

Treatment Policy After Poor Fertilization in the First IVF Cycle

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Purpose: The chance of recurrence of poor fertilization in a second in vitro fertilization (IVF) cycle was assessed.

Methods: Total fertilization failure was defined, and the relationship between the fertilization rate and the number of motile sperm cells per milliliter of semen was assessed. Patients with a total fertilization failure or poor fertilization (20% or less of the oocytes fertilized) were divided into three subgroups with different chances of fertilization and were followed in a subsequent IVF cycle.

Results: The recurrence rate of total fertilization failure was high in all three groups (45–70%), and poor fertilization frequently occurred in the second cycle (50–75%).

Conclusions: Poor fertilization frequently recurs in the second IVF cycle. The use of intracytoplasmic sperm injection could be considered after fertilization of 20% or less of oocytes in the first cycle, irrespective of the number of motile sperm cells per milliliter of semen.

KEY WORDS: fertilization failure; poor fertilization.

INTRODUCTION

The incidence of total fertilization failure (TFF) and its predictive significance for subsequent in vitro fertilization (IVF) cycles have been reported by several authors (1–5). In contrast, the incidence of low fertilization rate (LFR) in an IVF cycle and its significance for the treatment prognosis has not been given much attention. Apparently when, after a LFR, one or more embryos are available for replacement and, consequently, a true chance for pregnancy exists, the IVF attempt is seen as successful. However, if TFF and LFR are both expressions of a defective interaction

between the oocyte and the sperm cell, the recurrence rate in a subsequent cycle and the treatment prognosis of LFR and TFF could be comparable.

The chance of recurrence of TFF in a subsequent cycle as reported by others is approximately 20%, irrespective of the indication for IVF (1–5). Because of this low recurrence rate, it has been advised to undertake two more IVF attempts before reverting to other therapeutic options such as the use of donor sperm or micromanipulative techniques (3,5). However, with the introduction of intracytoplasmic sperm injection (ICSI), a micromanipulative technique has become available that has proved to be a good alternative after TFF. For ICSI a TFF rate of only 3% has been reported (6).

In this study the chance of successful fertilization in a subsequent IVF cycle after TFF or LFR in the first cycle is assessed. The aim of the study was to investigate whether TFF and LFR in the first IVF cycle are indications for assisted fertilization in following cycles.

MATERIALS AND METHODS

In IVF cycles with a low oocyte yield, TFF can be seen as a chance occurrence in a substantial number of cases. Consequently, for definition of TFF, an analysis of the relationship between the chance of occurrence of TFF and the number of oocytes retrieved was carried out. As reported previously (7), the average fertilization rate in our population is 50%. The theoretical chance of fertilization failure is therefore 50% for one oocyte, 25% for two oocytes, 12.5% for three oocytes, etc. The a priori chance of TFF in relation to the number of oocytes retrieved is indicated in Fig. 1. The actual incidence of TFF in the population studied is also indicated in this figure. Based on the data obtained, TFF was defined as fertilization failure in cycles with four or more oocytes retrieved.

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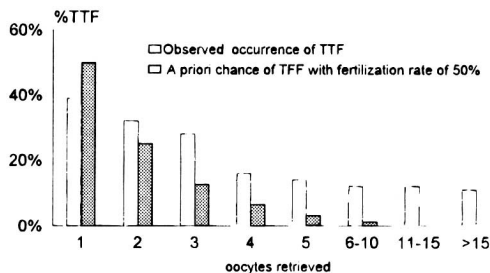


Fig. 1. The a priori chance of TFF in relation to the number of oocytes retrieved and the actual incidence of TFF in the population.

At our IVF laboratory the number of motile sperm cells per milliliter in the semen obtained on the day of oocyte retrieval is considered the most important parameter of semen quality. After analyzing the relationship between the chance of an oocyte being fertilized and the number of motile sperm cells per milliliter in the semen used in 1211 consecutive first IVF cycles, three subgroups with different chances of fertilization were defined for separate analysis.

