The Effect of Single-Dose Oxytocin Application on Time to Ejaculation and Seminal Parameters in Men

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Purpose: To report the effect of a single dose of oxytocin on ejaculation time and seminal parameters.

Methods: The prospective randomized clinical study was performed at a private assisted reproduction technology center and included 103 consecutive healthy men (semen donors or husbands of IVF patients). Oxytocin (16 IU) were administered intranasally to 49 subjects, randomly assigned to the study group just before masturbation to ejaculation. The time needed for ejaculation as well as the semen parameters was recorded according to the WHO standards, and compared to the control group of 54 subjects with no prior oxytocin treatment.

Results: No significant difference was noted between the two groups concerning ejaculation time and semen parameters.

Conclusions: Although the administration of oxytocin stimulates sexual behavior and performance in mammalian species, our data indicate that oxytocin has no detectable effect on ejaculation time and seminal parameters after intranasal application in normal, healthy men.

KEY WORDS: ejaculation; masturbation; oxytocin; seminal parameters; sperm output.

INTRODUCTION

The peptid hormone oxytocin has well-established functions in many mammalian species including humans. It is effective not only in the central nervous

system in memory processing (1,2) or in the induction of maternal behavior (3), but also has systemic effects, as a mediator of uterine contractions during partition or of milk ejection during lactation (4). In the male mammal, the hormone is produced in concentrations similar to those found in the female, yet for the male little is known about its function associated with reproductive physiology.

Various animal models have shown that oxytocin has a distinct sexually stimulating effect in certain mammalian species and increases the willingness to copulate (5,6). Previous studies described a significant increase of oxytocin during sexual arousal in men (and women), also immediately after ejaculation (4,7,8). Furthermore, it has been postulated that the circulating hormone—beside the central modulation of sexual behavior (9,10)—could also stimulate smooth muscle cells in the male reproductive tract, enhancing sperm transport. It is, therefore, hypothesized to be involved in the control of male fertility (11–19).

A possible potential to improve sexual performance would be of obvious interest, especially in IVF centers. There, the harvest of a high quantity of spermatozoa of optimal quality is crucial, and a decline in sexual behavior is a common problem for the male patient during the stressful semen collection.

The aim of our clinical study, therefore, was to investigate the possible ameliorative effect of oxytocin on sexual performance and sperm quality after intranasal application of this neuropeptide.

MATERIALS AND METHODS

A total of 103 men, aged between 26 and 59 years (mean 35.4 years), who were referred to our private assisted reproduction technology center either for

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IVF treatment or to volunteer for semen donation for artificial insemination between September and November 1995 were included in the trial. Written informed consent was obtained from all participants. The exclusion criteria were any metabolic, endocrine, or neurological disease, any malfunction or illness in the sexual tract. From all participants, a control spermogram was obtained prior to the study to evaluate the sperm quality and to exclude individuals with OAT 3 syndrome. The subjects were asked to produce a semen specimen by masturbation after 4 days of sexual abstinence, which should increase the stabilization of epididymal spermatozoal reserves.

Forty-nine donors were assigned to the study group by randomization, and the others were assigned to the control group. The two groups did not vary significantly in age and semen quality checked by the prior examination. The study group received oxytocin, applied as a nasal spray (Syntocinon-Spray®, Sandoz Pharma, Basel, Switzerland) prior to masturbation. Two puffs per nostril were applied, which correlates to 16 IU of oxytocin. During this, all subjects were assisted by a staff member of the institute to guarantee proper application of the drug. The subjects were instructed to commence with masturbation within less than 5 min after application. Then they were left alone for semen collection. The control group produced the semen specimen without prior oxytocin treatment.

The time from beginning of masturbation until completion of the specimen was measured. Then the sperm parameters were determined in the laboratory as follows. After complete liquefaction at room temperature, all samples were evaluated by light microscopy using a single Makler counting chamber, according to the WHO standards. Each specimen was evaluated for sperm volume, total sperm count, count per milliliter, total motility, percentage of progressive motility, and pathologic morphology. All laboratory work was performed by the same expert who had no

knowledge of the source of the specimen, so as to eliminate any possible subjective evaluation. ANOVA was performed as statistical analysis, and the mean and standard deviation (in brackets) are presented in Table I. A *p*-value of <0.05 was considered statistically significant.

RESULTS

In the study group as well as in the control group, all participating men were successful in producing an ejaculate. No correlation was found between age and masturbation time. Subjective responses were similar and independent of the prior treatment. In the oxytocin group, no major side effects were registered. Minor side effects such as feeling flushed, slight transient headache, or a strange peculiar taste disappeared in all subjects within 10 min after application of the hormone.

The results of the study group and the control group are shown in Table I. Although the mean time to ejaculation was slightly shorter in the oxytocin group, the difference was statistically not significant. The mean sperm volume was almost equal in both groups, and the mean total sperm count and the mean sperm density were even slightly lower in the oxytocin group. Mean total sperm motility and progressive motility were found to be slightly higher in the oxytocin group, as well as the mean pathological sperm count. However, none of the sperm parameters analyzed showed a statistically significant difference between the two groups (Table I).

