

# Insemination with man's sperm: results of fertility recovery in married couples with male infertility

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The paper analyzed the results of reproductive function restoration in 140 married couples with male infertility, which passed the program of insemination with man's sperm in 2013–2015 at the Institute of Reproductive Medicine (Kyiv).

It was found that the number of pregnancies and childbirths after 3 attempts (420 cycles) with an interval of 3–5 months was reached in  $17,0 \pm 1,8\%$  and  $15,0 \pm 1,8\%$  cases, respectively. The presence of a linear relationship between the fact of fertility recovery and factors such as the woman's age, duration of non-set of natural pregnancy, and the response of the ovulatory function to stimulation was confirmed. The influence of the spermogram indicators on the result is objectified: the type of pathospermia, the concentration of sperm, which is inversely dependent on the presence of predictors and determinants that burden the general condition of the man, as well as the percentage of actively moving sperm fractions.

**Key words:** male infertility factor, insemination with man's sperm.

## Інсемінація спермою чоловіка: результати відновлення фертильності подружньої пари з чоловічою безплідністю

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У статті проаналізовані результати відновлення репродуктивної функції у 140 подружніх пар із безплідністю, які пройшли програму запліднення спермою чоловіка у 2013–2015 рр. в Інституті репродуктивної медицини (Київ).

Було встановлено, що кількість вагітностей та пологів після 3 спроб (420 циклів) з інтервалом 3–5 міс було досягнуто відповідно у  $17,0 \pm 1,8\%$  та  $15,0 \pm 1,8\%$  випадків. Підтверджено наявність лінійної залежності між фактом відновлення фертильності і такими факторами, як вік жінки, тривалість невстановленої природної вагітності та реакцією овуляторної функції на стимуляцію. Продемонстровано вплив показників спермограми на результат: тип патоспермії, концентрація сперми, що обернено залежить від наявності предикторів та детермінант, які обтяжують загальний стан чоловіка, а також відсоток активно рухливих сперматозоїдів.

**Ключові слова:** чоловічий фактор безпліддя, інсемінація спермою чоловіка.

## Инсеминация спермой мужа: результаты восстановления фертильности супружеской пары с мужским бесплодием

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В статье проанализированы результаты восстановления репродуктивной функции у 140 супружеских пар с бесплодием, которые прошли программу оплодотворения спермой мужа в 2013–2015 гг. в Институте репродуктивной медицины (Киев).

Было установлено, что количество беременностей и родов после 3 попыток (420 циклов) с интервалом 3–5 мес было достигнуто соответственно в  $17,0 \pm 1,8\%$  и  $15,0 \pm 1,8\%$  случаев. Подтверждено наличие линейной зависимости между фактом восстановления фертильности и такими факторами, как возраст женщины, продолжительность неустоановленной естественной беременности и реакцией овуляторной функции на стимуляцию. Продемонстрировано влияние показателей спермограммы на результат: тип патоспермии, концентрация спермы, обратно зависящая от наличия предикторов и детерминант, которые обременяют общее состояние мужчины, а также процент активных подвижных сперматозоидов.

**Ключевые слова:** мужской фактор бесплодия, инсеминация спермой мужа.

Over the years, the importance and place of assisted reproductive technologies (ART) among existing types of fertility recovery in the infertile couples becomes more important and one of the leading [3, 6, 7, 9, 12, 13]. Most authors specify the need to adhere to a comprehensive, systematic approach subject to personalized choice of treatment method. When addressing the infertility, which is an urgent problem from the point of view of social, medical and economic aspects, one should take into account the male factor, share of which is growing rapidly [1, 4, 8, 11, 14]. Despite the fact that in case of application of the ART the direct treatment of a particular disease, which is determined as its cause is not a question, the biological/general clinical features of the individual can not be ignored. Experience and data of publications testify to this [2,10,15].

Therefore, it is obvious to this day that strict selection and clear criteria of the sperm parameters should be considered as an indispensable requirement for achieving fertility function of couples with male infertility. The foregoing motivates the need to critically analyze the results of fertility recovery of infertile

couples with the male factor by insemination with the man's sperm in order to clarify the causal relationship between them and, in fact, the known factors that became the purpose of the study.

### MATERIALS AND METHODS

The paper analyzes the results of fertility recovery in 140 married couples with male infertility by insemination with male's sperm (IMS) under the auspices of the Institute of Reproductive Medicine (IRM) (Kyiv) during 2013–2015. Existing clinical protocols were followed when examining and implementing the program procedure. Most of both partners were aged under 30; males were  $52.1 \pm 4.2\%$ , females –  $62.1 \pm 4.1\%$  ( $p < 0.05$ ). Regardless of gender, every third person was 30–39 years old. Men aged 40 and over were predominant ( $15.0 \pm 3.0\%$  vs.  $9.3 \pm 2.4\%$  women;  $p < 0.05$ ).

