhattacharya et al., 1997 [41]	RCT	372 (184)	1 year	91%	49%	20%
Vercelleni et al., 1999 [84]	RCT	91 (44)	1 year	Not reported	48%	5%
Pellicano et al., 2002 [85]	RCT	82	1 year	63%	Not reported	15.7%
			2 years	60.5%	Not reported	24.2%
Perino et al., 2004 [67]	RCT	116 (58)	1 year 3 years	Not reported Not reported	23% 24%	Not reported
	RCT	51	1 year	79%	29%	Not reported

randomized controlled trials

Table 3 Results of rollerball endometrial ablation

Study	Study	No of patients	Follow-up	Satisfaction rate	Amenorrhea rate	Failure rate
Paskowitz, 1995 [49]	Observational	200	2.5 years	90%	Not reported	Not reported
	Observational	142	4.2 years	84%	28%	Not reported
	RCT	255	1 year	87%	23%	Not reported
Vercelleni et al., 1999 [84]	RCT	91 (47)	1 year	Not reported	36%	0%
Corson, 2001 [86]	RCT	276 (89)	1 year	Not reported	51%	Not reported
Cooper et al., 2002 [87]	RCT	265	1 year	94%	35%	Not reported
Cooper J et al., 2004	RCT	322	1 year	Not reported	28.9%	Not reported

randomized controlled trials

Thermal balloon endometrial ablation The technique consists of a balloon for insertion in the endometrial cavity and a generator. After insertion, the balloon is filled with hot liquid that causes a destructive thermal effect to the surrounding endometrium. There are several devices that are commercially available: Thermachoice®, Cavaterm®, Menotreat®, and Thermablate®. A preoperative preparation of the endometrium with GnRH-a is suggested, although this is not necessary.

Thermachoice® was the first of the second-generation ablation technique, and its effectiveness has been evaluated intensively. After the application of Thermachoice®, a satisfaction rate is reported to be up to 90%, while the amenorrhea rate was up to 20% 1 year following treatment [55]. Following clinical evaluation of Thermachoice®, improved devices were introduced in 1998 (Thermachoice® II) and 2004 (Thermachoice® III). The efficacy of Thermachoice® III was evaluated and amenorrhea rates up to 32.6% were reported [56]. Thermachoice® has been compared to first-generation endometrial ablation techniques in several studies. Overall, the existing evidence suggests that success and satisfaction rates are equal, while the duration of surgery was significantly shorter with balloon [47]. Thermachoice® is one of the most safe endometrial ablation devices. According to MEDLINE and MAUDE databases, the complication rate of the method, including minor and major, is reported to be only 0.03% [57, 58].

Cavaterm® is the second most often used device based on thermal balloon. Its application results seem slightly improved compared to Thermachoice® in nonrandomized studies (satisfaction rate varying between 91% and 96%, amenorrhea rate ranging between 15% and 68%, overall success rate of 92–98% and failure rate up to 7%) [55]. There are few randomized trials comparing Cavaterm® with first- and second-generation ablative techniques, showing no evidence of significant differences in the rates of amenorrhea at any follow-up time, from 6 months to 5 years after surgery [54]. There is just one limitation in the application of Cavaterm® in comparison to Thermachoice®; Cavaterm® cannot be used in women whose endometrial cavity length exceeds 10 cm, while Thermachoice® can be used even when endometrial cavity measures 12 cm.

The Menotreat® thermal balloon is similar to the Cavaterm® endometrial ablation system. There is only one small observational study in the literature regarding the effectiveness of this device reporting an amenorrhea rate of 10% at 1 year follow-up [59], and just one small randomized control study comparing Menotreat® and Cavaterm® [60], reporting amenorrhea rates up to 19% in the Menotreat® group and up to 13% in the Cavaterm® group.

The Thermablate® thermal balloon was developed in 2004, and since then, various authors have studied the application results of this device. Amenorrhea rate ranges between 22.2% and 35% with a failure rate varying between 3% and 5.5% [55].

Endometrial ablation by hysteroscopic instillation of hot saline (hydrotherm ablator) This technique, although applied hysteroscopically, is categorized as a second-generation endometrial ablation technique. Externally heated saline of 90°C is infused into the uterine cavity through the external sheath of a diagnostic hysteroscope. The pressure used for the infusion is less than 45 mmHg, thus preventing flow through the fallopian tubes. Under direct hysteroscopic view, the hot saline causes ablation of the endometrium. The application experience of the method is tested in several observational studies and in one randomized controlled trial compared to rollerball. Amenorrhea rates are reported up to 53%, cure rate up to 94%, and satisfaction rate up to 98% [61].

