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Prognostic of IUI depends of the number of motile spermatozoa inseminated and patient age, however high concentrations are always detrimental: an analysis of 9618 cycles

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STUDY QUESTION

What is the impact of the number of motile spermatozoa inseminated (NMSI) on clinical pregnancy rates (CPR) in intrauterine insemination (IUI) according to female age?

WHAT IS KNOWN ALREADY

Many authors have studied the effects of the NMSI on the success of IUI, but a real consensus has not yet been achieved. A minimum of 1 Million (M) motile spermatozoa inseminated is often quoted as required to optimize IUI but several authors question this threshold. Some studies have shown that the pregnancy rates were higher if the NMSI exceeds 2M or 5M[1,2]. However, according to a recent study, female age is the only variable significantly correlated with IUI success rates[3]. NMSI and female age have rarely been studied together[4].

STUDY DESIGN

This is a retrospective cohort study, in which 4394 couples completed 9618 IUI cycles with partner sperm, between January 2011 and December 2015, at a University-affiliated private ART clinic in Montreal.

MATERIALS & METHODS

All couples had been trying to conceive without success for at least 1 year. Indications for IUI included moderate male factor, dysovulation and unexplained infertility. IUI was performed after a natural cycle (n=180) or an ovarian stimulation by clomiphene citrate or letrozole (n=7611) or gonadotropins alone (n=218) or in addition to letrozole (n=1609). The primary outcome measure was clinical pregnancy rates defined by an intrauterine gestational sac with fetal heartbeat visible with ultrasonography at 7 weeks. Factors that may influence CPR were compared according to Chi2 test.

Table 1: Parameters influencing Clinical Pregnancy Rates (CPR) in IUI

| Parameters	Clinical Pregnancy Rate (%)	P
Female Age:		
- **< 30 years**	13.8 (n= 250)	
- **30-34 years**	14.0 (n= 489)	
- **35-39 years**	12.9 (n=398)	P < 0.001
- **≥ 40 years**	8.6 (n= 105)	
NMSI (×10⁶):		
- **< 1**	4.6 (n= 20)	
- **1 - 4**	10.5 (n= 119)	
- **5 - 9**	11.5 (n= 80)	
- **10 - 19**	13.5 (n= 165)	P < 0.001
- **20 - 99**	14.0 (n= 781)	
- **100 - 149**	14.7 (n= 72)	
- **≥ 150**	10.0 (n= 5)	
Range:		
- **N°1**	14.4 (n= 518)	
- **N°2**	12.4 (n= 328)	
- **N°3**	10.3 (n= 191)	P= 0.001
- **N°4**	13.8 (n= 108)	
- **≥ N°5**	13.4 (n= 97)	
Stimulation Protocols:		
- **Oral ovarian stimulation**	12.4 (n= 941)	
- **Oral + Gonadotropins**	15.4 (n= 247)	
- **Gonadotropins**	17.4 (n= 38)	P= 0.001
- **Natural cycle**	8.9 (n= 16)	

RESULTS

The 9618 cycles were divided into four groups based on the NMSI as follows: group 1, < 1M ; group 2, 1 to 4M; group 3, 5 to 10M; group 4, ≥ 10M. In women younger than 30 years (n= 1814 cycles), CPR were not significantly different between the four groups (6.4%, 14.8%, 13.7% and 14.1%, respectively; p=0.20). Nevertheless, the CPR appeared clinically lower in group 1. In women 30 to 34 (n= 3499 cycles), CPR were significantly different between groups (2.9%, 10.2%, 15.6%, and 15.0%, respectively; p<0.001). In women 35 to 39 (n= 3083 cycles), CPR were also different between the groups (5.5%, 10.5%, 8.0%, 14.2%, respectively; p=0.001). Thus, better results are observed if the NMSI is ≥ 5M between 30 and 34 years, and if the NMSI is ≥ 10M between 35 and 39 years. For patients ≥ 40 years (n= 1222 cycles), CPR were not different by groups of NMSI (4.7%, 5.4%, 6.3%, 9.7%, respectively; p=0.21), although the CPR seemed to double between groups 1 and 4. Less pregnancies in the older age group could explain the lack of significance. Interestingly, we noted that an NMSI ≥ 150M had a detrimental effect on CPR any age combined (10.0%, p<0.001).

