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Embryo quality is the main factor affecting cumulative live birth rate after elective single embryo transfer in fresh stimulation cycles

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ABSTRACT

Objective: The study was aimed to evaluate which factors affect the cumulative live birth rate after elective single embryo transfer in women younger than 36 years. Additionally, number of children in women with more than one delivery per ovum pick-up after fresh elective single embryo transfer and subsequent frozen embryo transfers was assessed.

Study design: Retrospective cohort study analysing data of a university hospital's infertility clinic in 2001–2010. A total of 739 IVF/ICSI cycles with elective single embryo transfer were included. Analyses were made per ovum pick-up including fresh and subsequent frozen embryo transfers. Factors affecting cumulative live birth rates were examined in uni- and multivariate analyses. A secondary endpoint was the number of children born after all treatments.

Results: In the fresh cycles, the live birth rate was 29.2% and the cumulative live birth rate was 51.3%, with a twin rate of 3.4%. In the multivariate analysis, having two (odds ratio (OR) 1.73; 95% confidence interval (CI) 1.12–2.67) or ≥3 top embryos (OR 2.66; 95% CI 1.79–3.95) was associated with higher odds for live birth after fresh and frozen embryo cycles. Age, body mass index, duration of infertility, diagnosis or total gonadotropin dose were not associated with the cumulative live birth rate. In cycles with one top embryo, the cumulative live birth rate was 40.2%, whereas it was 64.1% in those with at least three top embryos. Of women who had a live birth in the fresh cycle, 20.4% had more than one child after all frozen embryo transfers. Among women with three or more top embryos after ovum pick-up, 16.1% gave birth to more than one child.

Conclusion: The cumulative live birth rate in this age group varies from 40% to 64% and is dependent on the quality of embryos. Women with three or more top embryos have good chance of having more than one child per ovum pick-up without elevated risk of multiple pregnancies.

Introduction

In in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI), elective single embryo transfer (eSET) is an effective method to decrease multiple births which cause increased maternal and perinatal morbidity and mortality [1]. Largely due to the introduction of eSET, the multiple delivery rate per embryo transfer has declined steadily in Europe from 26.9% in 2000 to 19.2% in 2010 [1]. eSET is widely practiced in the Nordic countries. Accordingly, statistics from 2011 show a low proportion of multiple births after IVF/ICSI – from 5.1% (Sweden) to 16.5% (Denmark) [2].

Embryo freezing is an essential component of eSET policy. Frozen embryo transfer (FET) cycles account for 31.8% of all assisted reproduction technology (ARTs) in the Nordic countries. The rate is highest in Finland (45.1%) [2]. Previous studies have confirmed that the cumulative pregnancy and live birth rates (cLBR) evaluating the outcome of ovum pick-up (OPU) and all following FETs indicate the real efficiency of ART and should be used when compared with other transfer policies [3,4]. eSET, combined with an effective cryopreservation programme, has been shown to result in a high cumulative pregnancy rate (44–62%) per oocyte retrieval [5–8]. The success in IVF treatment has been shown to have association with morphological parameters of the embryo [9]. On the other hand, a recent study indicated that embryo quality has no effect on maternal or

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neonatal outcomes in SET cycles [10]. There are few studies on factors affecting cumulative outcomes in eSET cycles.

According to earlier analyses, eSET diminished the costs in the general IVF/ICSI population [11], especially among women aged 36 years or less [12]. Studies comparing cLBR in eSET and double embryo transfer (DET) cycles in older women also suggest eSET is a viable treatment option [13,14]. Currently, eSET is more commonly applied to women younger than 36 years [1]. eSET has been suggested as a treatment of choice in this age group, even in countries with low eSET use [12,15].

The primary aim of the present study was to investigate the factors that affect cLBR after eSET in a cohort of women younger than 36 years. The results could be useful in counselling couples undergoing infertility treatment. A secondary aim was to analyse how many children were born in women with more than one delivery after single IVF stimulation, including deliveries after eSET in fresh cycle and subsequent FET cycles. This aspect has not been studied previously, although from the point of view of the couples information on the possible number of children gained with a single stimulated cycle is undoubtedly important.

