FERTILITY AND STERILITY®
VOL. 81, NO. 4, APRIL 2004

Published by Elsevier Inc.
Printed on acid-free paper in U.S.A.

Clinical management of men producing ejaculates characterized by high levels of dead sperm and altered seminal plasma factors consistent with epididymal necrospermia

Sperm quality and viability can be improved in healthy men with epididymal necrospermia by requesting a second ejaculate 60 minutes after the first specimen is obtained. (Fertil Steril® 2004;81:1148–50. ©2004 by American Society for Reproductive Medicine.)

Epididymal necrospermia is a phenomenon that has been described in healthy men, as well as men suffering from spinal cord injury and adult polycystic kidney disease (1–3). It has been estimated that this condition affects fewer than 1 in 200 healthy men undergoing infertility work-up (1, 2). Characteristics of this condition include poor sperm motility (<20% to 30%) and a low sperm viability (<30% to 40%) in the ejaculate; the cause is a hostile environment in the epididymis contributed to by a dysfunction of the epididymis itself, among other factors (1–4). Improvements in obtaining viable and motile spermatozoa have been realized in men with this condition by depleting epididymal stores via frequent ejaculation at 12-hour intervals over consecutive days (1). The purpose of the intense ejaculatory regimen is to decrease the time of exposure of "younger" spermatozoa arriving into the epididymis to the hostile environment (1–4). However, frequent ejaculations over the course of various days may not be a viable option for men undergoing infertility therapy because of the stress imposed by the intense ejaculatory regimen.

In cases of oligozoospermia, production of a second ejaculate within a short-term period of approximately 60 minutes has been shown to be beneficial for improving the seminal quality as compared with the first ejaculate (5). In one study describing this methodology, the second ejaculate was improved in the majority of cases (70%) as compared with the baseline sperm count (5). Others have reported no statistically significant changes in sperm concentration in the second ejaculate, but the sperm motility increased significantly (6). In our experience with similar patients, this approach has been more acceptable than the intense ejaculatory method. Thus, it was decided to implement a similar approach in patients with epididymal necrospermia in light of the positive results previously reported in men with different conditions (5, 6).

The aim of this study was to evaluate whether the condition of epididymal necrospermia could be improved by requesting a second ejaculation after production of a first semen specimen characterized by high levels of necrospermia.

The average age for male and female patients was 37.8 ± 15.8 (range: 29 to 56 years) and 32.0 ± 6.0 years (range: 24 to 39 years), respectively. All couples were undergoing evaluation for primary infertility with a mean duration of 3.6 ± 1.5 years (range: 2 to 5 years). Associated female factors diagnosed were as follows: three patients with polycystic ovary syndrome (PCOS), and two with endometriosis and tubal factor infertility. Approval was obtained from the institutional review board of Centro de Fertilidad del Caribe.

Received May 14, 2003; revised and accepted September 8, 2003.

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0015-0282/04/$30.00
doi:10.1016/j.fertnstert.2003.09.047

Epididymal necrospermia, as described by Wilton et al. (1), was characterized by ejaculates with poor motility and a high proportion of dead sperm in the semen. This parameter enables patients with epididymal necrospermia (<30% to 40% live sperm) to be easily distinguished from other patients who had poor sperm motility but sperm vitality (>50% live sperm) within normal parameters (1–3). A semen sample after 3 to 4 days of abstinence (sample 1) was request from each patient for routine semen analysis. After identification of high levels of necrospermia and 60 minutes after collection of sample 1, the second semen sample (sample 2) was collected.

The seminal plasma was evaluated for the presence of round cells, amount of debris, pH, bacterial activity, and particulate matter. The semen specimens were assessed according to World Health Organization (7) criteria for the following quantitative and qualitative characteristics: volume (mL), concentration ($\times 10^6$/mL), percentage of total motility and forward progression (grade), percentage of normal morphologic characteristics, and percentage of live cells. The supravital stain used to determine the percentage of live to dead cells

TABLE 1

Seminal profiles of patients producing one ejaculate after 3 to 4 days of abstinence, followed by a second ejaculation 60 minutes after the first collection.

Semen source[b]	Semen characteristics[a]					
	Volume (mL)	Concentration ($\times 10^6$/mL)	Motility (%)	Grade (%)	Morphology (% normal)	Live sperm (%)
Patient 1						
Sample 1	0.5	16.0	0.0	0.0	0.0	0.0
Sample 2	0.2	51.0	8.0	4.0	10.0	13.0
Patient 2						
Sample 1	0.25	2.6	8.0	2.0	10.0	10.0
Sample 2	0.75	114.0	58.0	33.0	41.0	65.0
Patient 3						
Sample 1	2.0	30.0	5.0	1.0	2.0	6.0
Sample 2	0.3	70.0	32.0	17.0	4.0	48.0
Patient 4						
Sample 1	2.0	0.4	4.0	2.0	2.0	20.0
Sample 2	1.0	0.4	12.0	4.0	4.0	28.0
Patient 5						
Sample 1	2.0	27.0	30.0	11.0	6.0	50.0
Sample 2	1.0	22.0	60.0	39.0	8.0	73.0

[a] Observations for semen characteristics represent individual values. Criteria used for evaluation of seminal characteristics was applied according to World Health Organization values (7).

[b] Sample 1 = Ejaculate collected after 3 to 4 days of abstinence. Sample 2 = Ejaculate collected 60 minutes after production of sample 1.