The obtained data were studied, analyzed by quantitative, attributive, factorial and resultant features. The validity of the compared sets was determined by the Student's t-test.

Table 1

**Pregnancy and childbirth rates taking into account the age of women in couples with male infertility factor under IMS program (n=140)**

Age	Abs.	%	Number of cycles	Quantity of pregnancies			Quantity of childbirth		
				abs	%	m	abs	%	m
under 24	47	83,6	141	31	22,0	3,6	30	21,3	3,4
25–29	40	28,6	120	25	20,8	3,7	23	19,2	3,6
30–34	16	11,4	48	8	16,7	5,3	6	12,5	4,7
35–39	24	17,1	72	5	6,9*	2,9	3	4,2*	2,3
40–44	13	9,3	39	2	5,1*	3,5	1	2,6*	2,5
≥45	-	-	-	-	-	-	-	-	-
Total	140	100	420	71	17,0	1,8	63	15,0	1,8

Note: \* – the difference between the values in column is reliable; p<0,05.

Table 2

**Percentage of fertility recovery in married couples with male infertility factor based on their age under the IMS program**

Age	Abs.	%	Number of cycles	Quantity of pregnancies			Quantity of childbirth		
				abs	%	m	abs	%	m
under 24	29	20,7	87	20	23,0	4,5	19	21,8	4,4
25–29	44	31,4	132	26	19,7	3,4	25	19,0	3,4
30–34	29	20,7	87	17	19,5	4,2	15	17,2	4,0
35–39	17	12,2	51	4	7,8*	3,8	3	5,9*	3,2
40–44	14	10,0	42	3	7,1*	3,9	1	2,4*	2,3
≥45	7	5,0	21	1	4,8*	4,5	-	-	-
Total	140	100,0	420	71	17,0	1,8	63	15,0	18

Note: \* – the difference between the values in the first three lines and in three bottom lines is reliable; p<0,05.

Table 3

**Percentage of pregnancies and childbirths in women from married couples with male infertility under IMS program depending on the number of follicles as a result of ovulation stimulation**

Follicles	Number of cycles		Pregnancy		Childbirth		Twins		Triples	
	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
1	95	22,6	10	10,5*	9	9,5*	0	0	0	
2	135	32,2	22	16,3	21	15,6	2	9,5	0	
3	127	30,2	23	25,2	20	15,7	3	15,0	0	
4	63	15,0	16	25,4	13	20,6	4	30,8	1	7,7
Total	420	100,0	71	17,0	63	15,0	9	14,3	1	15,9

Note: \* – the difference between the values in the column is reliable; p<0,05.

## RESULTS AND THEIR DISCUSSION

We present the results of the applied IMS program for fertility recovery in 140 married couples, whose infertility is caused by a male factor. Data obtained from 3 fertilization attempts at intervals of 3-5 months, in total for 420 cycles, were analyzed. It should be noted that the main baseline parameters of the female hormonal status from couples were within the confidence intervals typical for healthy, and they remained the same after stimulation of the ovaries. First of all, we will give an overall assessment of the effectiveness of the Program of insemination with male's sperm (IMS). It was found that according to the results of 420 stimulation cycles, 71 pregnancy cases were obtained in 140 married couples (17.0±1.8%), 63 of which resulted in childbirth, i.e. in reality, the program was implemented in 15.0±1.8% of married couples. Then we represent the features that have been found in the course of work and reveal the main causal relationship between the outcome and the main baseline parameters of the clinical laboratory tests.

The analyzed percentage of pregnancy and childbirth depended on the age of women, while not the age but the number

of unfavorable conditions and the severity of sperm disorders were more important for men. The Table 1 presents the pregnancy and childbirth rates in IMS program, depending on the age of the women.

According to the Table 1, there is a clear tendency towards decrease in pregnancy and childbirth, and it acquires significant difference from 35 years and older. Thus, if under 30 years the pregnancy was reached after 261 cycles in 56 of 140 couples (40.0±4.1%), at the age of 30–39 years –after 120 cycles in 13 of 140 couples (9.3±2.4%) , and aged 40 and older – only in 2 couples (1.4±0.9%) after 39 cycles. Accordingly, the percentage of birth was 37.8±4.0%, 6.4±2.0%, and 0.7±0.3%. The significance of the difference is obvious.

We found it interesting to conduct a similar analysis for the age of men. The results of this study are presented in table. 2.

