Clinical practice and short-term efficacy of 2.45-GHz microwave endometrial ablation to treat menorrhagia

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A B S T R A C T

Objective: To evaluate the clinical practice and short-term efficacy of microwave endometrial ablation (MEA) to treat menorrhagia, and to identify prognostic factors for optimal outcomes.

Methods: We performed MEA in 22 women with menorrhagia between October 2012 and December 2013. To evaluate efficacy, objective and subjective variables were measured using medical records and patients’ pre- and postoperative responses to a written questionnaire with a visual analog scale (VAS) scored from 0 to 10 for each symptom. MEA outcome was evaluated 6 months after treatment. Patients with amelioration of menorrhagia and no anemia were defined as the effective group, and the others were defined as the noneffective group. Effective patients requiring no hormonal therapy were defined as the highly effective group. To identify prognostic factors, background factors were compared between the highly effective group and the other groups.

Results: Uterine fibroids and adenomyosis were diagnosed in 68% and 32% of patients, respectively. The median VAS score of postoperative pain was 1.0, and that of satisfaction was 8.1. Hemoglobin concentration, menstrual bleeding volume, menstrual duration, menstrual pain, vaginal discharge, and fatigue were ameliorated in the postoperative period. The effective group, the highly effective group, and the noneffective group included 95%, 84%, and 5% of patients, respectively. The uterine corpus cavity was significantly shorter in the highly effective group than in the other groups.

Conclusion: MEA was safe and effective. The short-term efficacy rate of MEA for alleviating menorrhagia symptoms was 95%. Optimal outcomes were correlated with a shorter uterine corpus cavity.

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Introduction

Endometrial ablation is considered an important surgical option for the treatment of menorrhagia.1 In Japan, microwave endometrial ablation (MEA) using a frequency of 2.45 GHz was described and developed as an original applicator for use by Kanaoka et al2 in 2001. After the Japanese Ministry of Health, Labour, and Welfare authorized the use of MEA as an advanced medical therapy in 2009, MEA has been offered in a few approved institutions and facilities.

In April 2012, MEA was approved by the national health insurance system in Japan as a covered treatment for menorrhagia. At that time, we began providing MEA in our hospital. Several researchers evaluated the efficacy of MEA based on the condition during 3–24 months after operations. Ishikawa et al3 showed that no patient experienced recurrent menorrhagia for > 6 months after MEA. Therefore, the short-term postoperative condition was evaluated in 6 months in this research. The purposes of this research were to evaluate the clinical practice and short-term efficacy of 2.45-GHz MEA to treat menorrhagia and to identify the prognostic factors associated with optimal MEA outcomes.

Materials and methods

Patient selection

Patients with symptoms of menorrhagia who were no longer bearing children and with no uterine malignancy were initially
deemed eligible to receive MEA. After initial screening, eligibility to receive MEA was individually decided on the basis of preoperative assessment using ultrasonography and/or magnetic resonance imaging. In principle, patients whose menorrhagia was not easy to control by conservative therapy were deemed to be good candidates. Patients whose uterine cavity was too large or too complex in shape to appropriately and safely provide MEA were excluded. Patients who preferred hysterectomy, which would furnish a perfect effect for menorrhagia in exchange for the invasiveness, were excluded as well. Before undergoing MEA, patients received an iron supplement, pseudomenopausal therapy (subcutaneous leuprolide acetate), and an oral hormonal medication (dienogest or an estrogen—progestin combination) if necessary.

Research design

We performed MEA in 22 women with menorrhagia between October 2012 and December 2013. To evaluate MEA efficacy, subjective and objective variables were measured. Objective variable data were drawn from patients’ medical records, including their laboratory test results, and subjective variables were measured using patients’ responses to a written questionnaire survey. Pre- and postoperative subjective symptom ratings of each patient were obtained using a questionnaire with a visual analog scale (VAS) scored from 0 to 10 for each symptom. The questionnaire survey obtained using a questionnaire with a visual analog scale (VAS) and postoperative subjective symptom ratings of each patient were data were drawn from patients’ medical records, including their objective and objective variables were measured. Objective variable

Ablation procedure

The microwave system used in this research was composed of a Microtaze device and a Sounding Applicator (Alfresa Pharma, Osaka, Japan). The former is a power generator of 2.45-GHz microwaves, and the latter is an intrauterine applicator that irradiates microwaves from its tip. The applicator is 4 mm in diameter and curved to access the endometrium easily, and it reaches to a maximum distance of 18 cm. MEA was performed according to the procedure guidelines described previously. The microwave generator’s output was set to 70 watts for 50 seconds for each irradiation. Transabdominal ultrasonography was used for intraoperative monitoring. Immediately before and after the procedure, as well as during the procedure if necessary, hysteroscopy was used to visualize the ablated area. Microwave irradiation was repeated until a sufficient area of the uterine corpus endometrium had been ablated. General anesthesia was used, and a nonsteroidal anti-inflammatory drug was administered intraoperatively.

