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Subtle Motility Abnormalities Diagnosed by Computer-Assisted Semen Analysis Not Found to Correlate with Infertile Males Better than Conventional Analysis

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One of the theoretical advantages of the computer-assisted semen analysis (CSA) is that by objectively isolating different motility factors some abnormalities may be noted by CSA that will correlate with male fertility that are not detected by routine semen analysis. Some data have been presented demonstrating that routine semen analysis (RSA) determined 50% of the male partners of a group of infertile couples that were found to have a subnormal RSA but the CSA was more sensitive detecting 80% abnormalities in the males [1].

However, the ability to detect a higher percentage of 'abnormal' males does not necessarily indicate that these males are truly subfertile. A recent study demonstrated no significant differences in the 6 month pregnancy rates of couples where a female factor was identified and corrected in the subset where the male partner had a normal motile density (83%) versus those males with subnormal levels (69%) [2]. Perhaps some CSA parameter(s) would be identified that could predict a fertile male even when the RSA was subnormal.

Not only has the RSA failed to adequately identify fertile males with subnormal parameters but the opposite has been found, i.e. males with normal RSA but who are subfertile. This was illustrated by demonstrating a high 6-month pregnancy rate after therapeutic donor insemination (TDI)

in a group of infertile couples failing to conceive despite the male seemingly normal by RSA and all female infertility factors corrected (and given at least 8 corrected cycles) [3].

A study was thus initiated to evaluate a group of infertile couples where a female factor was identified and believed to be correctable to determine if the CSA would better discriminate the fertile versus subfertile male.

Materials and Methods

A group of 405 couples with a minimum of 1 1/2 years of infertility were evaluated in this study. An additional requirement for inclusion was that a female factor(s) be identified and thought to be corrected. In this first group of 155 couples the semen analysis was performed manually, employing the Makler chamber for count and motility. The quality of motility and sperm morphology was estimated using the phase-contrast microscope. This group of tests is known as RSA. The other group consisted of 250 couples. The semen was evaluated by CellSoft (Cryo Resources, Ltd., New York, N.Y.) for a CSA; RSA was also performed. The group of parameters for CSA included: velocity, linearity, lateral head displacement, and beat/cross frequency, the normals were suggested by Cryo Resources, and correlates with lowest values obtained from our sperm donor specimens. The norms (parameters of normal males) for routine semen analysis were suggested by the World Health Organization (WHO) (table 1).

Quality of motility for RSA was judged on a scoring system of 1 to 4. The specimen was considered to be of subnormal quality if grade was 1 or 2. Grade 1 = minimal forward progression; grade 2 = poor to fair motility; grade 3 = good activity with linear forward progression; grade 4 = full activity with both fast and linear forward progression.

An RSA was considered subnormal if the motile density was below $10 \times 10^6/\text{ml}$ or morphology was < 50% normal. A CSA was abnormal if any parameter fell below normal standards.

Table 1. Normal values for RSA and CSA

	Normal values
Count	$\geq 20 \times 10^6/\text{ml}$
Motility	$\geq 50\%$ grade 3 or 4
Morphology	$\geq 50\%$ normal forms
Velocity	$\geq 40 \mu\text{m/s}$
Linearity	≥ 5.5
ALH mean	$\geq 1.8 \mu\text{m}$
ALH max	$\geq 2.3 \mu\text{m}$
Beat/cross frequency	$\geq 13 \text{ Hz (1/s)}$

Results

The pregnancy rates according to RSA and CSA parameters are shown in tables 2-4. The data showed that 70% of the time the RSA and CSA correlated with each other as to whether it was normal or subnormal. Interestingly, the pregnancy rates were almost identical whether the semen analyses were normal or subnormal (60 and 62%, respectively).

Table 2. Pregnancy rates according to RSA and CSA parameters

	155 couples			250 couples		
	patients		pregnancy rates %	patients		pregnancy rates %
	n	%		n	%	
RSA only subnormal	48/155	31	63	59/260	24	58
RSA only normal (CSA not performed)	107/155	69	85			
CSA only subnormal				16/250	6	31
RSA + CSA normal				55/250	22	60
RSA + CSA subnormal				120/250	48	62

Table 3. Computerized semen parameters vs. pregnancy rates for the group of 250, evaluated by RSA and CSA

	Number normal	Pregnant		Number subnormal	Pregnant	
		n	%		n	%
Count	86+131 = 217	131	60	18+15 = 33	15	45.5
Motility	41+56 = 97	56	58	63+90 = 153	90	59
Velocity	74+97 = 171	97	57	30+49 = 79	49	62
Linearity	76+106 = 182	106	58	28+40 = 68	40	59
ALH mean	74+107 = 181	107	59	30+39 = 69	39	57
Beat/cross	88+131 = 219	131	60	16+15 = 31	15	48
Morphology	70+87 = 157	87	55	34+59 = 93	59	63

Total number of pregnant couples = 146; total number of non-pregnant couples = 104.

Table 4. Comparison of semen variables in the group of couples who conceived and the group who did not (means \pm SD)

Semen variables	Pregnant	Non-pregnant
Count $\times 10^6$ /ml	90.5 \pm 95.4	84.5 \pm 70.2
Motility, %	44.1 \pm 20.2	44.5 \pm 17.9
Velocity, μ m/s	44.8 \pm 9.2	44.1 \pm 9.7
Linearity	6.2 \pm 1.2	6.0 \pm 0.9
ALH (mean), μ m	2.1 \pm 0.5	2.2 \pm 0.6
Beat/cross frequency, 1/s	15.5 \pm 1.8	15.3 \pm 1.8

A priori, the theoretical advantage of the computer would be to identify an abnormal male factor that the naked eye could miss and might falsely consider a semen analysis normal. When there was a discordancy between RSA and CSA (30%) only 16/75 (21.3%) found the RSA normal but the CSA detected a 'subtle abnormality'; in fact, the majority of the discrepancies centered on the RSA subnormal but the CSA normal 59/75 (78.7%).

Though the group with the exclusive abnormality in the CSA did have the lowest pregnancy rate at 31% (5/16), the numbers are too small to show statistical significance. The fact that the larger group with both subnormal RSA and CSA had a 62% pregnancy rate (74/120) suggests that it would be highly unlikely that the group with RSA normal but CSA subnormal would continue to demonstrate the lowest pregnancy rates.

Evaluating the CSA slightly differently, i.e. considering 2 or more parameters abnormal, 61/104 (58.7%) of non-pregnant cases were abnormal compared to 87/146 (59.6%) of the pregnant cases. Finally, no single parameter of the CSA that predicted a male with subfertility was found.

Discussion

Some of the potential physical pitfalls present in various CSA analyses have been described by Vantman et al. [4]. Most instruments are very expensive. Thus, a very important question is whether these instruments should be purchased by the average clinician practicing infertility or restricted just to research uses. If studies would indicate that CSA as

opposed to RSA could better predict the subnormal male than the expensive purchase would be justified.

Unfortunately, CSA proved no more effective than RSA in distinguishing the fertile from the subfertile male and, in fact, except possibly for extremely poor specimens, neither of these tests were useful as fertility potential tests. These data emphasize the need to find other methods of evaluating the semen analysis. Some preliminary data indicates that evaluating motion characteristics of sperm after being washed (capacitated) may prove useful [5]. CSA may be used for the latter. Thus, the main role of CSA in andrology should be limited to research.

References

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