A study on the etiology of uterine pressure rise on semen deposition in the vagina or uterus

A. Shafik, M.D., Ph.D.; A.A. Shafik, MCh, M.D.

Department of Surgery and Experimental Research, Faculty of Medicine, Cairo University, Cairo (Egypt)

Summary

Purpose of investigation: In a recent study we have demonstrated that semen deposition into the vagina or uterus effects uterine pressure rise which is suggested to assist in "sucking" semen into the uterine cavity. The purpose of this study was to investigate whether the uterine pressure rise is effected by the sperm or the substances contained in the seminal plasma, and to test the response of the vagina and uterus to abnormal semen deposition.

Methods: Semen was obtained from 60 men divided into four groups: A) obstructive azoospermia, B) Sertoli cell-only syndrome, C) oligozoospermia and D), fertile subjects. Before and after semen deposition into the vagina and uterus both vaginal and uterine pressure were recorded.

Results: Semen from groups A and B produced no significant vaginal or uterine pressure changes (p > 0.05) when it was deposited into either the vagina or uterus. Group C and D semen when placed in the vagina or uterus separately effected significant intrauterine pressure rise (p < 0.05) but no vaginal pressure changes (p > 0.05). The pressure rise was higher when the semen was deposited in the uterus than in the vagina (p < 0.05) and with the normospermic than oligozoospermic semen (p < 0.05). In groups C and D, the seminal plasma produced no vaginal or uterine pressure changes (p > 0.05), whereas the sperm effected intrauterine pressure rise (p < 0.05) which was more elevated with sperm from normospermic than oligozoospermic semen (p < 0.05).

Conclusions: Aspermic semen did not effect vaginal or uterine pressure rise, while oligozoospermic and normospermic semen produced rise of uterine but not vaginal pressure. Uterine pressure rise was induced by the sperm and not the seminal plasma. Further studies are required to define the sulstances secreted by the sperm which produce this increased uterine pressure.

Key words: Azoospermia; Oligozoospermia; Semen; Sperm; Spermatozoa; Infertility.

Introduction

Semen consists of spermatozoa and seminal plasma which during coitus are deposited into the vagina. The sperm find their way up to the oviduct and fertilize the ovum. They are transported through various luminal fluids of different physiologic and biochemical characteristics such as testicular, epididymal, vasal, seminal, vaginal, uterine, oviductal and peritoneal fluids [1-4].

Seminal plasma is derived from the vas deferens, the seminal vesicles, the prostatic gland and the mucus, especially bulbourethral, glands [5]. In addition it contains scant fluid from the testes and epididymis [6]. The seminal vesicles produce fructose, phosphorylcholine, ergothioneine, ascorbic acid, flavins and prostaglandins; spermine, citric acid, cholesterol, fibrinolysin, zinc and acid phosphatase are obtained from the prostate [6-8]. Other substances existing in the seminal plasma are phosphate and bicarbonate which act as buffers, as well as hyaluronidase [6, 7, 9].

A recent study [10] has shown that semen deposition into either the vagina or the uterus separately, effected a significant intermittent uterine pressure rise with no significant change in the vaginal pressure. This intermittent uterine pressure rise seems to indicate uterine contractile activity which is suggested to act as a "suction-ejection pump" that might help sucking semen from the vagina and pushing it up to the oviducts.

The cause of the uterine pressure rise is not exactly known. We hypothesized that it could be an effect of the sperm or the substances contained in the seminal plasma. This hypothesis was investigated in the current study.

Material and Methods

Subjects: The semen was obtained from 60 men (mean age 37.3 ± 10.9 , range 26 - 48 years) divided into four equal groups representing: A) obstructive azoospermia, B) Sertoli cell-only syndrome, C) oligozoospermia and D) healthy fertile subjects. The individuals had given an informed consent before entering the study. Age and semen characteristics are depicted in Table 1. Semen examination was done three times with a 2-week interval. Testicular biopsies were performed for patients in groups A and B. All the subjects of group D fathered children, while the other groups did not produce any pregnancies.

The semen of groups A and B was used as it was ejaculated. Meanwhile the semen of groups C and D was first used as it was ejaculated and then after separating the sperm from the semen by centrifugation; each of the supernatant and the sperm were used separately.

The wives of the aforementioned groups (40 women) volunteered for the study to which they had given an informed consent. Ages ranged from 22 to 36 years (mean 30.6 ± 2 SD). All of them had normal menstruation and were gynecologically disease-free and sexually active. Physical and neurologic examination of the women and their husbands showed normal

Methods: Both vaginal and uterine pressure were determined under basal conditions and after semen deposition into the vagina and uterus separately.

Revised manuscript accepted for publication April 16, 2006

Table 1. — Age and semen characteristics of the four groups studied+.