To evaluate MEA efficacy in detail, pre- and postoperative variables of each patient were compared. An iron supplement was administered to 81.8% and 5.3% of patients (p < 0.001 by McNemar test), pseudomenopausal therapy was administered to 68.2% and 10.5% (p < 0.001), and oral hormonal medication was administered to 5.3% and 10.5% (p = 1.0) of the 22 women in the pre- and postoperative periods, respectively. Changes in hemoglobin concentration and patients’ subjective symptom ratings are presented in Figure 1. Hemoglobin concentration (median preoperative score, median postoperative score, and median variation were 8.6, 13.5, and 5.0, respectively) ameliorated in the postoperative period.

| Factors | Median | Range | n | % |
|---------|--------|-------|---|---|
| Age (y) | 48.5   | 39–54 |   |   |
| Parity | 2      | 0–4   |   |   |
| Previous cesarean delivery | 6 | 27.3 |   |   |
| Obesity (BMI > 25) | 4 | 18.2 |   |   |
| Initial anemiaa | 18 | 81.8 |   |   |
| Initial hemoglobin concentration (g/dL) | 8.6 | 4.0–13.6 |   |   |
| Organic diagnosis causing menorrhagia | | | | |
| Uterine fibroids | 15 | 68.2 |   |   |
| Multiple fibroids | 9 | 60.0 |   |   |
| Submucosal fibroids | 8 | 53.3 |   |   |
| Adenomyosis | 7 | 31.8 |   |   |
| Functional menorrhagia | 0 | 0 |   |   |
| Patient complaints | | | | |
| Heavy menstrual bleeding | 22 | 100 |   |   |
| Prolonged menstruation | 10 | 45.5 |   |   |
| Painful menstruation | 11 | 50.0 |   |   |
| Uterine corpus cavity length (cm) | 5.5 | 3.4–7.5 |   |   |
| Preoperative use of iron supplement | 18 | 81.8 | | |
| Preoperative pseudomenopausal therapy | 15 | 68.2 | | |
| Preoperative oral hormonal medication | 1 | 4.5 | | |

BMI = body mass index.

Table 1

Results

The characteristics of the 22 patients who received MEA are shown in Table 1. No patients received a diagnosis of functional menorrhagia; all patients had either uterine fibroids or adenomyosis. Summarized data concerning the MEA procedures are shown in Table 2. On the whole, MEA yielded high levels of patient satisfaction with minimal postoperative pain. The only clinically problematic adverse event occurred in a patient with a single intramural fibroid of 55 mm in diameter. The patient had a fever with purulent vaginal discharge 1 week after MEA. The condition was diagnosed as bacterial endometritis, and she had to be briefly admitted to our hospital for intravenous antibiotics.

Data were analyzed using JMP version 8.0 (SAS Institute, Cary, NC, USA) and R version 2.13. Two-tailed p values were calculated using univariate methods including the Mann–Whitney U test, Wilcoxon signed rank test, McNemar test, Chi-square test, and Pearson product–moment correlation coefficient. A p value < 0.05 was considered significant.

Table 2

| Factors | Median | Range | n | % |
|---------|--------|-------|---|---|
| Age (y) | 48.5   | 39–54 |   |   |
| Parity | 2      | 0–4   |   |   |
| Previous cesarean delivery | 6 | 27.3 |   |   |
| Obesity (BMI > 25) | 4 | 18.2 |   |   |
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| Preoperative oral hormonal medication | 1 | 4.5 | | |

BMI = body mass index.

Characteristics of the 22 patients who received microwave endometrial ablation to treat menorrhagia.
In the 19 patients whose postoperative conditions were obtained, amenorrhea was observed in 52.6% (10/19) in the postoperative period. Only one patient reported no improvement in the menstrual bleeding volume. She received a diagnosis of multiple uterine fibroids, including a 56-mm submucosal fibroid. Her uterine corpus cavity measured 7.5 cm, and the operator performed 12 microwave irradiation sessions during the patient’s MEA procedure. Her pre- and postoperative ratings of menstrual bleeding volume were 10 and 10, respectively.

