The management of retrograde ejaculation: a systematic review and update

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Objective: To determine the best management of retrograde ejaculation to optimize the chance of conception.
Design: Systematic review.
Setting: Tertiary reproductive medicine center.
Patient(s): Subfertile men with retrograde ejaculation.
Method(s): Systematic search of studies using search terms "management" or "therapy" or "treatment" and "retrograde ejaculation." We excluded case reports and papers not in English.
Main Outcome Measure(s): Pregnancy and live birth rates and rates of achievement of antegrade ejaculation.
Result(s): Thirty-four studies met our criteria. Studies were mostly observational. Descriptions of predictive and confounding variables were often insufficient. The treatment options included urinary sperm retrieval and medical management with anticholinergics and sympathomimetics. Successful pregnancies and live births were also achieved using surgical techniques and electroejaculation; however, numbers were small.
Conclusion(s): Many treatment options exist in the management of retrograde ejaculation; however, current literature is insufficient to allow firm comparisons between interventions. Treatment should be tailored, therefore, to the individual. Our findings support the need for further research in this area—including large randomized controlled trials. However, these would be difficult logistically and may not be possible. (Fertil Steril® 2012;97:306–12. ©2012 by American Society for Reproductive Medicine.)
Key Words: Retrograde ejaculation, male factor subfertility, fertility agents, male, infertility, sympathomimetics, cholinergic antagonists, electroejaculation, ejaculation, reproductive techniques, assisted, pregnancy rates, conception, live birth rate

Ejaculation is a complex process controlled by a spinal reflex triggered by tactile stimulation of mechanoreceptors within the penis. Sympathetic efferent fibers (T10-L3) trigger the two phases of ejaculation—1) emission and 2) expulsion—through contraction of the penile musculature. During the expulsive phase, it is necessary that the bladder neck (internal urethral sphincter) be closed to prevent the reflux of semen into the bladder as the urethral pressure increases. Closure of the bladder neck is also under sympathetic control. Failure of closure of the bladder neck and resulting reflux of semen into the bladder is known as retrograde ejaculation (RE). This results in a low-volume ejaculate and a low or absent sperm count with subsequent subfertility. The condition can occur as a result of congenital abnormality, spinal trauma, retroperitoneal lymph node dissection, diabetes mellitus, and bladder neck surgery or can be idiopathic. Retrograde ejaculation accounts for less than 2% (1, 2) of cases of subfertility presenting to a fertility clinic.

Treatment methods aim to restore antegrade ejaculation either medically or with surgery or to retrieve spermatozoa from the urine. Medical management aims at increasing tone of the bladder neck and therefore preventing retrograde flow of semen into the bladder by either stimulating sympathetic activity or blocking parasympathetic stimulation. Surgical interventions in the management of retrograde ejaculation aim at restoring integrity of the bladder neck. Urinary sperm retrieval aims to extract sufficient viable sperm from the postejaculatory urine for insemination, IVF, or intracytoplasmic sperm injection (ICSI).

Although numerous treatment options for RE exist, there is little guidance on the most effective way to achieve pregnancy. A previous review article (3) attempted to answer the same question but was not a systematic review and included case reports. In this article, we aim to systematically review studies investigating the management of retrograde ejaculation to achieve pregnancy with three different groups of interventions—urinary sperm retrieval, medical management, and surgical intervention—using the predefined measurable outcomes of pregnancy rate (PR), live birth rate, and achievement of antegrade ejaculation.

MATERIALS AND METHODS

Information Sources

We performed a systematic journal search using Medline and Web of

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Knowledge databases. Keywords used for the search were "Retrograde Ejaculation" and Manage* or Treat* or Therap*. Papers referenced in these articles found in the searches were also included in our analysis. Finally we performed a hand-search of six journals: *Journal of IVF and Embryo Transfer* (later known as *Journal of Assisted Reproduction and Gynecology*), *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *Reproductive Medicine and Biology* online, *Fertility and Sterility*, *Human Reproduction*, and the *British Journal of Obstetrics and Gynaecology*.

There was no limitation on the year of publication. We reviewed all abstracts, excluded papers that were obviously not covering the management of retrograde ejaculation or were duplicate reports, and obtained full text copies of all other papers. We contacted authors of included studies, when their details were available, for relevant current and unpublished projects.

