



Evaluation of the effects of shockwave application on intrauterine adhesion in a rat model

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Intrauterine adhesion (IUA) is a major cause of female secondary infertility and is typically caused by damage to the uterus during postpartum curettage. The annoying symptoms are abnormal menstruation, pelvic pain, recurrent abortion, and infertility which are accompanied by psychological distress. Epidemiological data showed the incidence of IUA in females who have undergone hysteroscopic surgery and abortion ranges between approximately 4–46%. In addition, there is a high probability of complications and perforation-induced bleeding during reconstructive surgery, while the probability of a successful pregnancy is only 23 to 33%. Clinical data also indicate that the prognosis of IUA could be related to failed endometrial regeneration, with a recurrence rate of up to 62.5%. Therefore, the therapeutic of IUA is an absolutely important issue. Many studies have indicated some pharmacotherapy, such as hormones, vasoactive agents, and antibiotics treatment can help regenerate the endometrium and accelerate wound repair for repairing endometrial tissue in intrauterine adhesion. However, with these strategies, the possibility of adhesions recurrence persists, even after adhesiolysis, depending on the disease severity.

In the clinical study, extracorporeal shock wave therapy (ESWT) has been used for treating chronic pelvic pain, and vulvodynia in gynecology disease. I hypothesized that ESWT can ameliorate inflammatory effects in IUA. Our successfully established IUA rat model during preventive and therapeutic stages showed ESWT increased the number of glands, enhanced vascular endothelial growth factor (VEGF), facilitated vimentin expression in the IUA-affected endometrium, decreased the fibrotic scarring formation compared with only IUA-damaged endometrium. In addition, we also detected inflammatory, anti-inflammatory, angiogenesis, and fibrosis-associated genes underlying ESWT treatment and/or PRP transplantation during these two stages, transforming growth factor- β (TGF- β), collagen-I $\alpha 1$ (COL1 $\alpha 1$), fibronectin, nuclear factor kappa B (NF- κ B), interleukin (IL)-6 and tumor necrosis factor (TNF- α) were dramatically downregulated following ESWT treatment, PRP alone, and PRP transplantation. Conversely, the mRNA expression levels of VEGF, progesterone receptor (PR), insulin-like growth factor-1 (IGF-1), and IL-4 are significantly upregulated following ESWT, or PRP alone or ESWT treatment combined with PRP transplantation. ESWT treatment, PRP transplantation, or ESWT combined with PRP enhanced VEGF expression in protein levels during the two stages. Importantly, PRP transplantation or ESWT combined with PRP ameliorates pregnancy outcomes during the therapeutic stage of the *in vivo* study. Moreover, TGF- β and nuclear factor kappa B (NF- κ B) not only decreased the levels of mRNA expression but also down-regulated the protein levels of endometrium cells in molecular mechanisms, especially during the therapeutic stage. PRP transplantation or ESWT combined with PRP significantly suppressed inflammation in the IUA uterus, indicating that these treatment strategies potentially participate in vascularization, endometrial growth, and downregulation of pro-inflammatory-associated genes in the IUA-damaged uterine cavity. PRP transplantation or PRP combined with ESWT treatment is a valuable strategy to treat IUA.

Curriculum Vitae

Current Appointments :

- Professor, Department of Obs. & Gyn., Chang Gung Memorial Hospital, Kaohsiung, Taiwan
- Professor, Department of Obs. & Gyn., Chang Gung University, Taiwan.
- Superintendent, Jen-Ai Chang Gung Hospital, Taichung, Taiwan
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- Director, Taiwanese Society for Reproductive Medicine
- Director, Kaohsiung County Medical Association

- President, The Taiwanese Menopause Society

Education :

1987-1994	Graduated with a Bachelor's Degree from College of Medicine, China Medical University
2001-2007	Graduated with a Master's Degree from Graduate Institute of Clinical Medical Sciences, Chang Gung University
2007-2014	Graduated with a Doctorate Degree from Graduate Institute of Clinical Medical Sciences, Chang Gung University

Awards :

1999, 2000	Outstanding Teaching Attending Physician of the Year
2003, 2004	Outstanding Paper Award, Taiwanese Society for Reproductive Medicine
2004, 2005, 2007	Outstanding Teaching Attending Physician of the Year
2007	Candidate, 2007 Ministry of Science and Technology Academic Research Award IS Award, 59 th Annual Congress of Japan Society of Obstetrics and Gynecology
2008,2014,2015,2020	Outstanding Paper Award, Taiwanese Society for Reproductive Medicine
2009	Guide Author of Resident Physician Excellent Paper Award
2011	IS Award, 63 th Annual Congress of Japan Society of Obstetrics and Gynecology
2014	IS Award, 66 th Annual Congress of Japan Society of Obstetrics and Gynecology Outstanding Paper Award, Taiwanese Society for Reproductive Medicine
2015	IS Award, 67 th Annual Congress of Japan Society of Obstetrics and Gynecology
2016	IS Award, 68 th Annual Congress of Japan Society of Obstetrics and Gynecology
2018	IS Award, 70 th Annual Congress of Japan Society of Obstetrics and Gynecology
2022	Prize Poster Award, Taiwanese Society for Reproductive Medicine