

Uterine peristalsis and infertility: evaluation with cine MR

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Introduction Infertile couple has been increasing these days and numerous factors are considered as potential etiologies for infertility (1). Although various techniques are available to address such factors, many undetectable abnormalities in the process of conception still prevent gestation for infertile couples, resulting in a large number of women with an unknown cause of infertility. Uterine peristalsis is thought to represent a factor involved in infertility, although reports examining this subject using transvaginal ultrasound (TVUS) and MR imaging remain small in number (2, 3). Uterine peristalsis has been reported to change according to the menstrual cycle phase and are thought to facilitate sperm transport toward the fecundation site, as well as help conserve a conceptus (3-5). Malfunction of such movements is thought to lead to an implantation disorder, although the underlying etiology for such malfunction is not well clarified (2). In addition to such an intrinsic mechanism, uterine contractions are also known to be affected by neurogenic activity, since uterine myometrium is smooth muscle (6). Administration of anti-cholinergic agents has been shown to suppress uterine peristalsis (7). This study is designed to evaluate uterine peristalsis in women with an unknown cause of infertility, observing outcomes following anti-cholinergic administration to suppress adverse peristalsis at the time of *in vitro* fertilization (IVF).

Material and Methods 1) **Study population:** Eight infertile women (age range: 30-38 years) recruited from a private hospital specialized in assisted reproductive technology (ART) and 16 healthy female volunteers (age range: 24-42 years) were evaluated at periovulatory phase. To confine the cause of the infertility to an implantation disorder, inclusion criteria of the infertile group were no abnormality on hematologic examination, including estrogen and progesterone levels, male factor, tube patency, TVUS or MR imaging examination and more than three failed attempts at IVF and embryo transfer (IVF-ET) including cryo-preservation and fusion transfer or blastocyst transfer. Two subjects were excluded due to the presence of an endometrial polyp (n=1) and an endometrial cyst (n=1). 2) **MR scanning protocol:** MR studies were performed with a 1.5 T magnet (Symphony, Siemens Medical Systems) using a body array coil. In addition to sagittal fast-spin echo T2WI and spin echo T1WI, sequential T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) images were obtained sequentially in a mid sagittal plane of the uterus under quiet breathing, and displayed in cine mode. One image was obtained every three seconds allowing 60 serial images to be obtained within three minutes. Image analysis was performed by a computer-assisted software program. 3) **Image Analysis and Statistical analysis** Uterine peristalsis was evaluated for the following: 1) detectability of uterine peristalsis; and 2) peristaltic frequency and direction, if present. Comparisons of peristaltic frequency for two groups were performed with the unpaired Student's t-test. Peristaltic direction was compared with the chi-square test for the two groups. The results of MR imaging were reported to the patient's primary attending physician. The clinical course of the patients, focusing on infertility treatment, IVF trials, and outcome of infertility intervention, was observed.

Result Uterine peristalsis was identified in 5 of 6 studies for the infertile group, whereas in all studies of the control group. The peristaltic frequency was 4.2±2.6/2 min for the infertile group and 6.9±1.4/2 min for the control group and the difference was statistically significant (p<0.01). A cervico-fundal direction was observed in 2 of 6 subjects in the infertile group and 12 of 16 subjects in the control group. Fundo-cervical direction was observed in 3 of 6 subjects in the infertile group and only 2 of 16 subjects in the control group. The difference in peristaltic direction was not statistically significant (p=0.20). For three women who showed fundo-cervical peristalsis on MR imaging, anticholinergic agent was administered at the time of next embryo/blastocyst transfer. As a result, two of them got pregnant and one got ectopic pregnancy.

Discussion The present study, although preliminary, demonstrates that uterine peristalsis during the peri-ovulatory phase of infertile women exhibited different characteristics than that of controls. Although uterine peristalsis was detected in five of six infertile subjects, three of the five subjects exhibited fundo-cervical peristaltic direction. Such a high rate of fundo-cervical peristaltic direction in the peri-ovulatory phase is abnormal, as previous reports have demonstrated that the normal uterus in the peri-ovulatory phase exhibits a cervico-fundal peristaltic direction in 62%-95% of cases examined with TVUS and cine MR imaging. MR imaging in the present study of the control group agrees with such results (5, 8). In accordance with the report by Ijland et al., which demonstrated that fundo-cervical peristalsis was more frequent in an infertile group compared with a parous group (9), the present study revealed a frequency of cervico-fundal peristalsis in infertile women less than that observed for controls. Ijland et al. explored the relationship between uterine peristalsis and infertility using TVUS (9). Nonetheless, their inclusion criteria for infertile women differed from the present study. Their inclusion criterion was nulligravida women with infertility caused by a wide variety of possible causes, excluding the tubal factor, the male factor and anovulation. In contrast, the present study strictly selected women with unknown causes of infertility, repeated IVF failure, and only an implantation disorder. Fundo-cervical waves, which oppose the usual cervico-fundal waves, may, at the very least, adversely affect sperm transport, or, worse yet, act to expel the embryo from the uterine cavity, resulting in infertility (4) (5). All three patients who showed fundo-cervical peristalsis on MR imaging and underwent IVF-ET with administration of an anti-cholinergic agent to suppress such reversed waves became pregnant. It has been reported that uterine peristalsis tends to be suppressed by anti-cholinergic agents (7). The mechanism underlying the effects of anti-cholinergic agents on uterine myometrium is thought to be related to the parasympathetic nervous system though the uterus receives dual nervous system control, parasympathetic and sympathetic (10, 11). Since anti-cholinergic agents block only the parasympathetic nervous system and its effect lasts for only 10-15 minutes, not all uterine contractions are blocked. Accordingly, although the effect of anti-cholinergic agents might be weak, it may possible that uterine contractions are suppressed at the time of embryo transfer.

In conclusion, although preliminary, infertile women appear to exhibit an abnormal uterine peristaltic direction and reduced peristaltic frequency during the peri-ovulatory phase on cine MR imaging. In addition, subjects with fundo-cervical peristalsis became pregnant with administration of anti-cholinergic agents at the time of IVF-ET. It would appear that a malfunction in uterine peristalsis might result in infertility, which might be possibly corrected with anti-cholinergic agents.

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	N	Peristalsis		Frequency			Direction		
		Presence		(/3min)	CF	FC	CF+FC		
Infertile	6	5		4.2±2.6	2	3	0		
Control	16	16		6.9±1.4	12	2	2		
				(p<0.01)					(p=0.20)

CF=cervico-fundal, direction, FC=fundo-cervical direction