Microwave endometrial ablation (MEA®) Sharp et al. [62] first developed in 1995 the use of microwave energy for the treatment of abnormal uterine bleeding. Microwave energy of 9.2 GHz is generated in a magnetron and is applicated by a probe within the endometrial cavity. The ablation effect is achieved when the temperature in the uterus reaches 95°C. In the meantime, the surgeon moves the probe in all

directions within the uterus, and therefore, successful ablation of the endometrial lining is achieved. A pretreatment preparation of the endometrium with GnRH-a or danazol is necessary.

The microwave endometrial ablation system has been compared to first-generation ablative techniques (TCRE and rollerball) in randomized trials with similar results in terms of amenorrhea and satisfaction rates, even 10 years following surgery with low complication rates [47, 53, 63]. There is also one randomized controlled trial comparing MEA and thermal balloon ablation, showing similar results in relation to menstrual scores and satisfaction [64].

Endometrial laser intrauterine thermal therapy (ELITT®) The technique was developed by Donnez et al. in 1996 and causes endometrial ablation by laser photocoagulation [65]. Preparation of the endometrium prior to laser application is considered necessary. The technique has been evaluated in a prospective observational study. Satisfaction rate was reported up to 90% at 12 months after treatment, while amenorrhea rate was 71% [66]. There is only one randomized controlled trial comparing ELITT and TCRE, reporting at 12 months amenorrhea rates of 56% and 23%, respectively [67] .

Cryo-endometrial ablation (Her Option®) Endometrial ablation is achieved by a cooling gas, which achieves a temperature of −90 to −100°C within the endometrial cavity. The treatment has been evaluated in prospective observational studies with encouraging results (amenorrhea 28% and satisfaction up to 91%) [53], while there is only one randomized trial comparing cryoablation and rollerball, showing no significance difference in terms of amenorrhea [47].

Bipolar impedance controlled endometrial ablation (Novasure®) The device consists of a radio frequency generator and a single-use bipolar ablation probe. The probe consists of a three-dimensional expandable bipolar electrode, which comes in touch with the entire endometrial cavity, when opened. There is also a vacuum pump within the generator, which provides continuous suction of the endometrial lining and debris; therefore, preoperative preparation of the endometrium is not generally needed. The generator operates at 500 KHz and has a power cutoff limit of 50 Ω of tissue impedance. Once the myometrial layer is reached, immediately the tissue impedance increases to 50 Ω, and the generator automatically switches off.

This method has been evaluated in prospective observational studies and women reported a satisfaction rate of up to 87%, an amenorrhea rate of up to 58%, and a failure rate of up to 3% 1 year after treatment, while amenorrhea rate at 3 years postablation reported to be 65% [68]. At 5 years following treatment, women report an impressive amenorrhea rate of 75%, while the study reveals an overall success of the method up to 98% [68]. There is one clinical trial comparing Novasure® with combined loop excision plus rollerball ablation, reporting an amenorrhea rate of 41% and a satisfaction rate of 93% in the Novasure® arm, compared with 35% and 94%, respectively in the rollerball arm [69]. Novasure® has been compared in prospective randomized controlled trials with other second-generation ablation techniques. In the Novasure® versus the Cavaterm® trial, at 1 year follow-up, an amenorrhea rate of 43% was reported for Novasure® compared with Cavaterm® [70]. In the Novasure® versus Thermachoice® trial, an amenorrhea rate of 56% in the Novasure® arm was reported 12 months after the ablation [71], while the overall cost, including re-treatment in the balloon ablation group is lower [72].

Despite the safety features of the device, Della Badia et al. [73] reported a high number of complications caused by Novasure® in comparison to other ablation devices, a feature that caused great skepticism in the medical community.

Hysterectomy

Hysterectomy is the only method that guarantees permanent treatment of DUB and 100% amenorrhea rates. It is a major operation, performed either by laparotomy, laparoscopy, or vaginally [74], with associated morbidity and even mortality that requires hospitalization for a few days and several weeks for full recovery. TCRE or ablation is an effective and possibly cheaper alternative to hysterectomy with faster recovery although re-treatment is sometimes needed [75]. The CREST study on the complication rate for minor and major operations, reports a 25% complication rate for vaginal hysterectomy and a 43% for abdominal hysterectomy [76]. The VALUE study confirmed that more than 10% of women treated by hysterectomy for DUB reported immediate or long-term complications [77]. These complication rates are significantly higher than those of first-generation endometrial ablation techniques. Despite this fact, the satisfaction rate remains higher in women treated with hysterectomy, so does quality of life [75].