Patients with poor fertilization (PF = fertilization of 20% or less of all oocytes) in their first IVF cycles who continued treatment were followed in the subsequent cycle. The stimulation protocol used was described previously (7). In cases of PF, a differentiation was made between TFF and LFR, defined as fertilization of greater than 0% and 20% or less of all oocytes. In 1049 of 1211 patients four or more oocytes were retrieved in the first IVF cycle. Of these, 207 had PF in the first cycle, and 119 proceeded to a second attempt. In the second IVF cycle, 3 patients had fewer than four oocytes retrieved and were excluded from the study, leaving 116 patients for further analysis. The second cycles of the patients in the three subgroups with TFF or LFR in the first IVF cycle were analyzed separately, and the chance of recurrence of PF in the second cycle was studied. The stimulation protocol used in the first and the second cycles were identical because no poor responders to controlled ovarian hyperstimulation (fewer than four oocytes retrieved) were included in the study.

RESULTS

The theoretical incidence of TFF as a chance occurrence and the actual incidence of TFF in relation to the number of oocytes retrieved in the first IVF cycle are shown in Fig. 1.

As the number of retrieved oocytes increases, the incidence of TFF as the result of chance occurrences

decreases. The observed incidence in cycles with four oocytes retrieved was 16%, while the theoretical incidence of TFF in these cycles was 6%. For further analysis TFF in cycles with four or more oocytes was considered indicative of a defective interaction between the oocyte and the sperm cell. Consequently, all patients with fewer than four oocytes retrieved in the first IVF cycle were excluded from further analysis.

The relationship between the chance of fertilization per oocyte and the number of motile sperm cells per milliliter of semen is shown in Fig. 2. Based on this graph, the patients were divided into three subgroups: group 1, less than 5×10^6 motile sperm cells/ml; group 2, $5-19 \times 10^6$ motile sperm cells/ml; and group 3, 20×10^6 or greater motile sperm cells/ml.

The incidence of TFF in the first IVF cycle and the chance of recurrence of TFF and occurrence of LFR in the subsequent cycle are shown in Table I. The last column in the table shows the cases with PF. The recurrence rate of TFF in the subsequent cycle was high in all subgroups. Poor fertilization occurred in 60% of all cycles following TFF. The number of clinical pregnancies obtained in the second cycles of those who continued is shown in Table II.

The results of subsequent cycles of patients with a low fertilization rate in the first cycle are shown in Table III. Total fertilization failure in a second cycle occurred frequently (37%) after LFR in the first IVF attempt. Poor fertilization occurred in 50% of all subsequent cycles. The numbers of clinical pregnancies obtained in the first and second IVF attempts of patients with LFR in the first cycle are shown in Table IV.

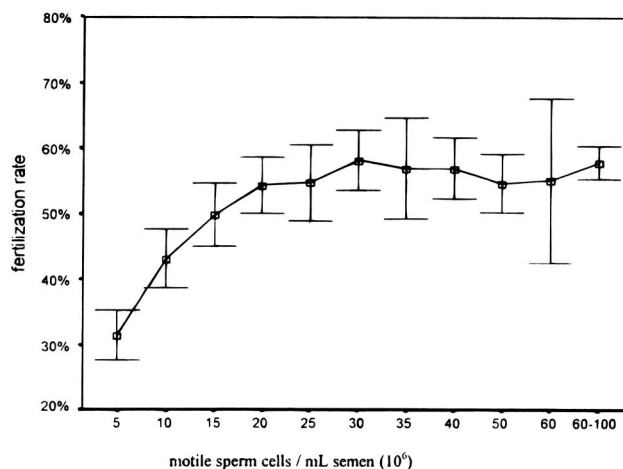


Fig. 2. Relationship between the chance of fertilization per oocyte and the number of motile sperm cells per milliliter of semen.

Table I. Total Fertilization Failure in the First Cycle and Poor Fertilization in the Second Cycle in the Three Groups

	TFF 1st cycle	Continued ^a	Second cycle		
			TFF	LFR	PF
Group 1 (<i>n</i> = 196)	39 (20%) ^b	20 (51%) ^c	14 (70%) ^d	1 (5%) ^d	15 (75%) ^d
Group 2 (<i>n</i> = 232)	46 (20%)	20 (45%)	8 (40%)	5 (25%)	13 (65%)
Group 3 (<i>n</i> = 621)	51 (8%)	38 (75%)	17 (45%)	2 (5%)	19 (50%)
Total (<i>n</i> = 1049)	136 (13%)	78 (57%)	39 (50%)	8 (10%)	47 (60%)

^a Patients with fewer than four oocytes in the second cycle (*n* = 3) were excluded.

