Simultaneous Use of Ultrasonically Guided Transcervical Microwave Myolysis for Myomas and Adenomyosis and Microwave Endometrial Ablation for Menorrhagia

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Abstract

Objective: Microwave endometrial ablation is widely used instead of hysterectomy for menorrhagia. However, it can not be used for large myomas or deep adenomyosis. To treat myomas and adenomyosis, we developed a transcervical microwave ablation system, and performed ultrasonically guided transcervical microwave myolysis.

Materials and Methods: Microwave (2.45 GHz) was introduced through coaxial cables to 2 types of microwave applicators: 1) a curved (diameter: 4 mm) for endometrial ablation, and 2) a needle-type (diameter: 1.6 mm) for myolysis. Once microwave endometrial ablation was completed, the needle-type applicator was placed in the myoma by transcervical introduction into the uterine cavity and puncturing, using a puncture adaptor attached to a transvaginal ultrasonic probe. Microwave irradiation was administered at 17 W for 10 min. Five patients waiting for microwave endometrial ablation of organic menorrhagia, caused by myomas or adenomyosis entered the study after giving complete informed consent. The study was approved by the Ethics Committee of Osaka City University Hospital.

Results: In 4 patients with myomas, the major part consisting of a submucous or an intramural node of 6 to 7 cm in size, was irradiated by microwave and necrotized. The myoma nodes shrank by 17 to 53% in the following 3 months. The patient with adenomyosis showing a uterus greater than a newborn’s head in size became amenorrheic, and the uterus size decreased by 31% three months after the operation. No remarkable complications were encountered.

Discussion: Transcervical microwave myolysis is feasible, and can quickly treat usual myomas or adenomyosis.

Keywords: microwaves, endometrial ablation, myolysis, transcervical, myoma

Özet

Transservikal Ultrasonografi ile Yönlendirilerek Mikrodalga ile Eşzamanlı Miyom ve Adenomiyom Miyolizi ve Menorajiyi Önlemek Üzere Endometriyum Ablasyonu

Amaç: Menoraji için hysterektomi yerine, mikrodalga ile endometriyum ablasyonu yaygın olarak uygulanmaktadır. Miyom ve adenomiyomların tedavisi için transservikal uygulan mikrodalga ile ablasyon sistemi geliştirilerek ultrasonografik yönlendirme ile miyoliz için kullanıldı.

Materyal ve Metot: Endometriyum ablasyonu için kavısı (4 mm çaplı) ve miyoliz için içe bağlı (1.6 mm çaplı) iki ayrı mikrodalga uygulayıcısına, orta akısi kablo ile mikrodalga (2.45 GHz) iletildi. Mikrodalga ile endometriyum ablasyonu tamamlanınca ultrason ucuna takılan bir adaptöre bağlanan içe bağlı mikrodalga uygulayıcı servisken rahim boşluğuna uzatılarak miyomun içine sokuldu ve 10 dakika süreyle 17 W mikrodalga iletildi. Bilgilendirilerek onaylı alınmış, miyom ve adenomiyom nedeniyle organik menoraji tedavisi için endometriyum ablasyonu beklenecek hasta, bu çalışmaya katıldı. Osaka Şehir Üniversitesi Hastanesi Etki Kurulu onayını aldı.
Introduction

Uterine myomas and adenomyosis are the major causes of enlarged uteri associated with menorrhagia or dysmenorrhea. Endometrial ablation is widely used as an alternative to hysterectomy for menorrhagia. However, it is not applicable to uterine cavity occupied by large submucous myomas. Also, deep adenomyosis may sometimes deteriorate its effects, leading to subsequent hysterectomy (1). Techniques destroying myomas in situ instead of myomectomy are termed myolysis. They have been performed by transabdominal cryosurgery under magnetic resonance monitoring (2), radiofrequency ablation with transabdominal, transvaginal or laparoscopic approach (3), or laparoscopic interstitial laser ablation (4). Because, these methods do not adopt a transcervical approach, a minimal incision or puncture of the abdominal wall or the vaginal wall is needed. Focused ultrasound (FUS) myolysis (5) is an elegant method without invasive access to myomas; however, its indication is limited depending on location, size, or vascularity of the target node. Uterine artery embolization (UAE) has been widely performed, and some authors report successful delivery after UAE (6). However, UAE is occasionally accompanied by complications of intra-arterial catheterization (7).

