

O-009

Ovarian stimulation in IUI cycles in couples with unexplained subfertility: follicle stimulating hormone (FSH) or clomiphene citrate (CC)?

N. Danhof¹, M. van Wely¹, C. Koks², H.R. Verhoeve³, J.P. Bruin⁴, M. Verberg⁵, M. van Hooff⁶, B.J. Cohlen⁷, C. van Heteren⁸, J. van Disseldorp⁹, F.J.M. Broekmans¹⁰, B.W.J. Mol¹¹, S. Repping¹, F. van der Veen¹, M.H. Mochtar¹

¹*AMC, Center for Reproductive Medicine, Amsterdam, The Netherlands*

²*Maxima Medical Center, Obstetrics and gynaecology, Veldhoven, The Netherlands*

³*OLVG, Obstetrics and gynaecology, Amsterdam, The Netherlands*

⁴*Jeroen Bosch ziekenhuis, Obstetrics and gynaecology, Den Bosch, The Netherlands*

⁵*Fertility Clinic Twente, Fertility, Hengelo, The Netherlands*

⁶*Sint Franciscus Gasthuis, Obstetrics and Gynaecology, Rotterdam, The Netherlands*

⁷*Isala, Obstetrics and gynaecology, Zwolle, The Netherlands*

⁸*Canisius Wilhelmina Hospital, Obstetrics and gynaecology, Nijmegen, The Netherlands*

⁹*St. Antonius hospital, Obstetrics and gynaecology, Nieuwegein, The Netherlands*

¹⁰*UMCU, Reproductive Medicine, Utrecht, The Netherlands*

¹¹*The Robinson institute, School of Paediatrics and Reproductive Health, Adelaide, The Netherlands*

Study question:

Is 75 IU FSH or 100mg CC the best ovarian stimulation (OS) regimen in couples with unexplained subfertility undergoing intra uterine insemination (IUI)?

Summary answer:

In IUI-OS with adherence to strict cancellation criteria, FSH is not superior to CC to achieve ongoing pregnancies, while multiple pregnancy rates are comparable.

What is known already:

IUI-OS is the first line treatment in couples with unexplained or mild male subfertility. OS aims to increase the number of dominant follicles per cycle, thus increasing pregnancy chances, but at the expense of multiple pregnancies. To reduce the risk of multiple pregnancy, IUI-OS with strict cancellation criteria, i.e. when ≥ 3 dominant follicles develop, has been suggested. With such a strategy, it is unclear whether the ovarian stimulation should be done with FSH or with CC.

Study design, size, duration:

We performed a multicentre, non-blinded, superiority randomised controlled trial in the Dutch Consortium for Healthcare Evaluation in Obstetrics and Gynaecology. Based on a power

calculation, we needed to include 732 women to be able to prove a difference in ongoing pregnancies of 10%. We randomly allocated 738 couples with unexplained or mild male subfertility and an unfavourable prognosis according to the model of Hunault for natural conception, to 4 cycles of IUI-FSH or IUI-CC.

Participants/materials, setting, methods:

The primary outcome was ongoing pregnancy within six months after randomisation. Secondary outcomes were multiple pregnancy, live birth, time to ongoing pregnancy, cancellation rates and number of cycles with monofollicular growth. We analysed the data on an intention to treat basis. We calculated relative risks and 95% CI.

Main results and the role of chance:

Between August 2013 and March 2016, we randomised 369 women to FSH and 369 women to CC. 115 women (31%) had an ongoing pregnancy following IUI-FSH and 100 women (27%) had an ongoing pregnancy following IUI-CC (RR 1.15, 95% CI .92 to 1.44, $p=.23$). 6 women (5%) had a multiple pregnancy following IUI-FSH and 9 women (9%) had a multiple pregnancy following IUI-CC (RR 0.58, 95% CI 0.21 to 1.57, $p=.28$).

Limitations, reasons for caution:

At this moment, we have access to 92% of the data regarding ongoing pregnancy and 90% of the data regarding multiple pregnancies. Full data will be available before June 2017.

Wider implications of the findings:

In view of the data, we suggest to use the least expensive and least invasive stimulation agent, which is CC. A formal cost-effectiveness analysis for the ultimate interpretation of the data is planned.

Trial registration number:

Nederlands Trial Register *NTR4057*

Funding by national/international organization(s)
ZonMW