As can be seen from the Table 2, the nature of the dynamics was similar. Indeed, the male ability to restore reproductive performance becomes weaker with age. While at the age under 30 years the pregnancy occurred in 46 women (32.8±3.9%) for 219 cycles, then at the age of 30–39 years – in 21 women (15.0±3.0%)

Table 4

Percentage of fertility recovery in married couples with male infertility factor depending on the length of its natural absence under IMS program

Length of infertility and years	TOTAL		Number of cycles	Quantity of pregnancies			Quantity of childbirth		
	abs	%		abs	abs	%	m	abs	%
Below 4	23	16,4	69	23	33,3*	5,6	22	31,9*	5,6
>1 – <3	41	29,3	123	29	23,6*	3,8	28	22,8*	3,7
≥3 – <5	51	36,4	153	14	9,2	2,3	11	7,2	2,0
≥5 – <7	15	10,7	45	4	8,9	4,2	2	4,4	3,0
≥7	10	7,1	30	1	3,3	3,1	-	-	-
Total	140	100,0	420	71	17,0	1,8	63	15,0	1,8

Note: \* – the difference between the values in the column is reliable; p<0,05.

Table 5

Percentage of fertility recovery in married couples with male infertility factor taking into account the type of pathospermia under IMS program

Type of pathospermia	Abs.	%	Number of cycles	Quantity of pregnancies			Quantity of childbirth		
				абс	%	m	абс	%	m
Asthenozoospermia	53	37,9	159	33	20,8	3,2	31	19,5	3,1
Oligozoospermia	48	34,3	144	29	20,1	3,3	2,6	18,0	3,2
Teratozoospermia	26	18,6	76	8	10,3*	3,4	6	7,7*	3,0
Oligo-astheno-teratozoospermia	13	9,2	39	1	2,6*	2,1	-	-	-
Total	140		420	71	17,0	1,8	63	15,0	1,8

Note: \* – the difference between the values in the column is reliable; p<0,05.

for 138 cycles, and at the age of 40 and older in was achieved in (2.9±1.4%) for 63 cycles. Pregnancy ended with the birth of child respectively in 31.4±3.9%, 12.8±2.8%, 0.7±0.3%. According to the abovementioned information, it is evident that with the same tendency for the frequency of pregnancy with the change of age of married couples, it is more dependent on the female factor, i.e. the younger the woman, the higher the percentage of pregnancy and childbirth. As an example, at the age of 30–39 years for women the pregnancy rate is 9.3±2.4%, while for men it is 15.0±3.0%; p<0.05.

Below we will trace the dependence of the pregnancy and birth rates, including the number of live births, on the number of dominant follicles achieved under the program and stimulation of ovulation conducted according to the protocol (Table 3).

The data of the Table 3 demonstrates that the most women had two and three follicles at almost the same number of cycles. Since those who had two follicles, had 135 cycles, and those with three follicles had 127 cycles (32.2% and 30.2% respectively); together they accounted for 262 out of 420 – 62.4%. The group of women with 1 follicle was 1.5 times smaller – 95 cycles (22.6%), even smaller in cases where 4 follicles were reached – 63 (15.0%). There is a direct correlation between their number and pregnancy with the subsequent childbirth rate. In case of 3–4 follicles, it was in every fourth woman (25.0% each), while in woman with 1 follicle it was only in 10.5%, which is significantly less among other indicators.

A similar result was found as to the childbirth, they are more often realized in cases of more number of follicles and, at the same time, the percentage of multiple pregnancies increases under such conditions. Most of them were found in women with 4 follicles (30.8% – twins, 7.7% – triples). Twins were less than twice in cases of 3 follicles and twice in cases of 2 follicles. Apparently, the development of 2–3 follicles should be considered as the optimum variant when one can expect a low rate of multiple pregnancy.

An important factor in the achievement of result in all ART

methods is the length of absence of natural pregnancy. This also applies to the IMS program. The data presented in the Table 4 confirm this assumption.

According to the materials given in the Table 4 it follows that the best results were obtained in cases of early applying for specialized assistance (up to 3 years). They are significantly different from those with prolonged infertility. Even if it is ≥3 – <5 years, its value is 3.6 and 2.6 times smaller than for up to 1 year or >1 – <3 years, respectively.

However, one of the main factors of the effectiveness of IMS program is the spermogram parameters, and, in particular, the type of pathospermia. The Table 5 presents specific data on the pregnancy and childbirth rates, depending on the features of the pathospermia.

It was found that the most unfavorable situation is in case of teratozoospermia and oligo-astheno-teratozoospermia, which is quite justified in view of the nature of pathological changes. Almost the same positive result was found in types such as asthenozoospermia and oligozoospermia. In particular, among the total number of pregnancies (71), the most had it in case of asthenozoospermia 33 (46.5±5.9%), with no significant difference 29 (40.0±5.8%) in oligozoospermia, whereas it was twice rarely achieved in case of teratozoospermia 8 (10.3±3.7%), which is statistically different in frequency. Only in specific case the pregnancy without realized childbirth occurred in complex combined pathology – oligo-astheno-teratozoospermia (2.6±2.1%).