To treat myomas and adenomyosis by microwave ablation, we developed a transcervical microwave ablation system. Most submucous or intramural myomas, and adenomyotic lesions are accessible by a transcervical approach. Transcervical treatment is expected to be easy to perform, and involves minimally invasive access to symptomatic myomas and adenomyosis. However, transcervical microwave myolysis has not been reported. We report for the first time, ultrasonically guided transcervical microwave myolysis following microwave endometrial ablation at 2.45 GHz using a specifically developed microwave irradiation system, in 5 patients.

Materials and Methods

Microwaves at 2.45 GHz from a microwave tissue coagulator (Microtaze AZM-520, AlfresaPharma, Osaka, Japan) were introduced through a coaxial cable to 2 types of microwave applicators: 1) a curved applicator (diameter: 4 mm; length: 20 cm) (SoundingApplicator, AlfresaPharma, Osaka, Japan) for endometrial ablation; and 2) a custom-made needle type (diameter: 1.6 mm; length: 37 cm). Each patient was positioned in the lithotomy position under general anesthesia. First, microwave endometrial ablation was performed to treat menorrhagia using the curved applicator.

Procedures for microwave endometrial ablation at 2.45 GHz for menorrhagia in an enlarged uterus have been described (8). A 14-gauge guiding needle (Hakko, Chikuma, Nagano, Japan) was then transcervically introduced into the uterine cavity and inserted into the myoma node, until the end reached 10 mm from the distal margin of the node, using a puncture adaptor attached to a transvaginal probe and a Prosound alpha 10 ultrasonic imager (Aloka Co., Tokyo, Japan). Then, the inner needle of the guiding needle was replaced by the needle-type microwave applicator (Figure 1). Then, microwave irradiation was administered at 17 W for 10 min. In a patient with deep adenomyosis, irradiation sites were set more than 15 mm away from the uterine serosa and the endometrium. Microwave irradiation was administered at 17 W for 50 seconds at one irradiation site. Irradiation sites were arranged to cover as much of the adenomyotic lesion as possible. Patients were administered with fosfomycin during the operation.

The sharp end of the guiding needle was sheathed with a Teflon tube to protect the uterine canal from injury at insertion and from thermal damage during microwave irradiation. To avoid tissue drying and a decrease in the heat generation rate, saline was infused to the irradiation site at 0.2 ml/min through the space between the guiding needle and the applicator during microwave irradiation. The
puncture adaptor, the guiding needle, and the microwave applicator were thus cooled by flowing saline through the space between the adaptor and the guiding needle during microwave irradiation. Two syringe pumps were used for saline infusion.

Five patients waiting for microwave endometrial ablation for organic menorrhagia caused by myomas or adenomyosis entered the study after giving complete informed consent. The study was approved by the ethics committee of our hospital. Before operation, endometrial malignant diseases were ruled out by hysteroscopy followed by endometrial biopsy, when transvaginal ultrasonography or MRI revealed suspicious areas. One month after operation, Gd-enhanced MRI was performed to detect *de novo* avascular areas showing necrosis. Size of myoma nodes or the uterus were measured by MRI preoperatively, 1 month, and 3 months after the operation. Shrinkage of the treated node was defined as follows:

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\text{Shrinkage} = 100 \times \frac{(A_{\text{before}} \times B_{\text{before}} - A_{\text{after}} \times B_{\text{after}})}{(A_{\text{before}} \times B_{\text{before}})}
\]

\(A_{\text{before}}, B_{\text{before}},\) and \(A_{\text{after}}, B_{\text{after}}\) are sizes of the myoma node before and after operation in 2 dimensions, respectively.

**Results**

The described transcervical puncture system enabled easy introduction of a guiding needle into the cavity without injuring the cervical canal, and insertion of the guiding needle into a myoma node or adenomyotic tissue was easily performed under transvaginal ultrasonography. A saline infusion system to the irradiation site and a cooling system for the applicator and the puncture attachment functioned as expected. Temperature at the puncture adaptor did not rise above 40°C during microwave irradiation. After irradiation, the needle-type applicator was withdrawn smoothly without adhering to tissues on the surface. These results were the same as those reported for microwave irradiation using a surgical specimen (9).