Materials and methods

This retrospective cohort study population consisted of all first IVF/ICSI treatments with eSET performed in the fresh cycle on day 2 after ovum pick-up (ultrasound-guided oocyte aspiration under intravenous sedation) in the time period 2001–2010 in Oulu University Hospital, Department of Obstetrics and Gynaecology, Oulu, Finland. eSET was defined as a treatment in which one embryo was transferred in the fresh cycle and at least one embryo was frozen. All subjects were younger than 36 years at the time of OPU. The analyses were made per treatment (OPU). The study consisted only of couples treated with their own gametes. Cumulative analyses were carried out by identifying FET cycles following OPU using the identification code in the Babe® database for ART patients (Cleodora Software, Portugal). In the FET cycles one or two embryos were transferred at the time. As one of the key issues was to determine the impact of the embryo quality on the success rate, women with missing data on the quality of embryos were excluded. Ovarian stimulation was mainly performed using the long GnRH agonist protocol (93.0%, 688 cycles) or the GnRH antagonist protocol (3.5%, 26 cycles). In 25 cycles (3.5%), other stimulation protocols were used. The starting gonadotrophin dose was determined according to the patient's age, BMI, antral follicular count in the baseline ultrasonographic scan and the outcome of previous infertility treatments. A top quality embryo had 4–5 evenly sized cells and <20% of fragmentation [9]. Embryos not transferred in the fresh cycle were frozen on the day of embryo transfer, using a slow freezing protocol.

Data on the woman's age at the time of IVF or ICSI treatment, body mass index (BMI) (kg/m^2), duration of infertility at the time of IVF or ICSI (years), main cause of infertility, number of oocytes

Table 1
Characteristics, *N* (%).

	By the number of top embryos				
	All, *N* = 739	1	2	3 or more	*p* Value
Age (years)					
Younger than 30	354 (47.9)	132 (37.3)	80 (22.6)	142 (40.1)	0.22
30–35	385 (52.1)	154 (40.0)	100 (26.0)	131 (34.0)	
BMI (kg/m^2)[a]					
<20.0	97 (13.3)	42 (43.3)	22 (22.7)	33 (34.0)	0.06
20.0–24.9	432 (59.0)	171 (39.6)	100 (23.1)	161 (37.3)	
25.0–29.9	140 (19.1)	51 (36.4)	32 (22.9)	57 (40.7)	
30.0–34.9	51 (7.0)	17 (33.3)	15 (29.4)	19 (37.3)	
35.0 or more	12 (1.6)	1 (8.3)	8 (66.7)	3 (25.0)	
Duration of infertility (years)[b]					
Less than 1	9 (1.5)	1 (0.4)	1 (0.7)	7 (3.0)	0.04
1–2 years	201 (32.6)	72 (30.6)	42 (28.0)	87 (37.5)	
3–4 years	247 (40.0)	105 (44.7)	63 (42.0)	79 (34.1)	
5 years or more	160 (25.9)	57 (24.3)	44 (29.3)	59 (25.4)	
Main diagnosis					
Endometriosis	140 (18.9)	61 (21.3)	29 (16.1)	50 (18.3)	0.09
Hormonal	69 (9.3)	16 (5.6)	21 (11.7)	32 (11.7)	
Tubal	89 (12.0)	38 (13.3)	14 (7.8)	37 (13.6)	
Male	232 (31.4)	90 (31.5)	57 (31.7)	85 (31.1)	
Unexplained	161 (21.8)	59 (20.6)	45 (25.0)	57 (20.9)	
Multiple & other reasons	48 (6.5)	22 (7.7)	14 (7.8)	12 (4.4)	
Type of ART					
IVF	433 (58.6)	169 (59.1)	103 (57.2)	161 (59.0)	0.92
ICSI or IVF + ICSI	306 (41.4)	117 (40.9)	77 (42.8)	112 (41.0)	
Gonadotropin dose IU (mean + SD)	1920 (659)	2051 (776)	1865 (511)	1819 (586)	<0.001
Number of oocytes					
Less than 10	216 (29.2)	124 (43.4)	53 (29.4)	39 (14.3)	<0.001
10–20	419 (56.7)	140 (49.0)	104 (57.8)	175 (64.1)	
More than 20	104 (14.1)	22 (7.7)	23 (12.8)	59 (21.6)	
Number of embryos frozen					
1–4	344 (46.5)	200 (69.9)	90 (50.0)	54 (19.8)	<0.001
5–10	321 (43.4)	78 (27.3)	82 (45.6)	161 (59.0)	
More than 10	74 (10.0)	8 (2.8)	8 (4.4)	58 (21.2)	

BMI, body mass index; ART, assisted reproductive technology.
IVF + ICSI, IVF and ICSI used in 50%/50% of the oocytes.
[a] Data missing in 7 cases (0.9%).
[b] Data missing in 122 cases (16.5%).