

LETTER TO EDITOR

Mazindol to induce antegrade ejaculation in a patient with aspermia secondary to diabetic neuropathy

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To the Editor,

Erection and ejaculation are necessary processes for semen to be deposited naturally in the vagina, allowing sperm to migrate in search of the egg in the female reproductive tract and achieve fertilization (1).

However, in some cases, complete retrograde ejaculation (with absence of ejaculation – aspermia) or partial retrograde ejaculation (decreased seminal volume – hypospermia – and sperm concentration – oligozoospermia) may occur. In cases of aspermia or anejaculation, retrograde ejaculation should be suspected, and the diagnosis is confirmed by finding sperm in the post-ejaculatory urine.

For reproductive purposes, these men with retrograde ejaculation undergo urine alkalization to recover live sperm after orgasm and perform assisted reproduction techniques. However, it has been observed that the quality of sperm recovered from post-ejaculatory urine is low due to the effects of osmotic stress, the acidic pH of urine, and urea toxicity (2, 3).

Retrograde ejaculation can have anatomical, pharmacological, endocrine, or neurogenic causes (4), among the most common neurogenic causes are neurological disorders involving loss of sympathetic innervation in the bladder neck (multiple sclerosis, retroperitoneal lymph node dissection without nerve preservation, and spinal cord injuries) (5), such as secondary neuropathy in patients with poorly controlled diabetes mellitus, which causes failure of the sympathetic nervous system and, consequently, closure of the bladder neck.

On the other hand, mazindol (commercially known as *Mazano*, *Sanorese*, or *IFA Lose*) is an anorectic agent used in the short-term treatment of obesity, in combination with a low-calorie diet and physical exercise, in people with a body mass index greater than 30, or with a body mass index greater than 27 in the presence of risk factors such as hypertension, diabetes, or hyperlipidemia. Recently, our group reported for the first time that after treatment with mazindol, six out of seven patients (85.71%) presented with antegrade ejaculation (6). Mazindol activates alpha-adrenergic receptors, causing partial occlusion of the bladder neck, which allows antegrade ejaculation. Therefore, the objective of this letter is to present the case that successfully resolved its problem of antegrade ejaculation with a single dose of mazindol. Two years ago, a couple (a 31-year-old woman and a 44-year-old man) consulted for infertility due to the absence of ejaculation. The man weighs 83 kg and is 1.71 m tall (body mass index of 28.4 kg/m²). He has diabetes mellitus (fasting blood glucose of 89 mg/dL and glycated hemoglobin of 7.41), with high alcohol consumption and erectile dysfunction.

The patient developed secondary anejaculation, most likely due to diabetes mellitus. Over time, the volume of his ejaculate gradually decreased until he reported having orgasms without semen discharge.

During the medical examination, the volume of the right testicle (20.8 mL) and left testicle (20.6 mL) was determined, as well as bilateral varicocele (3.1 mm on each side).

Laboratory evaluation showed normal serum concentrations of the following hormones: total testosterone (561 ng/dL), free testosterone (8.85 ng/dL), and bioavailable testosterone (216 ng/dL), sex hormone-binding globulin (SHBG 51.3 nmol/L), luteinizing hormone 6.09 mIU/mL, follicle-stimulating hormone 5.53 mIU/mL, estradiol 17.8 pg/mL, and 17-hydroxyprogesterone 0.94 ng/mL.

After suggesting treatment with a single dose of mazindol (2.0 mg), masturbation was attempted two hours later, and antegrade ejaculation was achieved (the first in three years), which was analyzed by evaluating the parameters according to the guidelines of the World Health Organization's manual for semen analysis (7). The pH was 7.4, the semen volume was 0.5 mL, the concentration was 213 x 10⁶/mL, progressive motility was 73%, non-progressive motility was 15%, and immotile spermatozoa were 12%. In addition, sperm DNA fragmentation was evaluated using the sperm chromatin dispersion assay, with a result of 21%.

After observing that ejaculation was possible, he was advised to take the same dose of mazindol two hours before

attempting to conceive on partner's fertile days. The only adverse effect reported was mild and transient tachycardia and palpitations.

The patient provided informed consent in accordance with the current ethical standards of the *Uro-Andrology Center S.C. Guadalajara, Jalisco, Mexico*.

Retrograde ejaculation poses a significant clinical challenge in the management of male infertility, because semen, instead of being deposited in the vagina, is redirected to the urinary bladder, making natural conception difficult. Although classic pharmacological treatments exist, such as imipramine, midodrine, and sympathomimetic agents, their efficacy is limited and varies among patients, with recovery rates of antegrade ejaculation in only one-third of cases (8). In addition, the sperm quality of samples recovered from urine is often compromised by exposure to an inhospitable environment (3).

This case report suggests that the consumption of mazindol, a non-amphetamine anorectic agent with central stimulant properties, could induce bladder neck contraction through sympathomimetic effects, resulting in the recovery of antegrade ejaculation in a patient with diabetic neuropathy. The obtaining of semen with favorable parameters (volume, motility, and low sperm DNA fragmentation) underscores its potential clinical relevance. It is important, however, to consider the adverse effect profile of mazindol, such as its action on urinary and sexual function, and its use primarily in non-reproductive contexts.

Currently, there is little literature on the use of mazindol to treat retrograde ejaculation; this clinical report documents its immediate effectiveness after a single dose, providing a reversible, temporary effect solely to allow the semen sample to be analyzed or used (6). In the absence of any female factor that warrants oocyte retrieval, this would allow the couple to attempt pregnancy naturally and even use the semen sample for assisted reproduction procedures, avoiding unnecessary testicular retrieval and damage to the sperm by urine, which may improve the success rate (2, 3).

Therefore, these results open new research opportunities; however, controlled, large-scale clinical studies are needed to validate their safety and efficacy compared with traditional strategies.

In conclusion, this case documents the efficacy of a single dose of mazindol in inducing antegrade ejaculation in a patient with retrograde ejaculation secondary to diabetic neuropathy. Obtaining a semen sample is a potential alternative for managing male infertility associated with retrograde ejaculation. Avoid injecting oocytes with sperm that have been in contact with urine in the bladder or avoid testicular capture. However, its use should be approached with caution given its pharmacological profile and potential adverse effects.

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