DISCUSSION

One of the major aims in an in vitro fertilization center is the production of a sufficient amount of ejaculate in combination with the highest possible quality of the sperm cells. Steady search for ways to improve these

Table I. Time to Ejaculation and Seminal Parameters in Men

	Time (min)	Volume (ml)	Total count ($\times 10^6$)	Density (mio/ml)	Motility (%)	Progr. mot. (%)	Path. morph. (%)
Study group (<i>n</i> = 49)	10.24 (3.03)	3.56 (1.56)	180.76 (236.88)	53.7 (46.98)	50.17 (23.91)	46.11 (24.12)	62.48 (13.57)
Control group (<i>n</i> = 53)	10.74 (4.76)	3.57 (1.40)	200.76 (252.29)	59.67 (57.43)	45.58 (21.13)	41.43 (21.54)	59.31 (19.38)
<i>p</i> -value	0.53	0.96	0.68	0.57	0.31	0.31	0.36

Note. time: time to ejaculation; volume: total sperm volume; total count: total sperm count; density: sperm density; motility: total sperm motility; progr. mot.: progressive motile sperms; path. morph.: pathological morphology. Values in parentheses indicate standard deviation.

requirements has led to the question, as to whether neuropeptide hormone oxytocin could have a positive effect on masturbation time, and quantity and quality of the ejaculate after administration similar to other indications, i.e., as an intranasal spray. The idea is based on the following facts.

The neuropeptide oxytocin can be found in the mammalian testis (13,15) and cauda epididymidis (18–20) and plays a role in the male reproductive tract by modulating steroidogenesis (9,21). Furthermore, it enhances sperm transport by improving seminiferous tubular (11,15) and testicular capsule contractile activity (13). This oxytocin effect is partly mediated via stimulation of an increase in the synthesis of prostaglandins by the seminal vesicles (22).

There is evidence that oxytocin is one of the most potent mediators of drug-induced penile erections in laboratory animals (23,24), most likely by increasing NO-synthase activity in the paraventricular nucleus of the hypothalamus (25). Intracerebroventricular injection of synthetic oxytocin was followed by yawning and penile erection within 5 min in rats (23), whereas application of a potent nonapeptide oxytocin receptor antagonist as well as a competitive inhibitor of NO synthase reduced penile erections and copulatory behavior in a dose-dependent manner (10,26,27).

Another relevant observation is that several tactile erotic stimuli usually occurring during the precoital phase of sexual intercourse are among the most potent inducers of oxytocin release from the neurohypophysis (23). Some previous studies described higher circulating levels of oxytocin during sexual arousal and immediately after ejaculation in rabbits (4), and also in human sexual response (7,8). Considering the above findings, the marked rise of oxytocin during coitus must be postulated to play some essential role in coital physiology. This lead us to the idea of application of oxytocin just before semen collection.

The observations described above, however, seem to vary among several animal species. So administration of oxytocin just before electroejaculation in Hollstein bulls, for which semen collection was precluded by physical disabilities or inadequate libido—a condition quite common in humans during sperm collection for medical purposes, increased the number of spermatozoas in the first ejaculate, but did not alter spermatogenesis nor did it affect sperm quality (28). Additionally, in a similar study carried out on male rabbits in order to elucidate the importance of neurohypophyseal peptides, oxytocin was found to have no overall effect on the number of spermatozoa ejaculated (17).

On the other hand, oxytocin increased the willingness to copulate, to shorten the mount, and increased the intomission and ejaculation latencies as well as the post-ejaculation intervals in rats (5). The effect was proportionally greater in sexually sluggish individuals, and so the authors suggested that oxytocin might be useful in conditions of copulatory inadequacy.

In regard to seminal parameters, Zavos *et al.* (29,30) reported that the quality of an ejaculate produced during coitus and complete intercourse is superior to that obtained by masturbation with respect to semen volume, sperm concentration, progressive motility, and morphology. This means that the collected specimen should as closely as possible resemble the ejaculate delivered during intercourse, which is associated with a significant rise in oxytocin plasma levels as described above.

Therefore, in order to imitate the physiological sexual stimulated situation, we treated our patients with oxytocin, administered just before masturbation as an intranasal spray. This has been reported to be effective in a similar dosage (20 IU) and similar way of application (intranasal) in the treatment of post-traumatic stress disorders (2), and is widely used in women with problems in milk ejection.

The results of our investigation, designed to evaluate the effects of oxytocin, showed no statistically significant difference regarding time to ejaculation and quantity or quality of the ejaculates produced by masturbation with prior oxytocin administration as compared to those of the control group.

One could argue that in the study design a placebo spray should have been applied to the subjects of the control group, because of the possible psychological influence of any medication given prior to masturbation. The lack of a significant difference in the results of the two groups in our study, however, indicates no major psychological effect of the application of the nasal spray.

Our present findings confirm earlier observations, which have failed to reveal any obvious correlation between plasma oxytocin levels and sperm parameters (31). Our results are also in accordance with another study on oligospermatic human males, where intravenous injection of 10 IU oxytocin had no detectable effect on sperm count, seminal volume, or total ejaculated sperm number (32). In a more recent paper (33), where the relationship between oxytocin seminal plasma levels and sperm characteristics was investigated in three groups of patients—normozoospermatic, astheno/oligo/teratozoospermatic, and azoospermatic subjects, the seminal as well

as the blood concentration of the neurosecretory peptide had been found similar in all groups.

Our results are, however, in contrast to other studies, describing the ameliorative effect of oxytocin in impotentia erectionis treatment with 300 IU of the synthetic hormone, administered daily for a longer period (34). Oxytocin was also shown to produce a long-lasting reversal of the decrease in ejaculatory frequency and effectiveness produced by chronic depression treatment with fluoxetine (35). This confirms other previous results, which indicated that naturally occurring as well as synthetic oxytocin has a clear sexually stimulating effect in certain mammalian species with a sex cycle, and that oxytocin leads to an increase in sperm output and improvement of sexual performance (4–6).

CONCLUSION

In conclusion, we can state that oxytocin failed to produce a significant difference in sperm output and sperm quality after intranasal application in this study. Despite the effect of oxytocin on human male reproduction, the role of this neuropeptide in sexual behavior and sperm quality in infertility treatment remains uncertain.

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