

21. Others

Reference

Fujii S, Fukushi Y, Yamaguchi E, et al. A study of the addition of tokishakuyakusan during in-vitro fertilization cycles*. *Sanfujinka Kampo Kenkyu no Ayumi (Recent Progress of Kampo Medicine in Obstetrics and Gynecology)* 1997; 14: 121-5 (in Japanese).

1. Objectives

To evaluate the effect of ovarian stimulation by tokishakuyakusan (当帰芍薬散) (used during in vitro fertilization and embryo transfer [IVF-ET] cycles) on follicular growth, luteal function, pregnancy rate, and abortion rate.

2. Design

Randomized controlled trial (RCT).

3. Setting

Single institution (Department of Obstetrics and Gynecology, Hirosaki University Hospital), Japan.

4. Participants

Ninety-three patients who were diagnosed as infertile at the above-mentioned institution between April 1995 and September 1996 and underwent ovarian stimulation using gonadotropin-releasing hormone (GnRH) agonist (long protocol).

5. Intervention

Arm 1: IVF-ET with ovarian stimulation using GnRH agonist (long protocol) and hMG, combined with oral administration of TSUMURA Tokishakuyakusan (当帰芍薬散) Extract Granules 2.5 g t.i.d. before meals.

Arm 2: IVF-ET with ovarian stimulation using GnRH agonist (long protocol) and human menopausal gonadotropin (hMG).

6. Main outcome measures

The following measures were compared between two arms: number of dosing days and total dose of hMG as an ovarian stimulant, endometrial thickness at the last dose of hMG, number of retrieved oocytes, number of fertilized oocytes, fertilization rate, number of transferred embryos, number of cancelled transfer cycles per oocyte retrieval, pregnancy rate, abortion rate per pregnancy; blood concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), estradiol (E), and progesterone (P); and P/E ratio.

7. Main results

There were no between-arm differences in the number of dosing days and total dose of hMG as an ovarian stimulant, endometrial thickness at the last dose of hMG, number of retrieved oocytes, number of fertilized oocytes, and fertilization rate. There were trends toward higher number of transferred embryos and lower number of cancelled transfer cycles per oocyte retrieval in arm 2. There were no between-arm differences in pregnancy rate per oocyte retrieval and abortion rate per pregnancy. The blood estradiol concentration was relatively high in arm 2 throughout the treatment cycles. No significant differences were observed in the blood concentrations of PRL and progesterone and P/E ratio. The blood FSH concentration was significantly higher in arm 2 at the time of oocyte retrieval ($P < 0.01$).

8. Conclusions

During IVF-ET cycles (GnRH agonist-long protocol), oral tokishakuyakusan was not found to have a clear clinical significance, but it reduced the total dose of hMG required to induce follicular growth, suggesting that this drug may stimulate secretion of FSH at the times of human chorionic gonadotropin (hCG) administration and oocyte retrieval.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

The authors of this paper concluded that during IVF-ET cycles, combined tokishakuyakusan has no clear clinical significance. Yet it is noteworthy that, in IVF-ET, which we can consider an example of highly-advanced medical technology, tokishakuyakusan significantly reduced the dose of the drug used for ovarian stimulation, tended to reduce the rate of cancelled embryo transfer cycles per oocyte retrieval (to one fifth), and increased the number of transferred embryos. In this study, a sufficient number of cycles for clinical evaluation were administered, but rates of pathological conditions that require oral tokishakuyakusan were not compared between the two arms. Subgroup analyses would have been needed for, at least, cases with *oketsu* (瘀血, static blood) and *suidoku* (水毒, disorder of body fluid metabolism). I hope that the true clinical value of tokishakuyakusan-combined therapy will be found in future prospective studies that compare the effects according to the pathological conditions (with or without *ketsu-kyo* [血虚, blood deficiency], *oketsu*, or *suidoku*) with rigorous oriental medical diagnoses.

12. Abstractor and date

Ushiroyama T, 10 September 2008, 1 June 2010, 31 December 2013.