P-042

Kinderwunsch Zentrum

Making the embryologist's life easier during intracytoplasmatic sperm injection (ICSI): use of dimethylxanthine theophylline (SpermMobil®) for testicular sperm samples

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What is already known

Derivatives of theophylline increase intracellularly the levels of cyclic AMP (1), thus stimulating sperm motility and reducing the time required to find viable motile sperm (2-6). Those compounds have been used for absolute asthenozoospermia (2-4) but solutions were not standardized. Only one study shows the effects of the commercially available SpermMobil® on pregnancy rates (5) and one live birth report after the use of this compound (6).

Study Question and Summary Answer

Is it possible to facilitate the embryologist's work during ICSI when dealing with testicular biopsy samples (TESE) in the absence of motile sperm? *Yes!*

Would the use of dimethylxanthine theophylline compromise fertilization, implantation and pregnancy rates, or affect perinatal outcomes? *It improved fertilization but not implantation and pregnancy rates. Perinatal outcomes were also similar among the groups with the live birth of 21 children so far.*

Study Design, Size, Duration

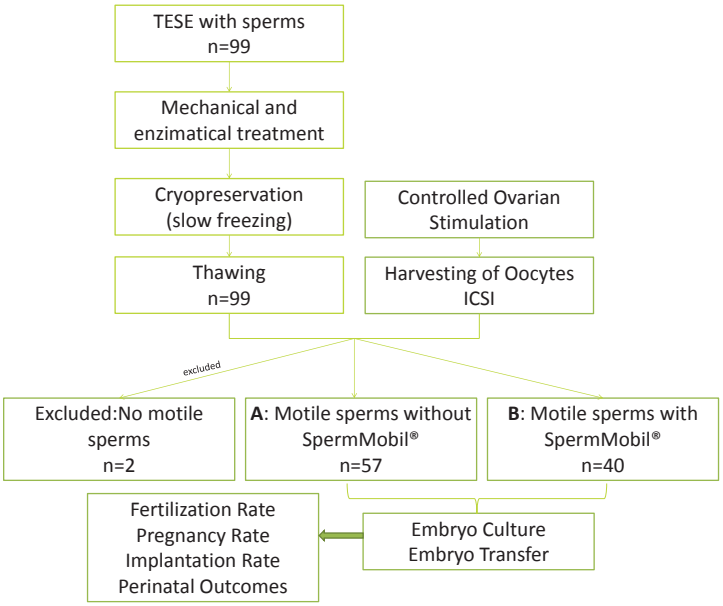


Figure 1. Study design and organization of experimental groups. ICSI cycles using TESE from January 2012 to October 2014 were analyzed retrospectively. 57 cycles did not require the use of SpermMobil® (group A), whereas 42 TESE (group B) presented no motility and were treated with SpermMobil® before ICSI. Two patients were excluded due to lack of motile sperm. TESE were treated mechanically and enzymatically, cryo-preserved, and thawed for therapy. Female partners underwent controlled ovarian stimulation and harvested oocytes were injected with motile sperm only. Embryos were cultured for up to 5 days. Statistical analysis were performed by Fischer's exact test, t-test, or Mann Whitney test.

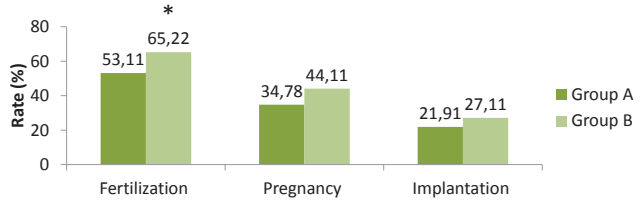
Results

	Group A		Group B		Mann-Whitney
	Mean	SD	Mean	SD	P-value
Female age (years)	34.11	4.216	33.5	4.668	n.s.
Male age (years)	39.81	8.221	38.83	8.221	n.s.
No. MII Oocyte	5.93	4.114	7.45	5.154	n.s.
No. Zygote	3.246	3.037	4.575	3.404	0.0168
No. of transfered embryos	1.587	0.5406	1.735	0.4478	n.s.
ET Day	3.766	1.237	4.343	1.027	0.0303

Table 1. Differences among groups were limited to number pronuclear zygotes obtained and consequently day of embryo transfer (ET). Statistical analysis was performed using the GraphPad Prism 6.0 software and $p < 0.05$ was considered significant. Unpaired t test for nonparametric variables (Mann Whitney test) was used as most of the data did not follow a normal distribution (D´Agostino & Pearson omnibus normality test). n.s., non significant.

Effects of SpermMobil®

I



II

	Group A		Group B		t-test
	Mean	SD	Mean	SD	P-value
Gestational Age at Birth (GA, weeks)	38.45	1.128	37.11	4.314	n.s.
Weight (g)	3169	532.5	3198	992.4	n.s.
Height (cm)	51.25	2.633	49.63	8.618	n.s.

Figure 2. I, SpermMobil increased fertilization rates. Fertilization rates were higher in group B, showing a beneficial effect of SpermMobil® (p=0.0431, Fischer's exact test). There were no statistically significant differences among the groups regarding pregnancy and implantation rates among groups, although group B tended to have higher rates.

Table 2. II, Perinatal outcomes. In group A, there were two biochemical pregnancies and two aborts, whereas in group B two aborts and 4 still ongoing pregnancies. GA, weight and height at birth also did not differ among the groups (A, n= 12 newborns; B, n= 9 newborns). The embryologist´s work was also facilitated, as the time required to obtain enough motile sperm decreased. Statistical analysis were performed by t-test.

Limitations and Reasons for Caution

This is a retrospective analysis of ICSI outcomes using testicular motile spermatozoa only. As the benefits of this compound have been already reported, we opted not to make a truly negative group (no spermatozoa motility, no SpermMobil® treatment) not to jeopardize patient's treatment outcome.

Wider Implications of the findings

This is the first report of multiple healthy births after the use of this chemical compound. The use of such a compound may facilitate not only the embryologist's work, by reducing the time needed to recover enough motile sperm, but also optimize patient's treatment outcomes by increasing the number of fertilized oocytes.

References

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