The MEA outcomes were largely positive: 94.7% (18/19) of patients were classified in the effective group, and 84.2% (16/19) also met the criteria for the highly effective group, whereas only 5.3% (1/19) of patients were classified into the noneffective group. Subsequent hysterectomies were performed in two patients, although these events occurred after the postoperative study period of 6 months. One case was the aforementioned patient who underwent hysterectomy 11 months after MEA. The second patient received a diagnosis of adenomyosis and pelvic endometriosis with severe anemia and dysmenorrhea. Although MEA reduced the patient’s reported menstrual bleeding volume, her dysmenorrhea was not relieved and pelvic endometriosis was exacerbated. After MEA, she received pseudomenopausal therapy, which also did not produce sufficient improvement in her symptoms. Therefore, the patient underwent hysterectomy with affected-side salpingo-oophorectomy 1 year after MEA.

To identify the prognostic factors associated with the optimal outcomes, background factors were compared between the highly effective group and the other groups (Table 3). The mean uterine corpus cavity length was significantly shorter in the highly effective group than in the other groups, and no patients in this group had a cavity length greater than 7 cm.

The correlation between the uterine corpus cavity length and the number of microwave irradiation sessions required for treatment was analyzed (Figure 2), and a positive linear correlation was observed ($r = 0.54$, $p = 0.008$).

**Discussion**

MEA was safely and effectively provided in our hospital. The short-term efficacy rate of MEA for the treatment of menorrhagia was estimated to be 94.7%. The optimal MEA outcomes were associated with a shorter uterine corpus cavity. A positive linear correlation was

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**Table 2**

Summarized data concerning microwave endometrial ablation procedures.

| Variables                                      | Median | Range | n  |
|------------------------------------------------|--------|-------|----|
| No. of microwave irradiation sessions per operation | 7.0    | 5–12  |    |
| Operative time (min)*                          |        |       |    |
| Postoperative use of painkiller on the operative day | 18     | 10–43 |    |
| Postoperative use of painkiller on and after the next day | 4      | 18.2  |    |
| VAS score of postoperative pain (points)*      | 1.0    | 0–10  |    |
| VAS score of satisfaction (points)*            | 8.1    | 2.5–10|    |

VAS = visual analog scale.

* The duration from starting the first irradiation to ascertaining necessary and sufficient ablation by hysteroscopy.

* A lower score indicates milder pain.

* A higher score indicates a higher level of satisfaction.
Table 3
Comparison of background factors between the highly effective group and the other groups in the 19 patients whose postoperative ratings were obtained.

| Factors                              | Highly effective group | Other groups | \( p \) |
|--------------------------------------|------------------------|--------------|--------|
| Age (y)                              | 45.5                   | 46           | 0.96   |
| Parity                               | 2                      | 2            | 0.39   |
| Previous cesarean delivery (%)       | 37.5                   | 0            | 0.20   |
| Obesity (BMI \( \geq 25 \)) (%)      | 25.0                   | 0            | 0.33   |
| Initial hemoglobin concentration (g/dL) | 8.4                   | 9.7          | 0.91   |
| Organic diagnosis causing menorrhagia (%) | 68.8                   | 33.3         | 0.25   |
| Uterine fibroids                     | 63.6                   | 100          | 0.46   |
| Submucosal fibroids                  | 63.6                   | 100          | 0.46   |
| Adenomyosis                          | 33.3                   | 68.8         | 0.25   |
| Patient complaints (%)               |                        |              |        |
| Prolonged menstruation               | 43.8                   | 33.3         | 0.74   |
| Painful menstruation                 | 50.0                   | 100          | 0.11   |
| Uterine corpus cavity length (cm)    | 5.5                    | 7.2          | 0.010  |
| VAS scores of patients’ subjective preoperative conditions (points) |          |              |        |
| Menstrual bleeding volume            | 10                     | 7.5          | 0.18   |
| Menstrual duration                   | 7                      | 5            | 0.19   |
| Abnormal vaginal bleeding            | 0                      | 5            | 0.068  |
| Menstrual pain                       | 5                      | 8            | 0.21   |
| Chronic pelvic pain                  | 2.5                    | 0            | 0.79   |
| Vaginal discharge                    | 5                      | 2.4          | 0.27   |
| Fatigue                              | 7.5                    | 5            | 0.28   |
| Preoperative pseudomenopausal therapy (%) | 68.8                   | 66.7         | 0.95   |

Data are presented as the median or proportion in each group. The \( p \) values were calculated using Chi-square or Mann–Whitney \( U \) tests. BMI = body mass index; VAS = visual analog scale.