Conclusions

DUB is a common problem in women of reproductive age with serious impact on their personal and social life. Treatment options vary among medical, levonorgestrel intrauterine device, first- and second-generation endometrial ablation techniques and hysterectomy.

Tranexamic acid is the most effective treatment in cases of DUB. NSAIDs and COC pills may be used as second-line drugs, the latter especially in cases of young women who also seek for contraception. Levonorgestrel releasing intrauterine device is a low-cost, simple, and quite effective medical method for the treatment of DYB, comparable to hysterectomy in terms of quality of life [78]. First-generation endometrial ablation techniques have been evaluated thoroughly in randomized controlled trials and found impressively effective in terms of blood loss and satisfaction, compared to hysterectomy. Second-generation endometrial ablation devices have been compared intensively to first-generation techniques in randomized controlled trials and found to have equivalent results in terms of definite blood loss, satisfaction, and effect on quality of life [47, 53]. Prospective randomized clinical trials comparing hysterectomy to second-generation ablation devices are needed to establish the effectiveness of these two treatment options. Surprisingly, there is a lack of RCTs between second-generation ablation devices. This may be partly due to the differences between the devices regarding their ability to treat women with concomitant uterine pathology and not just DUB. However, it seems more likely that there is a commercial resistance in comparing devices due to the possible effect on the market share that these trials could provoke.

It seems that none of the treatment options is significantly superior to the others, in terms of satisfaction, amenorrhea, failure, and complication rate. The role of the physician in counseling the patient is crucial in order to reach the abovementioned goals. Gynecologists should inform women suffering from DUB regarding all treatment options, published application results, and of course their complication rates. This way, every patient can participate in the decision-making process and provide a definite and mature consent, even accept a possible failure of the method [79-83]. Furthermore, the patient should be informed that contraception should be recommended in cases of not achieving permanent amenorrhea after endometrial ablation.

In conclusion, since none of the treatments for DUB is significantly superior to another, and all methods have their advantages and disadvantages, proper counseling of each woman suffering from DUB regarding all treatment modalities can provide the best choice for each patient. The only way forward is to perform well-designed clinical trials on the subject in order to reach definite conclusions on the effectiveness of all the treatment modalities.

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References

1. National Statistics Online (2001) Census. http://www.statistics.gov.uk/census2001/pop2001/england_wales.asp.2002 Accessed 21 April 2002
2. Prentice A (1999) Healthcare implications of dysfunctional uterine bleeding. In: Smith SK (ed) dysfunctional uterine bleeding. Bailliere Tindal, London, pp 325–341
3. Coulter A, Bradlow J, Agass M et al (1991) Outcomes of referrals to gynaecology out-patients clinics for menstrual problems: an audit of general practice records. Br J Obstet Gynaecol 98:789–796
4. Royal College of Obstetricians and Gynaecologists (1998) The initial management of menorrhagia. Evidence based guidelines no. 1. Royal College of Obstetricans and Gynaecologists, London
5. Chimbira TH, Anderson ABN, Turnbull AC (1980) Study of menstrual blood loss. Br J Obstet Gynaecol 87:603–609
6. Fraser IS, McCarron G, Markham R (1984) A preliminary study of factors infuencing perception of menstrual blood loss volume. Am J Obstet Gynecol 149:788–793
7. Hallberg L, Hogdahl A, Nilsson L, Rybo G (1966) Menstrual blood loss—a population study. Acta Obstet Gynecol Scand 45:320–351
8. Hallberg L, Nilsson L (1964) Determination of menstrual blood loss. Scand J Clin Lab Invest 16:244–248
9. Cannon MJ, Day P, Hammaddieh N, Johnson N (1996) A new method for measuring menstrual blood loss and its use in screening women before endometrial ablation. Br J Obstet Gynaecol 103:1029–1033
10. Higham JM, O' Brien PM, Shaw RW (1990) Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 97:734–739
11. Janssen CA, Scholten PC, Heintz AP (1995) A simple visual assessment technique to discrimitate between menorrhagia an normal menstrual blood loss. Obstet Gynaecol 85:977–982
12. Reid PC, Coker A, Coltart R (2000) Assessment of menstrual blood loss using a pictorial chart: a validation study. Br J Obstet Gynaecol 107:320–322
13. Wyatt KM, Dimmock PW, Walker TJ, O'Brien PMS (2001) Determination of total menstrual blood loss. Fertil Steril 76:125–131
14. Beazley JM (1972) Dysfunctional uterine haemorrhage. Br J Hosp Med 7:573–578
15. Vercellini P, Cortesi I, Oldani S et al (1997) The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia. Hum Reprod 12:1768–1771
16. Dijkuizen FPHLJ, De Vries LID, Mol BWJ (2000) Comparison of transvaginal ultrasonography and saline infusion sonography for the detection of intracavitary abnormalities. Ultrasound Obstet Gynecol 15:372–376
17. Lethaby A, Farquhar C, Cooke I (2000) Antifibrinolytics for heavy menstrual bleeding. Cochrane Database Syst Rev (4): CD000249
18. Wellington K, Wagstaff AJ (2003) Tranexamic acid: a review of its use in the management of menorrhagia. Drugs 63(13):1417–1433
19. Sundstrom A, Seaman H et al (2009) The risk of venous thromboembolism associated with the use of tranexamic acid and other drugs used to treat menorrhagia: a case-control study using the General Practice Research Database. BJOG 116 (1):91–97
20. Lethaby A, Augood C, Duckitt K, Farquhar C (2007) Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database Syst Rev (4):CD000400