**Cases**

**Patient 1**

Patient 1 had an intramural myoma node 72x77 mm in size before operation. As shown in Figure 2a, MRI in the prone position was performed using a magnetic resonance imager with the FUS system. Since signal intensity of the node was enhanced by the contrast medium like the myometrium, this indicated that FUS was unable to heat the node fully in a limited time. The patient was referred to our facility and underwent microwave myolysis (10 minutes) following microwave endometrial ablation. The patient experienced fever up to 38°C from day 2 to day 4 with elevation of serum lactate dehydrogenase level, which returned to normal level spontaneously. Gd-enhanced MRI, 7 days after the operation revealed that the node had become avascular. Three months after the operation, the node had shrunk by 52%.

**Patient 2**

Patient 2 had suffered from menorrhagia caused by adenomyosis. The patient was referred to our hospital 6 months after UAE for severe continuous menorrhagia. After microwave endometrial ablation, microwave myolysis was performed in the thick posterior wall. Three months after the operation, the uterus size decreased by 31% and the posterior wall decreased in thickness to almost half of that before the operation (Figure 3). The patient had been amenorrheic for 12 months.

**Patient 3**

Patient 3 had a submucosal myoma node 70x51 mm in size protruding by 30% into the uterine cavity. Once microwave endometrial ablation was completed, microwave myolysis was performed for 10 minutes. The patient showed increased discharge, and dull sense of uterine contraction after birth. The symptoms were controlled within 2 weeks after operation by administering non-steroidal anti-inflammatory drugs. During the postoperative period, small necrotic tissues passed out in 3 episodes. Three months after the operation, the myoma had shrunk by 41%.

**Patient 4**

Patient 4 had a submucosal node 67x53 mm in size protruding by 30% into the uterine cavity. Once microwave endometrial ablation was completed, microwave myolysis was performed for 10 minutes. The patient showed increased discharge, and dull sense of uterine contraction after birth. The symptoms were controlled within 2 weeks after operation by administering non-steroidal anti-inflammatory drugs. During the postoperative period, small necrotic tissues passed out in 3 episodes. Three months after the operation, the myoma had shrunk by 41%.

**Figure 2.** MRI images of Patient 1 before and after operation. **a)** An intramural node 7 cm in size can be seen in the sagittal T2-weighted image 1 cm left from the midline before operation. **b)** In the fat saturated enhanced T1-weighted image 7 days after operation, most of the node is avascular.

**Figure 3.** Axial MRI images of Patient 2 before and after operation. **a)** An enlarged uterus due to adenomyosis before operation can be seen in the T2-weighted image. The posterior wall is 7 cm thick. The thin endometrium is indicted by short arrows. The 3 irradiation sites are shown by closed circles. **b)** Fat-saturated enhanced T1-weighted image one month after operation, showing an avascular area in the lining of the uterine cavity with the posterior wall shrunken by half.
ablation and microwave myolysis were performed, resulting in 17% shrinkage of the myoma area.

Patient 5 had a submucosal node of 68x55 mm in size in the anterior wall. Diagnostic imaging by MRI and a power Doppler study showed that the node was hypovascular. Microwaves were irradiated for 10 min in the myoma tissues after microwave endometrial ablation. The postoperative course was uneventful. The node shrank by 53%.

Patients 1, 3 and 5 became hypomenorrheic and Patient 4 became eumenorrheic after operation.

Discussion

Conventional methods for myolysis utilizing radiofrequency, cryosurgery or a laser have been performed using transabdominal, transvaginal or laparoscopic access. To the best of our knowledge, transcervical microwave myolysis has not been previously reported. However, transcervical access is the shortest path to reach submucous, intramural myoma nodes, and adenomyotic lesions. It is clear that puncture via this shortest path is nearly non-invasive, because symptomatic submucous or intramural myoma nodes are usually located, at the most, 3 to 10 mm under the convex lining of the uterine cavity. Although, the superiority of the transcervical approach is beyond doubt, there are possible unrecognized or unpublished difficulties involved in transcervical myolysis in clinical practice. Therefore, we investigated the feasibility of ultrasonically guided transcervical microwave myolysis following ex vivo experiments using fresh surgical specimens of a uterus with submucous or intramural myomas. Results of ex vivo experiments showed that it was easy to introduce a guiding needle held in a puncture adaptor attached to a transvaginal probe to the uterine cavity, and to insert the needle into the intramural lesions with an ultrasonic guide. A Teflon sheath perfectly protected the cervical canal from injury at insertion, and thermal damage during microwave irradiation. In clinical practice, transvaginal scan in the vagina exposed by a speculum, clearly depicts intramural myoma nodes. No difficulty has been encountered at insertion of the guiding needle into the irradiation sites.