	Age* (years)		Volume/ml		Sperm count		Motility %		Abnormal forms %	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
A. Obstructed azoospermia	33.6 ± 7.2	25-40	2.4 ± 0.8	1.4-3.5	0	0	0	0	0	0
B. Sertoli cell syndrome	35.6 ± 8.2	24-42	2.7 ± 1.2	1.3-4.3	0	0	0	0	0	0
C. Oligozoospermia	31.2 ± 8.8	25-38	2.8 ± 1.2	1.8-4.6	3.9 ± 1.5	2.2-7.2	25.4 ± 8.8	13-38	71.2 ± 14.4	4 56-88
D. Fertile subjects	34.3 ± 6.9	26-39	3.6 ± 0.9	3-4.3	74.8 ± 8.2	62-86	78.3 ± 7.3	70-88	14.6 ± 2.6	11-18

^{*} Values are given as mean ± standard deviation.

The women were asked to abstain from coitus three days prior to testing so as to exclude the presence of residual semen in the uterus. With the subject in the lithotomy position, a selfretaining speculum was introduced into the vagina. The cervix uteri was dilated with Hegar's dilators of the size from 2/5 to 3/6 mm. Uterine pressure was measured by means of a manometric tube of 0.5 mm inner and 1 mm outer diameter. It was perfused by a pneumohydraulic perfusion system (Arndolfer Medical Specialities, Greentale, WI, USA). The tube was introduced into the uterine cavity for 3-4 cm and connected to a strain gauge pressure transducer (Statham 230b, Oxnard, CA, USA). The vaginal pressure was measured simultaneously by a similar manometric tube inserted into the vagina for 3-4 cm, and connected to a second Statham pressure transducer. The women as well as the vagina and uterus were allowed a 30minute lapse to adapt to the inserted tubes before the test was

At the start, the husbands were asked to supply the semen sample via sexual intercourse with their wives, while the pressure tubes were inserted. The tubes were so thin that they did not interfere with coitus, as was confirmed by the subjects. However, by this method, the amount of semen deposited in the vagina could not be assessed because a portion of semen was lost on the penile skin and outside the vagina. For this reason we asked the subjects to deliver the semen sample by masturbation. Two ml of semen were obtained from each individual and were placed in a seminal syringe connected to a polyethylene tubing. The latter was introduced into the posterior vaginal fornix while the woman was lying in the lithotomy position, and the semen was injected. Both vaginal and uterine pressure were recorded before and immediately after vaginal deposition of the semen and every ten minutes thereafter for 60 minutes.

One week later, the test was repeated with semen deposition into the uterus. Two ml of semen, provided by masturbation, were injected into the uterine cavity by means of a syringe and the connected polyethylene tube which was introduced through the cervix into the uterine cavity. Vaginal and uterine pressure were measured during a period of three to five minutes before and immediately after semen deposition into the uterine cavity and every ten minutes thereafter for 60 minutes. One week after the last test, the sperm of groups C and D were separated from the semen by the Percoll discontinuous gradient technique [12] and the effect of the sperm or seminal plasma, separately tested on the vaginal and uterine pressure, was determined.

The period between semen deposition into the vagina and uterus in each test ranged from seven to ten days so as to avoid the effect of one test interfering with the other. This was also the time interval between one test and the other.

All the pressure measurements were repeated at least twice to assure reproducibility in the individual subject. The results were analyzed statistically using the Student's t-test. Analysis of variance was used when it was found necessary. Significance was ascribed to p < 0.05, and values were given as mean \pm standard deviation (SD).

Results

No complications were encountered during or after performing the tests, and all women were evaluated. The basal vaginal pressure recorded a mean of 4.8 ± 1.6 cm H_2O (range 3-8) and the uterine pressure a mean of 11.2 ± 2.1 cm H_2O (range 9-13).

The semen of group A and B subjects produced no significant pressure changes in the vagina or uterus (p > 0.05) when it was deposited into either of them. The semen of the oligozoospermic patients (group C) when deposited into the vagina, effected no significant pressure change in the vagina (p > 0.05). Meanwhile, the intrauterine pressure showed a significant increase immediately after semen deposition into the vagina (p < 0.05) (Figure 1). When the semen of this group was deposited into the uterine cavity, it produced no vaginal pressure changes (p > 0.05), whereas the intrauterine pressure showed a significant pressure rise immediately and after semen deposition into the uterus (p < 0.05) (Figure 2). The pressure rise was higher (p < 0.05) when the semen was deposited into the uterus than in the vagina. The uterine pressure rise was momentary; it occurred for 15-25 sec (mean 19.6 \pm 3.8) and then dropped to the basal level, to rise again after another 35-60 sec (mean 52.6 \pm 7.3). Repeated uterine pressure elevations recorded similar values each time (p > 0.05). Intermittent uterine pressure rise was recorded for 6-11 minutes (mean 8.4 ± 2.2) from semen deposition after which it dropped to the basal level (p > 0.05).