21. Farquhar C, Brown J (2009) Oral contraceptive pill for heavy menstrual bleeding. Cochrane Database Syst Rev(4): CD000154
22. Fraser IS, McCarron G (1991) Randomized trial of 2 hormonal and 2 prostaglandin-inhibiting agents in women with a complaint of menorrhagia. Aust NZ J Obstet Gynaecol 31:66–70
23. Hickey M, Higham JM, Fraser I (2007) Progestogens versus oestrogens and progestogens for irregular uterine bleeding associated with anovulation. Cochrane Database Syst Rev (4): CD001895
24. Lethaby A, Cooke I, Rees MC (2005) Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Cochrane Database Syst Rev (4):CD002126
25. Beaumont HH, Augood C, Duckitt K, Lethaby A (2007) Danazol for heavy menstrual bleeding. Cochrane Database Syst Rev (3): CD001017
26. Duckitt K (2007) Medical management of perimenopausal menorrhagia: an evidence-based approach. Menopause Int 13 (1):14–18
27. French RS, Cowan FM, Mansour D et al (2000) Levonorgestrel-releasing (20 ug/day) intrauterine systems (Mirena) compared with other methods of reversible contraceptives. Br J Obstet Gynaecol 107:1218–1225
28. Irvine GA, Campbell-Brown MB, Lumsden MA et al (1998) Randomised comparative study of the levonorgestrel itrauterine system and morethisterone for the treatment of idiopathic menorrhagia. Br J Obstet Gynaecol 105:592–598
29. Lahteenmaki P, Haukkamaa M, Puolakka J et al (1998) Open randomised study of use of levonorgestrel releasing intrauterine system as alternative to hysterectomy. BMJ 316:1122–1126
30. Mukherjee K, Jones K (2005) The treatment of dysfunctional uterine bleeding with the Mirena IUS: a survival analysis. Gynecol Surgery 2(4):251–254
31. Luukkainen T, Toivonen J (1995) Levonorgestrel–releasing IUD as a method of contraception with therapeutic properties. Contraception 52:269–276
32. Hurskainen R, Teperi J, Rissanen P et al (2001) Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial. Lancet 357(9252):273–277
33. Haynes PJ, Hodgson H, Anderson AB, Turnbull AC (1977) Measurement of menstrual blood loss in patients complaining of menorrhagia. Br J Obstet Gynaecol 84:763–768
34. Ashermann JG (1948) Amenorrhea traumatica (atretica). Obstet Gynecol 55:23
35. Goldrath MH, Fuller TA, Segal S (1981) Laser photovaporization of the endometrium in the treatment of menorrhagia. Am J Obstet Gynecol 140:14–19
36. Garry R, Erian J, Grochmal SA (1991) A multi-centre collaborative study into the treatment of menorrhagia by Nd-YAG laser ablation of the endometrium. Br J Obstet Gynaecol 98:357–362
37. Erian J (1994) Endometrial ablation in the treatment of menorrhagia. Br J Obstet Gynaecol 101:19–22
38. Garry R, Shelley-Jones D, Mooney P, Phillips G (1995) Six hundred endometrial laser ablations. Obstet Gynecol 85:24–29
39. Shankar M, Naftalin N, Taub N et al (2003) The long-term effectiveness of endometrial laser ablation: a survival analysis. Eur Gynecol Reprod Biol 108:75–79
40. Philips G, Chien P, Garry R (1998) Risk of hysterectomy after 1000 consecutive laser ablations. Br J Obstet Gynaecol 105:897–903
41. Bhattacharya S, Cameron IM, Parkin DE et al (1997) A pragmatic randomised comparison of transcervical resection of the endometrium with endometrial laser ablation for the treatment of menorrhagia. Br J Obstet Gynaecol 104:601–607