The output of microwaves and the duration of radiation for myolysis were selected according to the size of the myoma node. If cooling by radiating effects from blood perfusion and cooling by conduction to the myometrium are ignored, microwaves are required to generate heat of 310, 736, 1.438, and 2.484 cal in myomas of 3, 4, 5, and 6 cm in size, respectively, to elevate temperature by 23°C, assuming that the node is a sphere. These estimations show that with 17 W of microwave output, the necessary irradiation times are 1.3, 3, 5.9 and 10.2 minutes, respectively. These irradiation times indicate the shortest values in ideal conditions where cooling is neglected. Thus, microwave radiation for shorter durations than these values is safe.

Ex vivo experiments revealed that an ellipsoid myoma tissue of 60x20x20 mm reached a temperature beyond 60°C after 10 minutes irradiation at 17 W with saline infusion at 0.2 ml/min (9). During microwave irradiation, tissues lose water when the temperature elevates beyond 100°C, which decreases the heat generation rate. Therefore, to maintain the heat generation rate, a small amount of saline is continuously infused to the irradiation site. Infused saline prevents tissues from charring and adhering to the applicator and the mediator of heat generation, based on ex vivo experiments.

Tissue necrosis occurs at temperatures above 60°C, because most proteins in tissue denature at 60°C in a few seconds. Generally, the area where temperature elevates beyond 60°C after microwave irradiation is smaller in in vivo experiments than in ex vivo experiments because of the cooling. In an animal experiment using porcine liver, it has been reported that for microwave tissue degeneration in vivo, degeneration reaches a relative plateau in contrast to ex vivo degeneration, and longer microwave irradiation results in an increase in thermal degeneration (10). For clinical application, irradiation conditions were selected so that the margins of the area above 60°C were located more than 10 mm away from the outer margins of the myoma node. Thus, safe conditions were preserved to prevent thermal damage of extra-uterine organs and the normal myometrium.

Despite that the expected necrosis area was restricted within the myoma node, the outer margins of necrotized tissues reached the borders between the myoma and the myometrium in some cases. We interpreted that as being that heat conducted and maintained the temperature of the marginal myoma tissues over 50°C for longer than 100 seconds during and after microwave irradiation; therefore, delayed necrosis or apoptosis was induced. However, necrosis never extended beyond the borders. This suggested that myoma tissue was more sensitive to thermal stress than normal myometrium because of poor blood perfusion in the myoma tissue; just as myoma tissue is selectively necrotized by UAE.

Microwave myolysis like other conservative techniques has the disadvantage that there is no possibility for histopathological examination. However, the risk of uterine sarcoma is minimized by MRI and needle biopsy. It has been reported that transcervical needle biopsy of the uterine fibroid effectively detect myometrial malignancy (11). In the present cases, MRI revealed usual myoma for Patients 1, 3, 5, and adenomyosis for Patient 2. MRI revealed that Patient 4 had rich vascularity in the node and so transcervical needle biopsy was undertaken to rule out malignant disease.

The present results showed that transcervical microwave myolysis simultaneously combined with microwave endometrial ablation was safe and minimally invasive, demonstrating the feasibility and safety of transcervical microwave myolysis. It was notable that the myoma node with abundant blood perfusion in Patient 4 showed less shrinkage at three months after operation, which suggests that the indication for
the present methods should be limited to usual myomas with poor vascularity.

More clinical studies will be necessary to assess the shrinkage rates of myoma nodes over longer follow-up periods. However, we believe that the usual techniques of hysterectomy and myomectomy for myomas and adenomyosis could be replaced by microwave myolysis in the near future. As well, child-bearing potential may be preserved after microwave myolysis.

Conclusions
Usual myoma and adenomyosis can be safely necrotized by ultrasonically guided transcervical microwave myolysis. Transcervical microwave myolysis can quickly treat usual myomas and adenomyosis.

References