

X-Prep (A Senna Preparation) Use As a Bladder Alkalinizing Agent in the Preparation of Sperm for IVF in Patients with Retrograde Ejaculation

RETROGRAD EJAKULASYON OLGULARINDA, IVF İÇİN SPERM HAZIRLIĞINDA MESANE ALKALİNLEŞTİRİCİ AJAN OLARAK X PREP (SENA PREPARATI) KULLANILMASI

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Abstract

Retrograde ejaculation (RE) is an uncommon cause of male infertility. In most cases the only possible treatment is recovery of spermatozoa from the urine for artificial insemination. Herein we describe a new and simple method in recovering sperm in such a case.

A patient with Type 2 diabetes (36 yrs) for 17 years who failed medical therapy for restoration of ejaculation was planned for COH/IUI (controlled ovarian hyperstimulation/intrauterine insemination). Following three failed IUI cycles using motile sperm obtained by bladder washings, with NaHCO₃ or X-prep (a senna preparation) use, the patient was finally scheduled for an IVF (in vitro fertilization) cycle. The patient had taken X-prep for urine alkalization in the last two IUI cycles and before IVF (in vitro fertilization). X-prep was better tolerated than the NaHCO₃ preparation.

The obtained urine volume with retrograde ejaculation was 40 ml. The sperm sample was prepared for IVF with a final count of 31 million/mL with 52% motility. Embryos were transferred on day 3 with an 85% fertilization rate.

Following implantation, a healthy baby was delivered at 38 weeks of gestation. X-prep may be a useful and well-tolerated simple method for recovering sperm in patients with retrograde ejaculation.

Key Words: Retrograde ejaculation, IVF, X prep

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Özet

Retrograd ejakülasyon erkek infertilitesinin sık rastlanmayan sebeplerinden biridir. Birçok vakada en olası tedavi şekli, yıkama sonrası, sperm elde edildikten sonra suni inseminasyon uygulanmasıdır. Bu vaka takdiminde, retrograd ejakülasyonu olan bir vakada spermin elde edilmesi için yeni ve basit bir yöntem sunduk.

Onyediyıldan beri Tip 2 diabeti (36 yaş) olan, antegrad ejakülasyon için medikal tedaviye yanıt vermemiş olan hasta için KOH (kontrollü ovarian hiperstimülasyon) sonrası, IUI (intrauterin inseminasyon) planlandı. NaHCO₃ ve X prep kullanımı sonrası, mesane yıkanması sonrası, elde edilen hareketli spermle, üç başarısız IUI denemesi sonrası, IVF (in vitro fertilizasyon) programına alındı. Hastanın, son iki IUI siklusunda ve IVF işlemi öncesinde idrar alkalizasyonu için X prep solüsyonu alması sağlandı. X-prep solüsyonu, NaHCO₃'a göre daha iyi tolere edildi.

Retrograd ejakülasyon sonrası elde edilen idrar hacmi 40 ml idi. IVF için hazırlanan sperm örneği sayısı 31 milyon/mL, motilitesi %52 idi. Embryolar %85 fertilizasyon oranı ile üçüncü gün transfer edildi.

İmplantasyon sonrası, 38 haftalık sağlıklı bir bebek doğurtuldu. X-prep kullanımı retrograd ejakülasyonlu olgularda spermin elde edilebilmesi için yararlı ve iyi tolere edilebilen basit bir yöntemdir.

Anahtar Kelimeler: Retrograd ejakülasyon, in vitro fertilizasyon, X prep

Retrograde ejaculation (RE) is the entry of semen into the bladder instead of the urethra during ejaculation. RE can be diagnosed in 0.3-2.0% of infertile patients.^{1,2} The post-ejaculatory urine sediment should always be examined in cases of low volume ejaculate.³ The

diagnosis is confirmed by finding spermatozoa in post ejaculatory urine.

RE's etiology is multifactorial. Different congenital anomalies can occasionally cause retrograde ejaculation, e.g. ejaculatory ducts entering into the bladder and ectopic ureters or ectopic ureteroceles terminating in the prostatic urethra.⁴ It may also be present in cases of spina bifida, meatal stenosis and posterior urethral valves.

Most common surgical procedures leading to this condition are prostatectomy, urethral surgery, bladder neck resection or extensive pelvic surgery.

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Diabetic neuropathy, multiple sclerosis and adrenergic blocking agents are among the other causes of RE.

For antegrade ejaculation, three successive events should take place which are stimulation of the sympathetic nerves, sympathetic contraction of the posterior urethra with closure of the bladder neck and parasympathetically (originating from S2-S4) induced contraction of the bulbocavernosus and ischiocavernosus muscles and pelvic floor activity.¹

Various treatments have been proposed for the treatment of infertility related to RE. However, the potential benefits or risks of individual treatment options are still unclear.¹

Medical treatment of RE is based either on increasing sympathetic tone of the bladder or on decreasing parasympathetic activity and is conducted with alpha agonistic or anticholinergic and antihistaminic drugs, mostly imipramine. At the given doses, side effects of the drugs given include various degrees of dizziness, sleep disturbances, weakness, restlessness, dry mouth, nausea or sweating which occur frequently in the responding patients. However, the effectiveness of medical therapy remains unclear. Although parasympathomimetics seem to be significantly better, they have potentially more severe side effects such as severe autonomic dysreflexia, headache, sweating and vomiting.⁵

If medical treatment of RE fails, sperm recovery from the bladder should be the second approach to retrieve spermatozoa for ART (Assisted Reproductive Technologies).⁶

Urine is considered to be spermicidal because of its acidic nature. Therefore urine alkalization is necessary before ejaculation.

