Neuromuscular Electrical Stimulation and Biofeedback Therapy to Improve Endometrial Growth in Patients with Thin Endometrium

A Randomized Controlled Study

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1 INTRODUCTION

Thin endometrium at time of ovulation can be a concern and may be one of the principal causes of embryo implantation failure, poor placental development and miscarriage in assisted reproductive technologies (ART). The aim of this study is to evaluate the efficacy of non-invasive NMES in the management of thin endometrium patients with history of at least two previous ART cycles failure in which the optimum endometrium thickness was less or equal to 7 mm.

2 METHOD

This was an open label, randomized controlled trial, interventional study, parallel assignment, comparing NMES with ASA in fertility unit, Memorial Hospital of Sun Yat-Sen University. Allocation to groups was by concealment. 115 patients with thin endometrium (≤7mm) and history of infertility were recruited for this work. NMES group received intermittent vaginal NMES according to the manufacturer’s recommended protocol for 20 to 30 minutes, 3 to 4 times during one menstruation cycle from day 9-10 to human chorionic gonadotropin (hCG) administration day and in comparison, a similar group of subjects receive d ASA (100mg/day from day 9 or day 10 until the day of pregnancy test). Pre and post-treatment endometrium thickness, endometrial volume and Power Doppler Angiography (PDA) related parameters measured by three-dimensional ultrasound using a 4D sonographic scanner (Voluson 730/ Voluson E8, GE Medical Systems, Kretz Ultrasound, Zipf, Austria) equipped with an automatic 6-12 MHz 4D probe at day 9-10 and at hCG administration day. Data analysis was performed using Mann–Whitney U-test and chi-square test where appropriated.

3 RESULTS AND DISCUSSION

A total of 55 and 48 women were randomized to NMES therapy and ASA treatment groups respectively and effectively participated to the study and were further analysed. The mean age of the study population was 30.74 ± 4.52 (range 21-39). The women in this study had mixed diagnosis. 51/103(50%) had primary infertility. 45 women out of 103 were diagnosed polycystic ovary syndrome (PCOS). 42 had tubal occlusion, and 71 with male factor. Their mean ages were 30.32 ± 4.57 and 31.23 ± 4.47 years for NMES and ASA group respectively. Their mean body mass indexes (BMI) were 20.78 ± 3.24 and 21.82 ± 2.92 kg/m² for NMES and ASA respectively. The endometrium was thicker in the NMES group compared with that in ASA group [8.00 versus 7.72; P=0.028]. 32/55(58%) developed endometrial thickness equal to or more than 8 mm after NMES therapy in the NMES group and 16/48(33%) in ASA group. The endometrial and sub-endometrial volumes at final point also differ significantly between groups [2.58 versus 2.28; P=0.008 and 1.40 versus 1.21; P=0.001 for endometrial volume and sub-endometrial volume respectively. The two groups did not differ significantly regarding endometrial vascularization index (VI) and vascularization flow index (VFI) at final point. But in another hand, endometrial flow index (FI), sub-endometrial vascularization index(sub-VI), sub-endometrial flow index (sub-FI) and sub-endometrial vascularization flow index (sub-VFI) differed statistically between groups (P=0.032, P=0.022, P=0.006 and P=0.018 respectively).

A good quality of endometrium is of great significance to human reproduction and therefore plays an important role as well as a good quality
embryo. Normally, in response to oestrogen, the uterine lining or endometrium grows about 1-2mm every other day. Thin endometrium more commonly occurs when the basal germinal endometrium, from which the full endometrial layer develops, is compromised in its response to oestrogen by damage or reduced blood flow. Many studies have been reported that a poor uterine receptivity in women with thin endometrium is associated with the impairment of blood flow impedance through the endometrium (Khairy, 2007) (Sher, 2002). Despite advancement of the ART, therapy for thin endometrium have gone without significant change for some women over the past few decades. One major impediment to treating women with this condition is the large range of aetiologies associated to thin endometrium. NMES is the application of electrical current to the pelvic floor muscles. NMES combined with biofeedback may be useful in that the electrical stimulation provides a passive contraction that increases awareness of pelvic floor muscle contractions in general. In a recently published pilot study, we have shown that NMES could be one of effective options to manage women with thin endometrium (Bodombossou-Djobo, 2011). To our knowledge, this is the first randomized trial examining the effect of NMES compared to ASA on endometrium thickness. Our main outcome of interest in this trial was the change in endometrial thickness and volume along with associated vascularization indices in the two groups. The data in this study have showed that NMES improved endometrial thickness, endometrial volume and endometrial vascularization in women with thin endometrium. There was no consistent decrease in impedance to uterine spiral arteries blood flow from baseline to final point in aspirin group patients. In contrast to these findings, there was a decrease in PI and RI values after NMES therapy in NMES group patients. This makes us believed that NMES not only improved endometrial thickness but also decreased PI and RI in patients with thin endometrium.

It is currently unclear how NMES exerted its action on the endometrium in term of mechanism but the hypothesis was that by stimulating uterine smooth muscle to repeated contraction and relaxation, there will be an increased in blood supply towards the whole endometrial and the sub-endometrial regions that leads to peripheral tissue trophicity. By this hypothetical mechanism, NMES will likely correct the impairment of uterine blood flow and will increase the endometrial thickness.

4 CONCLUSIONS

Our randomized controlled trial showed better endometrial thickness, endometrial volume and vascularization in NMES group than that in aspirin group. However, more studies with greater sample size and with uniformity regarding treatment protocols are needed for the implementation of the new therapy in clinic.

REFERENCES