The literature review was performed between July 2008 and April 2009 by the first two investigators (A.J. and D.S.). Subsequently an automatic update was set up. We followed MOOSE (4) and PRISMA (5) guidelines, and adhered to Cochrane principles (6).

Outcome Measures

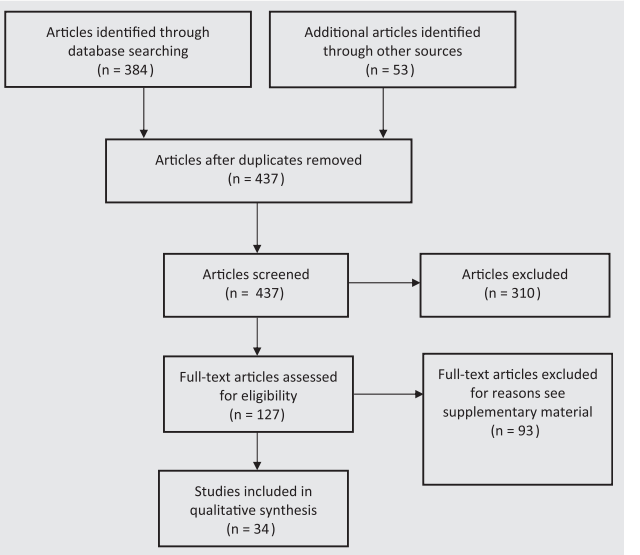
We selected outcome measures that reflect the success of treatments of retrograde ejaculation for the purposes of fertility, achievement of antegrade ejaculation, PRs, and live birth rates. For the purpose of comparing the success of interventions only studies with these outcome measures were included in the review. We stress that the lack of matched controls and the inadequate description of several studies make direct comparisons difficult.

Study Selection

Figure 1 demonstrates the study selection process for this review. Following MOOSE guidelines (4), we decided to focus on the key components of study design rather than arbitrary scoring schemes. All studies included had to assess more than one method (or variations on one method) of the management of retrograde ejaculation using the outcome measures described above. In many papers examined, variations on the method were quite subtle; for example, differences in the suspensory medium used, the route of fertilization, or whether or not the urine was alkalinized. These differences were, however, considered sufficient for inclusion in our review. For those papers where only one intervention was tested, there had to be a nontreatment group for inclusion. An assessment of quality of the study was made at the time of inclusion in the review by our investigators based on study size, documentation of methods and documentation of outcome measures. To reduce investigator bias as per Cochrane guidelines (6), the assessors included a generalist (A.J.), an obstetrician with interest in early pregnancy (D.S.), and an expert in reproductive medicine (P.W.). We excluded papers not written in the English language. A full list of citations excluded after review of the full text and the reasons for exclusion are detailed in the Supplemental Table 1. Most of the papers did not describe the methodology in detail. Therefore, we only collected data on participants, interventions, comparisons, outcomes, and study design (PICOS).

None of the authors are aware of any conflicts of interest in relation to the review. Our systematic review was not considered for IRB approval because of the nature of the study. It did not require access to patient data either directly or indirectly.

FIGURE 1



Study selection process. (Adapted from PRISMA Flowchart [5]).

Jefferys. The management of retrograde ejaculation. Fertil Steril 2012.

RESULTS

In all, 34 papers satisfied the above criteria and were included in this review (Fig. 1). Twenty-four papers looked at urinary sperm retrieval; 6 employed medical management of retrograde ejaculation; 2 assessed surgical and medical approaches; 1 evaluated electroejaculation, urinary sperm retrieval, and surgery; and 1 compared urinary sperm retrieval and medical management.

Urinary Sperm Retrieval

There are three different methods: centrifugation and resuspension of postejaculatory urine specimens, the Hotchkiss (7) or modified Hotchkiss technique, and ejaculation on a full bladder (Tables 1 and 2).

Centrifugation and resuspension of postejaculatory urine specimens. Nineteen studies employed this technique and 15 of these studies reported pregnancies and live births as outcome measures (Table 1). A postejaculatory urine specimen was obtained either by voiding or catheterization usually after alkalinization of the urine using oral sodium bicarbonate or increasing oral fluids to dilute the urine. The postejaculatory urine specimen was then suspended in medium, centrifuged and resuspended before used by either vaginal insemination, IUI, IVF, ICSI, or intraperitoneal insemination.