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OUTCOMES OF 1503 CYCLES OF MODIFIED NATURAL CYCLE IN VITRO FERTILIZATION : A SINGLE INSTITUTION EXPERIENCE

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INTRODUCTION

Modified natural IVF (mnIVF) is a technique performed using the natural female menstrual cycle, with the addition of certain agents to support follicular growth and prevent premature ovulation. It has gained popularity in recent years due to the many advantages it offers, which include lower costs, negligible risk of ovarian hyperstimulation syndrome, and patient-friendly treatment. Our center has been performing mnIVF since 2003, and since 2005 using the refined protocol. We sought to determine if it is a worthwhile treatment option for women seeking IVF.

OBJECTIVE

To study the outcomes of modified natural cycle in vitro fertilization (mnIVF) in a single center.

METHODS

A single center retrospective cohort study was performed using all mnIVF cycles performed between July 2005 and December 2011, according to the current mnIVF protocol used in our center. A total 1503 cycles of mnIVF were analyzed. These were performed in 782 patients, and there was a maximum of five cycles per patient. The main endpoints studied were clinical pregnancy rates (CPRs) per embryo transfer (ET) and per started cycle. Outcomes were stratified by cycle attempt, as well as by female patient age (≤ 35 years and ≥ 36 years). There were 1238 patients in the group ≤ 35 years of age, and 265 patients in the group ≥ 36 years of age. The causes of infertility in these patients in order of importance included male factor, unexplained, low ovarian reserve, tubal factor, endometriosis, and other.

In our mnIVF protocol, an ultrasound is performed on day 9 of the cycle to detect the presence of a dominant follicle. During this follicular surveillance period, a GnRH antagonist (orgalutran or cetrotide), a gonadotrophin (repronex or menopur), as well as indocid are given on a daily basis until ovulation induction day. Ovulation is induced by an hCG injection when the dominant follicle attains maturity. Oocyte retrieval (OR) is then performed 34 hours later and the embryo is transferred two days after the OR.

RESULTS

Table 1: Patient characteristics undergoing a maximum of five cycles of mnIVF

Number of patients (N)	782
Female patient age, mean (SD)	32.5 \pm 3.2
≤ 35 years, n(%)	657 (84.0)
36 years and more, n(%)	125 (16.0)
Male patient age, mean (SD)	36.7 (6.0)
Type of infertility, n (%)	
1°	494 (63.4)
2°	286 (36.6)
Cause of infertility, n (%)	
male factor	261 (33.4)
unexplained	118 (15.1)
low ovarian reserve	96 (12.3)
tubal	70 (8.9)
endometriosis	35 (4.5)
other (implantation failure, pcos)	11 (1.4)
mixed	191 (24.4)