42. De Cherney A, Polan ML (1983) Hysteroscopic management of intrauterine lesions and intractable uterine bleeding. Obstet Gynecol 61:392–397
43. A. Lethaby, M. Hickey and R. Garry (2005) Endometrial destruction techniques for heavy menstrual bleeding. Cochrane Database Syst Rev (4):CD001501
44. O'Connor H, Magos A (1996) Endometrial resection for the treatment of menorrhagia. N Engl J Med 335:151–156
45. O'Connor H, Broadbent JA, Magos AL et al (1997) Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia. Lancet 349:897–901
46. Papadopoulos NP, Magos A (2007) First-generation endometrial ablation: roller-ball vs loop vs laser. Best Pract Res Clin Obstet Gynaecol 21:915–929
47. Lethaby A, Hickey M, Garry R, Penninx J (2009) Endometrial resection/ablation techniques for heavy menstrual bleeding. Cochrane Database Syst Rev (4):CD001501
48. Vancaillie TG (1989) Electrocoagulation of the endometrium with the ball-end resectoscope. Obstet Gynecol 74:425–427
49. Paskowitz RA (1995) Rollerball ablation of the endometrium. J Reprod Med 40:333–336
50. Overton C, Hargreaves J, Maresh M (1997) A national survey of the complications of endometrial destruction for menstrual disorders the MISTLETOE study. Br J Obstet Gynaecol 104:1351–1359
51. Jansen FW, Vredevoogd CB, van Ulzen K et al (2000) Complications of hysteroscopy: a prospective, multicenter study. Obstet Gynecol 96:266–270
52. Vilos GA, Brown S, Graham G et al (2000) Genital tract electrical burns during hysteroscopic endometrial ablation: report of 13 cases in the United States and Canada. J Am Assoc Gynecol Laparosc 7:141–147
53. Practice Committee of American Society for Reproductive Medicine (2008) Indications and options for endometrial ablation. Fertil Steril 90(5 Suppl):S236–S240
54. Sowter MC, Lethaby A, Singla AA (2002) Pre-operative endometrial thinning agents before endometrial destruction for heavy menstrual bleeding. Cochrane Database Syst Rev (3): CD001124
55. Vilos G, Edris F (2007) Second-generation endometrial ablation technologies: the hot liquid ballons. Best Pract Res Clin Obstet Gynaecol 21(6):947–967
56. Garza-Leal J, Pena A, Donovan A et al (2010) Clinical evaluation of a third-generation thermal uterine balloon therapy system for menorrhagia coupled with curettage. J Min Inv Gynecol 17(1):82–90
57. Gurtcheff SE, Sharp HT (2003) Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 102:1278–1282
58. Weisberg M (2004) Complications associated with global endometrial ablations: the utility of the MAUDE database. Obstet Gynecol 103:995
59. Ulmsten U, Carstensen H, Falconer C et al (2001) The safety and efficacy of MenoTreat, a new balloon device for thermal endometrial ablation. Acta Obstet Gynecol Scand 80:52–57
60. Vihko KK, Raitala R, Taina E (2003) Endometrial thermoablation for treatment of menorrhagia: comparison of two methods in outpatients setting. Acta Obstet Gynecol Scand 82:269–274
61. Ciantar E, Jones K (2007) Preventing hysterectomies for dysfunctional uterine bleeding with the HTA^{TM}: a survival analysis. Gynecol Surgery 4(1):39–43
62. Sharp NC, Cronin N, Feldberg I et al (1995) Microwaves for menorrhagia: a new fast technique for endometrial ablIation. Lancet 346:1003–1004