The response of the vagina and uterus to normospermic semen (group D) deposited separately into the vagina and uterine cavity are shown in Figures 3 and 4. Vaginal pressure showed no response, whereas intrauterine pressure exhibited a significant rise which was higher when the semen was deposited into the uterine cavity (p < 0.01)than when deposited into the vagina (p < 0.05) and with normospermic than with oligozoospermic semen (p < 0.05). When the sperm were separated from the semen of groups C and D and the supernatant (aspermic semen) was separately deposited in each group into the vagina or the intrauterine cavity, both vaginal and intrauterine pressure showed no significant changes (p > 0.05). The test was repeated in both groups C and D using only the sperm which were injected immediately after their separation from the semen into the vagina and the uterine cavity separately. In both conditions, vaginal pressure showed no significant change (p > 0.05) while uterine pressure significantly increased (Figures 5 and 6). The latter increase was higher when the sperm were placed

^{*} Age was not significantly different between the four groups.

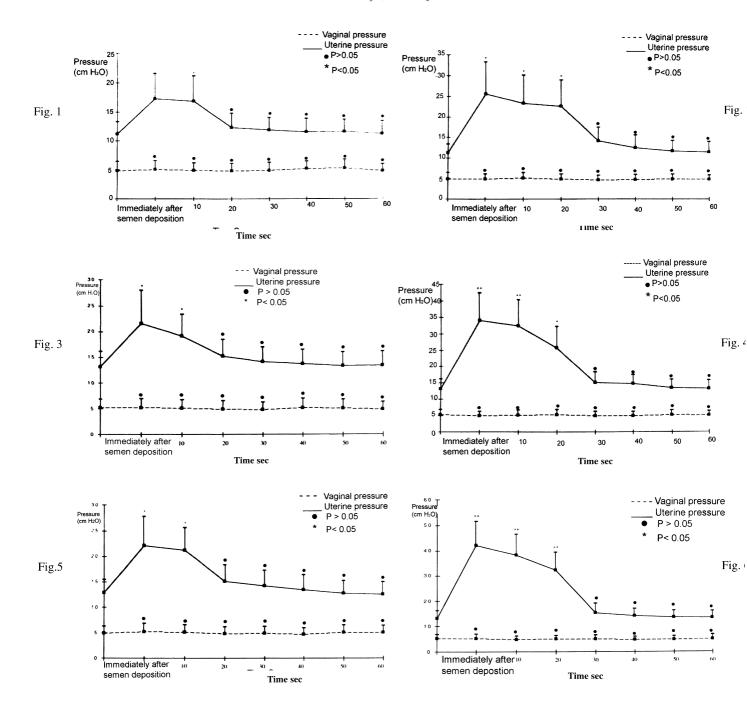


Figure 1. — Vaginal and uterine pressure recorded before and after semen deposition of oligozoospermic patients into the vagina and every 10 sec thereafter.

- Figure 2. Vaginal and uterine pressure recorded before and after semen deposition of oligozoospermic patients into the uterine cavity and every 10 sec thereafter.
- Figure 3. Vaginal and uterine pressure recorded before and after deposition of normal semen into the vagina and every 10 sec thereafter.
- Figure 4. Vaginal and uterine pressure recorded before and after deposition of normal semen into the uterine cavity and every 10 sec thereafter.
- Figure 5. Vaginal and uterine pressure recorded before and after deposition of sperm separated from normal semen into the vagina and every 10 sec thereafter.
- Figure 6. Vaginal and uterine pressure recorded before and after deposition of sperm separated from normal semen, into the uterine cavity and every 10 sec thereafter.

into the uterine cavity than into the vagina (p < 0.05) and with the normospermic than with oligozoospermic sperm (p < 0.05).

The uterine pressure response occurred after 1-3 sec (mean 2.2 ± 0.9) when the sperm were deposited into the vagina, and after 1-2 sec (1.3 ± 0.2) when they were deposited into the uterus. The uterine pressure rise was momentary. It lasted 16-28 sec (mean 21.6 ± 4.8) and then dropped to the basal level, to rise again after another 28-50 sec (mean 39.6 ± 10.3). The repeated uterine pressure elevations recorded similar values each time (p > 0.05).

The aforementioned measurements were reproducible with no significant difference (p > 0.05) when they were repeated in the same individual.

Discussion

The current study demonstrates the effect of the azoospermic, oligozoospermic, normospermic semen, and sperm and seminal fluid on vaginal and intrauterine pressure. The azoospermic semen and aspermic seminal plasma produced no significant pressure changes in the vagina or uterus. Meanwhile, the oligozoo- or normospermic semen produced an intrauterine pressure rise; this occurred also with sperm when they were deposited into the vagina or uterine cavity.

