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Title:

OPTIMAL TREAMENT STRATEGY FOR THE PATIENT WITH DOR: ESTROGEN PRIMING PROTOCOL VS. MICROFLARE

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Objective:

Optimal care for patients with natural or premature ovarian ageing continues to challenge clinicians in the reproductive medicine field. Women of reproductive age with DOR may have regular menses, but respond poorly to ovarian stimulation and/or have suboptimal fecundity compared to those of similar age. We sought to evaluate DOR patients engaged in an IVF cycle treated with either a luteal estradiol/gonadotropin-releasing hormone antagonist (antGnRH) (Estradiol-Priming (EP)) protocol (EPP) or with oral contraceptive pill (OCP) daily micro-dose leuprolide acetate (Microflare) protocol (MFP). Our goal was to use age, baseline hormone values, number of injections, and outcome to optimize choice of ovarian stimulation protocol.

Design:

Retrospective cohort analysis

Materials and Methods:

Patients who were identified as having DOR who underwent an IVF cycle utilizing a MFP or an EPP were included. DOR were defined by any of the following: 1) history of previously canceled IVF cycles; 2) poor response to stimulation (<3 dominant follicles or E2 <500 pg/mL); 3) basal follicle-stimulating hormone (FSH) levels >12 mUI/mL or basal antral follicle count (BAFC) <8. Freeze all cycles were included for clinical and laboratory outcomes and excluded for pregnancy outcomes. The primary outcome measures were cycle cancellation rate, number of oocytes retrieved, and clinical pregnancy rates. Student's t-test was used for continuous variables, and the X^2 test was used for categorical variables. Significance was confirmed a $p<0.05$.

Results:
Patient (n=2298) utilizing EPP (n=641) had a higher basal FSH (15.5±6.3 vs. 14.6±5.4), a lower peak E2 level (1102.0±663.2 vs. 1455.6±803.3), and a greater gonadotropin requirement (5067.5±1172.6 vs. 4583.3±1031.5) but achieved similar endometrial thickness, average number of fols>14mm and counts of oocytes retrieved and embryos transferred, when compared to the MFP group (n=859). There were 56 freeze-all cycles in the MFP and 39 in the EPP protocol. Patients using EPP exhibited similar clinical pregnancy rates (21.5% vs. 21.4%) and live birth rates (15.0% vs. 15.3%) per started cycle. Patients undergoing a MFP required more injections (~40 vs. ~26) than an EPP and spent an average of $4,375.00 compared to EPP patients who spent $5,485.00. When stratified by age, patients older than age 40 showed a trend towards higher pregnancy rates using EPP (PR 23.8 vs. 20.8%, clinical 15.7% vs. 13.7%, cancellation rate 30.9 vs. 32.8), while this difference was not demonstrated in the younger patients.

Conclusions:
Patients with DOR may require aggressive stimulation protocols to optimize cycle outcomes. Both EPP and MFP remain viable options, but the extra cost associated to an Estrogen Priming protocol in addition to extra gonadotropins may make Microflare the preferred protocol, especially in young patients. To corroborate this finding, a larger, powered randomized clinical evaluation is needed.

Support:
None.

	Microflare	Estrogen Priming	Statistics
Cycles	1657	641	2298
Age	39.5±3.5	40.4±3.5	p<0.05
BAFC	5.1±2.4	5.4±2.5	NS
Days of stimulation	9.8±1.8	10.2±1.7	p<0.05
Biochemical PR (per retrieval)	40.7% (459/1126)	41.2%% (169/410)	NS
Biochemical PR (per initiated pt)	28.6% (459/1601)	28.1% (169/602)	NS
Clinical PR (per retrieval)	30.4% (342/1123) 3 pnd	31.5% (129/409) 1 pnd	NS
Clinical PR (per initiated pt)	21.4% (342/1598) 3 pnd	21.5% (129/601) 1 pnd	NS
Miscarriage Rate(per retrieval)	17.7% (199/1126)	17.3% (71/410)	NS
Miscarriage Rate (per initiated pt)	12.6% (202/1601)	12.3% (74/602)	NS
Cancellation Rate (before retrieval)	28.7% (475/1657)	29.9% (192/641)	NS
Cancellation Rate (before ET)	13.9% (223/1601)	17.6% (106/602)	NS
Live Birth Rate (per retrieval)	21.9% (219/1000)	21.7% (73/336)	NS
Live Birth Rate (per initiated pt)	15.3% (219/1425)	15.0% (73/486)	NS