63. Jameel JK, Ahmed T, Noble W, Philips K, Tised J (2005) Microwave endometrial ablation (MEA) and bowel injury. Gynecol Surgery 2(2):131–133
64. Sambrook AM, Cooper KG, Campell MK et al (2009) Clinical outcomes from a randomized comparison of microwave endometrial ablation with thermal balloon endometrial ablation for the treatment of heavy menstrual bleeding. BJOG 116(8):1038–1045
65. Donnez J, Polet R, Mathieu PE et al (1996) Endometrial laser interstitial hyperthermy: a potential modality for endometrial ablation. Obstet Gynecol 87:459–464
66. Donnez J, Polet R, Rabinivitz R et al (2000) Endometrial laser intrauterine thermotherapy: the first series of 100 patients observed for 1 year. Fertil Steril 74:791–796
67. Perino A, Castelli A, Cucinella G et al (2004) A randomized comparison of endometrial laser intrauterine thermotherapy and hysteroscopic endometrial resection. Fertil Steril 82(3):731–734
68. Marlies B (2007) Second generation endometrial ablation treatment: Novasure. Best Pract Res Clin Obstet Gynaecol 21(6):989–994
69. Cooper J, Gimpelson R, Laberge P et al (2002) A randomized, multicenter trial of safety and efficacy of the Novasure system in the treatment of menorrhagia. L Am Assoc Gynecol Laparoc 9 (4):418–428, o
70. Abbott J, Hawe J, Hunter D, Garry R (2003) A double blind randomized trial comparing the Cavatherm and the NovaSure endometrial ablation systems for the treatment of dysfunctional uterine bleeding. Fertl Steril 80:223–232
71. Bongers MY, Bourdrez P, Mol BW et al (2004) Randomized controlled trial of bipolar radio frequency endometrial ablation and balloon endometrial ablation. Br J Obstet Gynaecol 111:1095–1102
72. Bongers MY, Bourdez P, Van Der Steeg JW, Heintz AP, Brolmann HA (2005) Thermal endometrial ablation in dysfunctional uterine bleeding: an economic comparison of bipolar ablation and balloon ablation. Gynecol Surgery 2(4):271–277
73. Della Badia C, Nyirjesy P, Ata A (2007) Endometrial ablation devices: review of a manufacturer and user facility device experience database. Jmig 14:436–441
74. Pados G (2005) Laparoscopic hysterectomy: why is it not popular. In controversies in obstetrics-gynecology and infertility. Ben-Rafaeln T, Creatsas G, Shoham T (eds) Oren Publisher Ltd, International Proceedings Division, pp 518–522
75. Lethaby A, Shepperd S, Farquhar C, Cooke I (1999) Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding. Cochrane Database Syst Rev (2):CD000329
76. Lumsden MA, Twaddle S, Hawthorn R et al (2000) A randomized comparison and economic evaluation of laparoscopic-assisted hysterectomy and abdominal hysterectomy. Br J Obstet Gynaecol 107:1386–1391
77. Maresh MJA, Metcalfe MA, McPherson K et al (2002) The VALUE national hysterectomy study: description of the patients and their surgery. Br J Obstet Gynaecol 109:302–312
78. Marjoribanks J, Lethaby A, Farquhar C (2006) Surgery versus medical therapy for heavy menstrual bleeding. Cochrane Database Syst Rev (2):CD003855
79. Coulter A, Peto V, Doll H (1994) Patient's preferences and general practitioners' decisions in the treatment of menstrual disorders. Fam Pract 11:67–74
80. Cooper KG, Grant AM, Garratt AM (1997) The impact of using a partially randomized patient preference design when evaluating alternative managements for heavy menstual bleeding. Br J Obstet Gynaecol 104:1367–1373
81. Coulter A (1997) Partnerships with patients: the pros and cons of shared clinical discision making. J Health Serv Res Policy 2:112–121
82. Gambone JC, Reiter RC (1997) Hysterectomy: improving the patient's decision-making process. Clin Obstet Gynecol 40:868–877
83. Nagele F, Rubinger T, Magos A (1998) Why do women choose endometrial ablation rather than hysterectomy? Fertil Steril 69:1063–1066
84. Vercelleni P, Oldani S, Yaylayan L et al (1999) Randomised comparison of vaporising electrode and cutting loop for endometrial ablation. Obstet Gynecol 94:521–527
85. Pellicano M, Guida M, Acunzo G et al (2002) Hysteroscopic transcervical endometrial resection versus thermal destruction for menorrhagia: a prospective randomized trial on satisfaction rate. Am J Obstet Gynecol 187:545–550
86. Corson S (2001) A multicenter evaluation of endometrial ablation by hydrothermablator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 8:359–367
87. Cooper J, Gimpelson R, Laberge P et al (2002) A randomized, multicenter trial of safety and efficacy of the NovaSure in the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 9:418–428