It is known that the main criteria for infertility include the number of sperm per 1 ml of ejaculate and their motility. They also determine the likelihood of adequate results when applying the IMS. The percentage of pregnancy depending on the concentration of sperm can be specified according to the data given in the Table 6.

According to the information given in the Table 6, the groups of men with the value of 5–14 and 15–30 mln/ml (36,4% and

Table 6

**Percentage of pregnancies and childbirths in married couples with male infertility depending on concentration of sperm under IMS program**

Number of sperm, mln/ml	Number of cycles		Quantity of pregnancies			Quantity of childbirth		
	abs	%	abs	%	m	abs	%	m
5–14	153	36,4	21	13,7	2,7	17	11,1	2,5
15–30	183	43,6	30	16,4	2,7	27	14,6	2,6
>30	84	20,0	20	23,8*	4,0	19	22,6*	3,9
Total	420	100,0	71	17,0	1,8	63	15,0	1,8

Note: – the difference between the values in the column is reliable;  $p < 0,05$ .

Table 7

**Percentage of pregnancies and childbirths in married couples with male infertility, taking into account the motility of sperm of «a» category under IMS program**

Number of sperm of «a» category, %	Number of cycles	Quantity of pregnancies			Quantity of childbirth		
		abs	%	m	abs	%	m
1–5	50	5	10,0*	4,0	3	6,0*	3,2
6–10	126	21	16,7	3,0	19	15,1	3,1
11–24	188	34	18,1	2,8	31	16,5	2,7
>25	56	11	19,6	5,3	10	17,9	5,0
Total	420	71	17,0	1,8	63	15,0	1,8

Note: \* – the difference between the values in the column is reliable;  $p < 0,05$ .

43,6% respectively) were the largest, and the groups with value of >30 mln/ml (20,0%) were much smaller. A comparative analysis of the data demonstrates that the rate of pregnancies and childbirths is statistically higher among men with sperm concentrations >30 mln/ml – 23,8±4,0% and 22,6±3,9%, respectively. They were close in the other two variants: in 5–14 and 15–30 mln/ml of the sperm the pregnancies and childbirths by groups were 13,7±2,7% and 11,1±2,5% and 16,4±2,7% and 14,6±2,6%, respectively. When emphasizing the importance of sperm concentration as a factor that significantly influences the end result of the program, the following feature should be noted. The proven existence of a significant inverse relationship ( $r = -0,82$ ) between the number of prerequisites in the form of predictors, determinants and the sperm concentration value confirms the need to take them into account and, if possible, to level out at the stage of preparation of the men for the program.

Below we comment on another criterion – the motility of sperm of «a» category, the data on the relationship between it and the result are given in Table 7.

4 groups are identified depending on the percentage of the progressively active fraction of «a» category sperm. The first and the fourth groups were equal in terms of the number of cycles, and the majority of cycles is concentrated in the third group.

One should pay attention to the low rate of pregnancy and, in particular, childbirth (10,0±4,0 and 6,0±3,2% respectively) when the motility percentage was <5%. It is 1,6 and 2,5 times higher, respectively, when the value is 5–10%. However, in case of its further increase the number of pregnancies and childbirths increases, but without a significant difference between the indicators. According to the data obtained, one can objectify the conclusion about the optimum minimum percentage of fast moving sperm of «a» category (>5%), when a positive consequence may be expected.

Summarizing the presented results, it can be argued that the effectiveness of the IMS program itself has proven to be quite low. Among 140 couples with male infertility, the pregnancy with subsequent delivery was in 17,0±1,8% and 15,0±1,8% cases, respectively. The dependence of the desired consequence on the age of women has been traced, whereas the age factor of men is not crucial. It has been proved that the fertility rate is subject to active ovarian response and ovulation stimulation.

A common factor for a married couple is a late treatment. In case of long-term non-onset of natural pregnancy (>3 years), there are prerequisites for negative impact on the result, for example, in the form of aging, reduction of reproductive reserves, including as a result of negative attempts of treatment, etc. Among the male-specific factors, the most important are the spermogram: type of pathospermia, the concentration of sperm, the percentage of their actively moving fractions, and the general state of their health is also relevant.

### CONCLUSIONS

It was found that the percentage of pregnancies and childbirths based on the results of 3 attempts (420 cycles) in 140 married couples with male infertility as a result of using the IMS program is 17,0±1,8% and 15,0±1,8%, respectively.

The causal relationship of the result with factors such as women's age, duration of non-onset of natural pregnancy, response of ovulatory function to stimulation has been confirmed, but the objectively proved indicators of spermogram are decisive: type of pathospermia, concentration of sperm and percentage of their active moving fractions, as well as the general state of health of the men.

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