ORAL CONTRACEPTIVE PILLS VERSUS ESTRADIOL VALERATE PRETREATMENT IN GONADOTROPHIN-RELEASING HORMONE ANTAGONIST PROTOCOL

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INTRODUCTION

In ICSI cycle's controlled ovarian hyperstimulation is an important parameter of the success rates.
Premature LH surge may complicate ovarian stimulation and decrease the pregnancy rate, suppression of endogenous LH can be achieved by GnRH antagonist protocols.
GnRH antagonists results in immediate down regulation of pituitary gland, thus allowing for shorter period of suppression, reduced duration of stimulation and associated with lower incidence of OHSS.
Advantages of pretreatment are more synchronous follicular development, higher number of oocytes, programming for cycle start and programming oocyte retrieval day.
Advantages of E2 versus OCPs are, duration of pretreatment is shorter, a good alternative for patients who have objections to or present contraindications for taking OCPs, E2 doesn't affect the fertility potential during the cycle preceding ovarian stimulation.
Follicular phase estradiol scheduling does not seem to increase gonadotropin consumption or hamper clinical outcome.

AIM OF THE WORK

The aim of the work was to compare pretreatment with OCPs with pretreatment with follicular estradiol valerate 8mg in antagonist protocol cycles for patients undergoing ICSI.

PATIENTS AND METHODS

This study was a prospective randomized controlled trial:

Group I: 250 female patients were pretreated with OCPs, the pill (Ethinyl Estradiol 0.03 mg + Gestodene 0.075 mg [Femogesal; Techno]) taken from the first day of the cycle for 7-14 days and then, 5 days wash out period before starting stimulation in GnRH antagonist cycles.

Group II: 250 female patients were pretreated with estradiol valerate (progynova 2mg; Bayer) given 8 mg/day orally from cycle day one for 7-14 days then, patients started stimulation cycles.

After the administration of FSH ampoules, antagonist Cetrotide 0.25 mg was administered on D5 of stimulation followed up by transvaginal ultrasound and hormonal measurement until ≥ 3 follicles reached 17-20 mm in diameter, at this moment ovulation was triggered. E2 and P4 level were measured on the trigger day.

Primary outcome: The clinical Pregnancy rate. Ongoing pregnancy rate.
Secondary outcome: Duration of stimulation, dose of gonadotrophins, number of oocytes retrieval, oocyte maturation rate, cleavage rate, blastulation rate, rate of top quality blastocyst, implantation rate, chemical pregnancy rate, miscarriage rate.

RESULTS

Table 1: Comparison between the two studied groups according to stimulation parameters and secondary outcomes

	OCPs pretreatment (n = 250)	Estradiol (n = 250)	Test of sig.	
No of days of pretreatment E2 or OCPS				
Min. – Max.	7.0 – 14.0	7.0 – 14.0	U= 12199.5*	<0.001*
Mean ± SD.	10.80±3.01	7.54±1.42		
Median (IQR)	11.0 (7.0 – 14.0)	7.0 (7.0 – 7.0)		
Stimulation (days)				
Min. – Max.	7.0 – 15.0	8.0 – 15.0	t= 1.085	0.278
Mean ± SD.	11.77±1.75	11.61±1.54		
Median (IQR)	12.0 (10.0 – 14.0)	12.0 (10.0 – 13.0)		
Total dose of(FSH/ IU)				
Min. – Max.	1309 – 6300	1600 – 6300	t= 1.271	0.204
Mean ± SD.	2774.5±945.2	2680.2 ± 696.1		
Median (IQR)	2537.5(2000-3300)	2400.0(2322 – 3000)		

Table 2: Comparison between the two studied groups according to secondary ICSI outcomes

	OCPs pretreatment (n = 250)	Estradiol (n = 250)	Test of sig.	P
Maturation rate				
Min. – Max.	20.0 – 100.0	25.0 – 100.0	t= 1.795	0.073
Mean ± SD.	82.58 ± 16.19	84.96 ± 13.20		
Median (IQR)	87.50 (73.0-95.0)	87.0(77.0-95.0)		
No of embryos				
Min. – Max.	1.0 – 44.0	1.0 – 37.0	U= 29570.50	0.298
Mean ± SD.	12.80 ± 7.49	11.90 ± 6.76		
Median (IQR)	11.0 (7.0 – 18.0)	11.0 (7.0 – 15.0)		
Blstuation rate				
Min. – Max.	12.50 – 100.0	10.0 – 100.0	U= 28416.50	0.079
Mean ± SD.	59.49 ± 22.71	63.24 ± 22.84		
Median (IQR)	60.0 (40.0 – 77.0)	62.50 (46.40 – 80.0)		

Table 3: Comparison between the two studied groups according to main outcomes

	OCPs pretreatment (n = 250)		Estradiol (n = 250)		Test of sig.	P
	No.	%	No.	%		
Clinical pregnancy						
Positive	102	40.8	111	44.4	χ^2= 5.309	^{MC}p= 0.068
Negative	143	57.2	139	55.6		
Ectopic pregnancy	5	2.0	0	0.0		
Ongoing pregnancy						
Positive	94	37.6	99	39.6	χ^2= 5.03	^{MC}p= 0.085
Negative	151	60.4	151	60.4		
Ectopic pregnancy	5	2.0	0	0.0		
Live birth rate						
Positive	93	37.2	97	38.8	χ^2= 4.961	^{MC}p= 0.093
Negative	152	60.8	153	61.2		
Ectopic pregnancy	5	2.0	0	0.0		

CONCLUSION

From the present study, the following can be concluded:
Our results failed to show statistically significant differences for the main measures of ICSI outcome between pretreatment with OCPs and follicular estradiol valerate in a dose 8 mg daily for COH with the GnRH antagonist protocol, so a short course of oral estradiol administration during the follicular phase of the stimulation cycle can be used to schedule antagonist cycles, it could be useful in avoidance of weekend retrievals, it is considered an efficient method for scheduling IVF and it does not negatively affect clinical outcome.