Sodium bicarbonate solution is the most commonly used preparation for urine alkalization. Its observed side effects are nausea and gastrointestinal discomfort.

X prep is a sennoside derived from Senna leaves. Sennosides have been commonly used as

natural safe time tested laxatives. They have both a stimulant and bulk forming laxative activity. The reported side effects for the indication of bowel evacuation are similar to NaHCO₃; nausea and abdominal pain.⁷

We present a case with RE in whom the spermatozoa were recovered after X prep intake.

Case Report

RE was diagnosed in a 36 year old man. The patient had type 2 diabetes mellitus for 17 years. The patient gave no response to medical treatment for antegrade ejaculation with imipramine. The couple had intrauterine insemination once after 1g sodium bicarbonate intake, and twice using motile sperm obtained by bladder washing after 150 mg X prep preparation intake, but no pregnancy followed. The patient stated that he had less abdominal bloating with X prep intake. Finally in vitro fertilization (IVF) was performed. The male had taken X prep (a senna preparation) orally one day before and on the morning of ejaculation. The patient reported no vomiting or dizziness, only mild abdominal bloating. The obtained urine volume with retrograde ejaculation was 40 ml. Recovery of spermatozoa from the urine was achieved. The sperm count was 31x10⁶/ml with 52% motility. Three grade 1 embryos were transferred on day 3 leading to a clinical pregnancy. At 38 weeks of gestation the wife delivered a healthy girl by cesarean section.

Recovery of Spermatozoa From Urine

Urine is considered to be spermicidal because of its acidic nature. Therefore urine alkalization is necessary before ejaculation.

In addition to the detrimental effect of urine pH, there is evidence that osmolarity should be a major concern. Studies have shown that decreased sperm motility is more closely related to reduced osmolarity rather than to pH.^{8,9} Osmolarity of urine can be manipulated via fluid intake.

A sexual abstinence of 3 days was recommended for the investigation of the post-

ejaculation urine sample. The patient was instructed to ingest 150 mg of X prep the night before and a further 150 mg on the morning of the procedure. He was asked to empty his bladder before masturbation to obtain the post-ejaculatory urine as quickly as possible after ejaculation, and to deliver the sample immediately to the laboratory. The urine samples were divided into 15 ml sterile aliquots and centrifuged for 10 min at 600 g at room temperature. The supernatant was removed and the pellet suspended in 3ml of G fert (Vitrolife, Englewood, Colorado, USA Innovative Cell and Tissue Technology) supplemented with 5% HSA before use and recentrifuged at 600 g for 10 min. The supernatant was removed and finally, the pellet was resuspended in 0.5 ml medium and incubated at 37°C and 6% CO₂

Sperm parameters were assessed according to World Health Organization guidelines.¹⁰ Swim-up method was used for the preparation of sperm.

The pellets were resuspended and transferred to a sterile dish, the volume was supplemented with sperm washing medium until the total volume reached 20 ml. Later, it was equally divided into 2 sterile 15 ml aliquots and further centrifugated at 600 g for 10 minutes.

The supernatant was removed and each aliquote was resuspended in sperm washing medium G-Rinse (Vitrolife, Kungsbacka, Sweden, Innovative Cell and Tissue Technology) until the total volume reached 10 mL. The sample was finally centrifuged at 600g for 10 minutes.

The supernatant was removed and 0.5 mL of G fert supplemented HSA was added for swim up. The sperm suspension was transferred to an Eppendorf container with a small amount of medium.

The semen sample collected after the swim up process was ready for the IVF procedure.

Discussion

Retrograde ejaculation is an uncommon cause of infertility. Medical treatment of RE with alpha agonistic or anticholinergic and antihistaminic drugs, mostly imipramine have been succesful in a

minority of cases. At the given doses, side effects of the drugs given include various degrees of dizziness, sleep disturbances, weakness, restlessness, dry mouth, nausea or sweating which occur frequently in the responding patients.

Electrovibration stimulation initiates reflex spinal cord activity causing ejaculation. Reported side effects are paroxysmal hypertension, headache and autonomic dysreflexia.

Transrectal electroejaculation stimulates nerves responsible for ejaculation. Its side effects are rectal mucousa injury, transitory erythema, thermal electrical injury to the rectum, autonomic dysreflexia with paroxysmal HT and vomiting. It is a traumatic procedure for the patient and requires general anesthesia.

If medical treatment of RE fails, sperm recovery from the bladder should be the second approach for the retrieval of spermatozoa for ART. IUI, IVF or ICSI is performed on the basis of the sperm criteria. Our patient reported less side effects with X prep than with NaHCO₃

X-prep may be a useful and well tolerated simple method for recovering sperm in patients with retrograde ejaculation. Further research is needed to make further conclusions.

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