Modified natural cycle IVF protocol

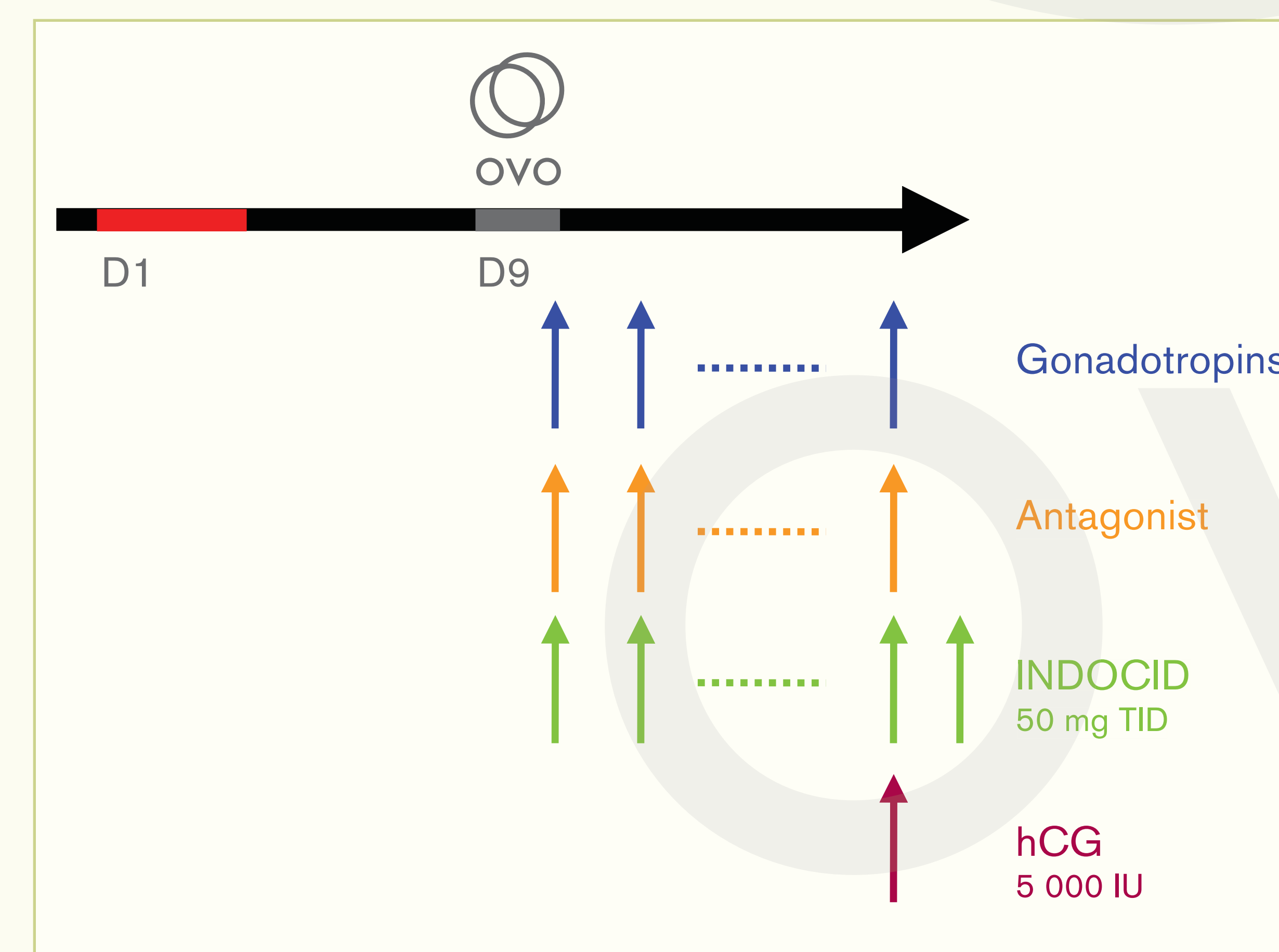


Table 2: Overall cycle outcomes according to cycle number of mnIVF

Cycle number	1	2	3	4	5	Total
Cycles started	782	436	189	75	21	1503
Cycles cancelled (%)	141 (18)	85 (19.5)	36 (19)	11 (14.7)	6 (28.6)	279 (18.6)
OR (oocyte retrieval) performed (%)	641 (82.0)	351 (80.5)	153 (81.0)	64 (85.3)	15 (71.4)	1224 (81.4)
Successful OR (%)	581 (74.3)	305 (70.0)	132 (69.8)	57 (76)	15 (71.4)	1090 (72.5)
Cycles with fertilization (%)	390 (49.9)	200 (45.9)	87 (46.0)	41 (54.7)	11 (52.4)	729 (48.5)
Embryo transfer (ET) (%)	334 (42.7)	170 (40)	80 (42.6)	37 (49.3)	7 (33.3)	628 (41.8)
Implantation rate per cycle, %	16.6	15.4	12.2	12.0	19.1	15.5
Implantation rate per ET %	38.2	39.4	28.4	24.3	57.1	36.7
Clinical pregnancy rate per cycle, %	15.0	13.5	10.1	10.7	14.3	13.7
Clinical pregnancies per OR, %	20.1	19.3	14.4	14.0	20.0	18.9
Clinical pregnancy rate per ET, %	34.5	34.7	23.5	21.6	42.9	32.5

Table 3: Overall outcomes stratified by female patient age

Cycle number	≤ 35 years	≥ 36 years	p value
Cycles started	1238 (82.4)	265 (17.6)	
Cycles cancelled (%)	216 (17.4)	63 (23.8)	0.12
OR performed (%)	1022 (82.6)	202 (76.2)	0.12
Successful OR (%)	910 (88.6)	180 (88.2)	0.88
Cycles with fertilization (%)	599 (65.8)	130 (72.2)	0.10
Embryo transfers, (%)	514 (41.6)	114 (43.0)	0.66
Implantation rate per cycle, %	16.5	10.9	0.02
Implantation rate per ET, %	39.2	25.2	0.01
Clinical pregnancy rate per cycle, %	14.5	10.2	0.06
Clinical pregnancy rate per OR, %	19.7	15.0	0.02
Clinical pregnancy rate per ET, %	34.5	23.5	0.02

CONCLUSIONS

To our knowledge, this is the largest series regarding mnIVF outcomes. The results of our study demonstrate that mnIVF is a reasonable treatment option for patients considering IVF. It offers a clinical pregnancy rate of 13.7% per cycle started and 32.5% per embryo transfer. These rates are slightly higher than those of a previous report (Pelinck 2007), and the cancellation rate of 18.6 % is on the lower side of those in other studies. (Pelinck 2007, Branco 2005). We also confirm that mnIVF is particularly advantageous for women aged 35 years or younger (Schimberni 2009), for which the CPR per ET is 34.5%. Further analysis into the different properties of each cycle, such as the timing of ovulation induction or endometrial thickness at induction can help refine the protocol to maximize chance of pregnancy in each cycle and to minimize chance of cancellation. Also, analysis by indication may help in the better selection of patients for this procedure since the results of this study pertain to several causes of infertility combined.

In summary, this study shows that mnIVF holds a valuable place in the treatment options of infertile couples. Moreover, it offers several benefits, including easy accessibility, minimal risk of ovarian hyperstimulation, a low rate of multiple pregnancies as well as low cost.

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