Correa-Pérez. Clinical management of men with epididymal necrospermia. Fertil Steril 2004.

consisted of 1% (*w*/*v*) eosin-Y in isotonic phosphate buffered saline (PBS) solution. A drop (5 μL) of fresh semen was mixed with an equal volume of the staining solution on a microscope slide, covered with a cover slip, and incubated for 30 seconds at 37°C. The cells were observed under phase-contrast microscopy at $\times$400. A total of 200 cells per specimen were observed for each characteristic.

The results of the semen analyses for the two consecutive collections requested for each patient are summarized in Table 1. The semen analysis data for each patient represent individual values. Alterations in seminal plasma properties observed in the first ejaculate (sample 1) of all patients included increased levels of the following constituents: amount of debris, bacterial activity, particulate matter, polymorphonuclear leukocytes, and other round cells. A low semen pH (range: 6.4 to 6.8) was characteristic of sample 1. Improvements of sperm qualitative characteristics were realized in sample 2, which was requested at 60 minutes after the first ejaculation for all patients.

The altered seminal plasma factors were reduced to within normal limits for patients 2 to 5. The seminal plasma factors for patient 1 were reduced compared with the first ejaculate but remained high. The semen pH returned to normal levels in the second ejaculate of all patients (range: 7.2 to 7.6). The most dramatic case was observed in patient 2, in whom the classification of the semen specimen went from oligoteratoasthenozoospermic in the first ejaculate, to normozoospermic in the second ejaculate.

The composition of ejaculate, seminal plasma and spermatozoa, can be affected by factors such as the collection method (i.e., masturbation vs. coitus), stimuli during collection, abstinence period, and ejaculatory frequency (8, 9). Thus, under normal circumstances, a degree of sperm senescence may be present at any given time while the spermatozoa are stored within the epididymis before ejaculation. In the case of semen exhibiting characteristics of epididymal necrospermia, it has been proposed that the spermatozoa are produced normally in the testis and that the degeneration of those spermatozoa occurs during transit through the epididymis (1–4). Evidence to support this observation has been provided by improvements in sperm quality in healthy men or those with spinal cord injury in samples obtained after depletion of epididymal reserves containing high levels of dead spermatozoa (1, 2).

The hostile environment in the epididymis may be caused by a dysfunction or partial obstruction of the epididymis itself, stasis of seminal fluids, accumulation of senescent–degenerating spermatozoa, packing of cells involved in the removal of aging sperm, and reproductive tract infections (1–4, 10). The properties of the seminal plasma may also indicate a possible dysfunction of the accessory glands and/or alterations in the fluid dynamics of the accessory sex glands and vas deferens after periods of ejaculatory activity and rest (10).

In this study, improvements in the presence of viable spermatozoa were realized in a second ejaculation obtained approximately 60 minutes after an original ejaculate that was characterized by high levels of necrospermia and poor motility. By removing the negative environment temporarily from the cauda epididymis/vas deferens area, the spermatozoa in the second ejaculate may have had less exposure to the epididymal environment than those that had been ejaculated for the first collection. However, the spermatozoa may still be affected by the hostile environment in the epididymis, as the viability after ejaculation tended to decrease during the first 3 hours after ejaculation. Thus, it is suggested that the semen should be

processed as soon as possible following ejaculation and evaluation to remove any residual effects contributed by the epididymal environment or accessory glands.

Increased ejaculation intensity of two ejaculations per day for at least 4 days in healthy men and those with spinal cord injuries results in qualitative improvements of the necrozoospermic factor (1, 2). In healthy men, a second ejaculation provided 60 minutes after the first one provides the same effect, improving sperm vitality and quality, and is easier and as efficient as the intense ejaculatory regimen (1, 2). Our observations support an alternative approach for improving the condition of epididymal necrospermia in patients undergoing infertility therapy.

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References

1. Wilton LJ, Temple-Smith PD, Baker HWG, de Kretser DM. Human male infertility caused by degeneration and death of sperm in the epididymis. Fertil Steril 1988;49:1052–8.
2. Mallidis C, Lim TC, Hill ST, Skinner DJ, Brown DJ, Johnston WIH, Baker HWG. Necrospermia and chronic spinal cord injury. Fertil Steril 2000;74:221–7.
3. Fang S, Baker HWG. Male infertility and adult polycystic kidney disease are associated with necrospermia. Fertil Steril 2003;79:643–4.
4. de Ktetser DM, Huidobro C, Southwick GJ, Temple-Smith PD. The role of the epididymis in human infertility. J Reprod Fertil 1998;53:271–5.
5. Check JR, Chase JS. Improved semen quality after a short-interval second ejaculation. Fertil Steril 1985;44:416–8.
6. Gulmez I, Tatlisen A, Karacagil M, Kesekci S. Seminal parameters of ejaculates collected successively with sixty minute interval in infertile men: effect of combination of prazosin and terbutaline on these parameters. Andrologia 1991;23:167–9.
7. World Health Organization. Laboratory manual for the examination of human semen and sperm-cervical mucus interaction. 4th ed. New York: Cambridge University Press, 1999.
8. Tyler JP, Crockett NO, Driscoll GL. Studies of human seminal parameters with frequent ejaculation. II. Spermatozoal vitality and storage. Clin Reprod Fertil 1982;1:287–93.
9. Zavos PM, Goodpasture JC. Clinical improvements of specific seminal deficiencies via intercourse with a seminal collection device versus masturbation. Fertil Steril 1989;51:190–3.
10. Prins GS, Zaneveld LJD. Radiographic study of fluid transport in the rabbit vas deferens during sexual rest and after sexual activity. J Reprod Fertil 1980;58:311–6.