^b Percentage of TFF in the group in the first cycle.

^c Percentage of patients with TFF in the first cycle.

^d Percentage of patients who continued after TFF in the first cycle.

Table II. Pregnancies Obtained in the Second Cycle of Patients with TFF in the First Cycle

	Pregnancies/cycles	
	Normal fertilization	Poor Fertilization
Group 1 (<i>n</i> = 20)	2/5	0/15
Group 2 (<i>n</i> = 20)	3/7	1/13
Group 3 (<i>n</i> = 38)	6/19	0/19
Total (<i>n</i> = 78)	11/31	1/47

DISCUSSION

Although low fertilization rates have been reported as an indication for the use of micromanipulative techniques (8), the incidence of LFR in IVF has not been given much attention. In contrast, the incidence of TFF and the treatment policy after TFF have been discussed by several authors. The most frequently given advice is to try conventional IVF treatment again for a second or even a third trial without resorting to assisted fertilization using micromanipulative techniques (3–5). The advice given by these authors is based mainly on the low recurrence rate for TFF found in their studies. However, the definition of TFF used in these studies

can be questioned. Failure of fertilization in cycles with only a few oocytes retrieved can be seen as a chance occurrence. In many of these cases there might be no abnormality in the interaction between the sperm cell and the oocyte. Therefore, based on the incidences of TFF in cycles with a low number of oocytes in our study, we excluded patients with fewer than four oocytes retrieved in their first IVF cycle from the analysis. Using this approach, we identified a subpopulation of patients with a recurrence rate of TFF in a second IVF cycle of 50% as shown in Table I. This rate is high compared with that in other reports (1–5). When the cases of LFR in the second cycle were included, the incidence of PF in the second cycle was 60%. The introduction of subgroups with different sperm parameters showed a comparable poor prognosis for all three groups.

Although potential selection bias is present because many couples did not attempt a second cycle, the results shown in Tables I and II appear to indicate that there is no essential difference between the mechanism of TFF and that of LFR. After LFR in the first cycle, 37% of patients had a TFF in the subsequent cycle and 50% of the patients who continued with IVF treat-

Table III. Low Fertilization Rate in the First Cycle and Poor Fertilization in the Second Cycle in the Three Groups

	LFR 1st/cycle	Continued	Second cycle		
			TFF	LFR	PF
Group 1 (<i>n</i> = 196)	8 (4%) ^a	2 (25%) ^b	1 (50%) ^c	2 (15%) ^c	1 (50%)
Group 2 (<i>n</i> = 232)	27 (12%)	13 (48%)	6 (46%)	2 (15%) ^c	8 (61%) ^c
Group 3 (<i>n</i> = 621)	36 (6%)	23 (64%)	7 (30%)	3 (13%)	10 (43%)
Total (<i>n</i> = 1049)	71 (7%)	38 (54%)	14 (37%)	5 (13%)	19 (50%)

^a Percentage of LFR in the group in the first cycle.

^b Percentage of patients with LFR in the first cycle.

^c Percentage of patients who continued after LFR in the first cycle.

Table IV. Pregnancies Obtained in the First and Second Cycles of Patients with a LFR in the First Cycle

	First cycle (pregnancies/cycles)	Continued	Second cycle (pregnancies/cycles)	
			Normal fertilization	Poor fertilization
Group 1 (n = 8)	0/8	2	1/1	0/1
Group 2 (n = 27)	3/27	13	3/5	0/8
Group 3 (n = 36)	4/36	23	3/13	1/10
Total (n = 71)	7/71	38	7/19	1/19

ment had PF in the second cycle. It seems that in our population LFR in the first cycle has a poor prognosis comparable to that of TFF. Possibly, TFF should not be regarded as a separate entity in IVF.

With the availability of ICSI, the therapeutic options for defective interaction between sperm cell and oocyte have improved considerably. The results of ICSI are good compared with those of other micromanipulative techniques such as subzonal insemination (9) and partial dissection of the zona pellucida (10). The results obtained in our population indicate that ICSI might be indicated after TFF in the first IVF cycle. The high recurrence rate of LFR shows that the use of ICSI could even be considered after LFR in the first cycle.

In conclusion, in the population studied, TFF and LFR both have a high recurrence rate. The use of ICSI could be considered after PF in the first cycle.

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