**Figure 2.** Correlation between the uterine corpus cavity length and the number of microwave irradiation sessions, measured using the Pearson product-moment correlation coefficient.

Table 4
Short-term efficacy of microwave endometrial ablation reported in the recent literature.

| Year     | Researchers          | \( n \) | Period of assessment for therapeutic effect (mo after MEA) | Reduction in menstrual bleeding volume | Postoperative amenorrhea rate | Amelioration of menstrual pain | Subsequent hysterectomy rate |
|----------|----------------------|--------|-----------------------------------------------------------|---------------------------------------|-------------------------------|--------------------------------|------------------------------|
| 2009     | Sambrook et al\(^\text{1}\) | 157    | 12                                                        | 76                                    | 41                            | 4                              | 4                            |
| 2012     | Singh et al\(^\text{2}\)  | 68     | 6–18                                                     | 84.4                                  | 41                            | 7                              | 7                            |
| 2012     | Tsuda\(^\text{3}\)      | 25     | 3                                                        | 96                                    | 32                            |                                | 6                            |
| 2012     | Ishikawa et al\(^\text{4}\) | 55    | 6–24                                                     | 92                                    | 31                            | 8                              | 2                            |
| 2014     | Nakayama et al\(^\text{5}\) | 76    | 6                                                        | 95                                    | 34                            | VAS score of 4.2 improved to 1.3 | 3                            |
| 2014     | This research         | 19     | 6                                                        | 95                                    | 53                            | VAS score of 7.5 improved to 0.5 | 9\(^\text{6}\)          |

Data are presented as %, unless otherwise indicated.

VAS – visual analog scale.

\(^{1}\) These were performed after the postoperative study period of 6 months.
sessions required for treatment. As a rough estimate, a uterine corpus cavity with a length of 5 cm generally required six microwave irradiation sessions, one of 6 cm needed seven sessions, and one of 7 cm required eight sessions. This guideline may assist MEA operators in selecting the number of microwave irradiation sessions, taking into account uterine size, uterine shape, organic diagnosis, and previous history of cesarean delivery.

Since the introduction of MEA for the treatment of menorrhagia in our hospital in 2012, the procedures have been shown to be both effective and safe. In our experiences, the cases that do not have very large cavities, protuberating submucosal myomas, and severe endometriosis outside the uterus are considered to be positive indications for MEA. Particularly for a case with large submucosal myomas, Kanaoka et al. developed and reported the system of transcervical microwave myolysis. It seems to have potency; however, it cannot be applied yet for approved treatment. We hope to continue contributing to improvements in the provision and research of this novel and useful therapy in Japan.

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Clinical practice and short-term efficacy of 2.45-GHz microwave endometrial ablation to treat menorrhagia

日本語要約
【目的】過多月経に対するマイクロ波子宮内膜焼灼術（MEA）の実践と短期的治療効果を検証し、さらに治療転帰を予測し得る背景因子を探索した。

【方法】MEAを行った全22例を研究対象とした。治療効果を検証するための変数は、客観的な評価に基づくものと患者アンケートによる主観的な評価に基づくものに分けた。患者アンケートは治療後（MEA後約6か月の時点）にし、治療前（初診時からMEA施術まで）と治療後の状態を同時に回答させた。回答方法には0から10までのvisual analog scale (VAS)を用いた。治療転帰を治療後に判定し、貧血なし・過多月経改善・ホルモン剤治療不要の全てを満たす状態を著効、前2項目を満たすがホルモン剤治療を必要とした場合を有効、有効に満たない場合を無効とした。治療前と治療後の各変数を比較し治療効果を検証した。さらに著効群と非著効群の背景因子を比較した。

【結果】患者背景に関して、年齢47歳（中央値、以下同様）、子宮筋腫68%、子宮腺筋症32%、初診時ヘモグロビン値8.6g/dL、術後疼痛VASスコア1.0ポイント、手術満足度8.1ポイント。ヘモグロビン値、経血量、月経期間、月経痛、帯下過多、体調全般が術後改善した。治療転帰は有効95%，著効84%，無効5%であった。著効群では非著効群より子宮体部腔長が短かった。

【結論】MEAを安全に実践した。短期的治療効果から判定した有効率は95%と高かった。子宮体部腔長が短いことが著効の転帰と関連していた。