Table 2: Clinical Pregnancy Rate (%) according to the NMSI and the female age

NMSI (×10⁶)	< 30 years	P	30-34 years	P	35-39 years	P	≥ 40 years	P
< 1	6.4% (n=6)		2.9% (n=5)		5.5% (n=7)		4.7% (n=2)	
1 - 4	14.8% (n=33)		10.2% (n=37)		10.5% (n= 40)		5.4% (n=9)	
5 - 10	13.7% (n=19)	0.198	15.6% (n= 42)	<0.001	8.0% (n=19)	0.001	6.3% (n=7)	0.213
≥ 10	14.1% (n=192)		15.0% (n=405)		14.2% (n=332)		9.7% (n=87)	

Figure 1: Clinical Pregnancy Rate (CPR) according to the NMSI (any age combined)
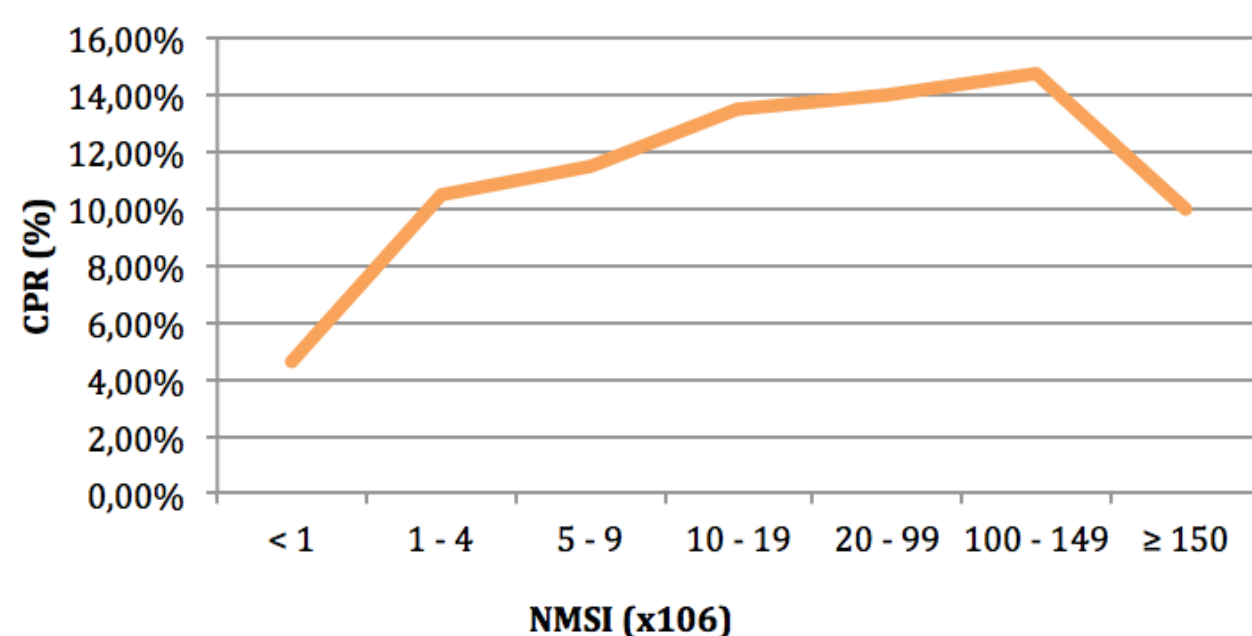
DISCUSSION

In this study, the NMSI positively influences the CPR of IUI for women between 30 and 39 years, while not for women under 30, or 40 and over. Our population was heterogeneous, all indications of inseminations combined, with ovulation stimulation treatments varied. However, the very high number of cycles adds strong value to our study and the NMSI is a standardized data.

CONCLUSION

Our study suggests that in couples with an NMSI <5M (if woman is between 30 and 34 years) or <10M (if woman is between 35 and 39 years), IVF should be considered as a first option. In addition, an NMSI ≥ 150M could have a negative impact and require prior dilution.

(1) Cao et al. A minimum number of motile spermatozoa are required for successful fertilisation through artificial intrauterine insemination with husband's spermatozoa. Andrologia. juin 2014
(2) Lemmens et al. Predictive value of sperm morphology and progressively motile sperm count for pregnancy outcomes in intrauterine insemination. Fertil Steril. juin 2016
(3) Sicchieri et al. Prognostic factors in intrauterine insemination cycles. JBRA Assist Reprod. janv 2018
(4) Badawy et al. Effect of sperm morphology and number on success of intrauterine insemination. Fertil Steril. mars 2009