These findings suggest that the sperm, and not the seminal plasma, produce the rise in intrauterine pressure. This is evidenced by the fact that both the sperm-containing semen and the sperm alone produced a uterine pressure rise, while the seminal plasma contained in the azoospermic, oligozoospermic and aspermic semen produced no vaginal or uterine pressure response. It seems that the sperm once deposited into the vagina secrete a substance that induces an intrauterine pressure rise. The latter denotes uterine contraction which being intermittent might act as a "suction ejection" pump that acts to suck the semen from the vagina into the uterine cavity and to push it up to the oviduct. It is suggested that the sperm, upon entering the intrauterine cavity, might effect a further increase of intrauterine pressure as has been demonstrated in the current study; semen deposition in the uterus produced an uterine pressure rise more than when semen was deposited in the vagina.

How the sperm induce an intrauterine pressure rise while they are in the vagina needs to be discussed. The substance that might be secreted by the sperm could act on the uterine musculature either directly or could be blood- or lymph-born. However, the instantaneous uterine pressure rise upon semen deposition into the vagina as well as the higher pressure rise upon semen deposition into the uterine cavity than into the vagina might favor the direct action of the substance secreted by the sperm. It is postulated that sperm secrete this subtance to facilitate reaching the oviduct. It seems that once semen is deposted into the vagina, some sperm pass

directly to the uterus effecting by virtue of their secretions, uterine contractions; alternately a blood- or lymphborn effect might be considered. The intermittent intrauterine pressure rise creates a form of "suction-ejection" pump which might act to help the ascent of the sperm to the oviduct. Further studies are needed to identify this substance.

In conclusion, aspermic semen did not produce vaginal or uterine pressure elevation; meanwhile oligozoospermic and normospermic semen did produce a rise of uterine but not vaginal pressure. The uterine pressure rise was induced by the sperm and not the seminal plasma. Further studies are needed to define the substances secreted by the sperm which produce this increase of the uterine pressure.

Acknowledgment

W. Reichelt and M. Yehia assisted in preparing the manuscript.

References

- Hafez E.S.E., Levasseur M.C., Thibault C.: "Folliculogenesis, egg maturation and ovulation". In: E.S.E. Hafez (ed), Reproduction in Farm Animals, 4th edition, Philadelphia, Lea & Febiger, 1980, 48.
- [2] Burkman L.J., Overstreet J.W., Katz D.F.: "A possible role for potassium and pyruvate in the modulation of sperm motility in the rabbit oviductal isthmus". J. Reprod. Fertil., 1984, 71, 367.
- [3] Guzick D.S., Overstreet J.W., Factor-Litvak P., Brazil C.K., Nakajima S.T., Coutifaris C. et al.: "Sperm morphology, motility, and concentration in fertile and infertile men". N. Engl. J. Med., 2001, 345, 1388.
- [4] Krause W., Viethen G.: "Quality assessment of computer-assisted semen analysis (CASA) in the andrology laboratory". *Andrologia*, 1999, 31, 125.
- [5] Guyton A.C.: "Male reproductive functions: the male sex hormones and the pineal gland". In: Human Physiology and Mechanisms of Disease. Editor, Guyton AC. 6th edition. WB Saunders, Philadelphia, Pa, 1997, 648.
- [6] Mann T., Lutwak-Mann C.: "Male reproductive function and semen: Themes and trends in physiology, biochemistry and investigative andrology". Berlin, Springer-Verlag, 1981, 28.
- [7] Ewald E.S.: "The reproductive system. In: Basic Physiology for Health Sciences". Boston, MA, Little Brown, 1982, 572.
- [8] Carrell D.T.: "Semen analysis at the turn of the century: an evaluation of potential uses of new sperm function assays". *Arch. Androl.*, 2000, 44, 65.
- [9] Rosecrans R.P., Jeyenran A.S., Perez P., Kennedy W.P.: "Comparison of the biochemical parameters of human blood serum and seminal plasma". *Andrologia*, 1987, *19*, 625.
- [10] Shafik A.: "Vaginal and uterine response to semen deposition". Mol. Androl., 1996, 8, 251.
- [11] Shafik A., Shafik I.A., El Sibai O.: "Vaginal and uterine pressure response to semen deposition into the vagina and uterus: human study". Clin. Exp. Obstet. Gynecol. (in press).
- [12] Berger T., Marrs R.P., Moyer D.I.: "Comparison of techniques for selection of motile spermatozoa". Fertil. Steril., 1985, 43, 268.

Address reprint requests to: A. SHAFIK, M.D., Ph.D. 2 Talaat Harb Street Cairo 11121 (Egypt)