### **ORIGINAL RESEARCH**

## New Methodology for Investigating Ejaculation Dysfunction: Measuring Intraluminal Seminal Vesicle Pressure in Rats with a Telemetric Device

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#### ABSTRACT-

*Introduction.* Ejaculation dysfunction is one of the most common male sexual disorders. Despite its prevalence and adverse impact on patients, little attention has been given to investigating ejaculation dysfunction.

Aim. We introduce a new method for evaluating ejaculation dysfunction in rats with a telemetric device.

*Methods.* A pressure transducer was surgically implanted in the seminal vesicles of 7-week-old male Sprague– Dawley rats. One week later, the rats were subcutaneously administered tamsulosin 3  $\mu$ g/kg, and intra-seminal vesicle pressure (ISVP) was recorded in freely moving rats after an injection of apomorphine (80  $\mu$ g/kg). Same rats repeated experiment with tamsulosin 10  $\mu$ g/kg, silodosin 1 mg/kg, and normal saline with 3-day intervals.

*Main Outcome Measure.* Sexual events were visually identified and recorded. Ejaculation was confirmed by visualization of a copulatory plug in the tip of the penis. We compared the maximal ISVP and area under the curve (AUC) of the ISVP.

**Results.** Adequate ISVP data were easily recorded and available in 66.6% rats (10/15) over a 6-week telemetric recording period (12 recordings). The mean number of ejaculations during an inspection time of 30 minutes was  $1.5 \pm 0.1$ . The maximal ISVP values in rats receiving  $3 \mu g/kg$  ( $30.0 \pm 5.2 \text{ mm Hg}$ ) and  $10 \mu g/kg$  tamsulosin ( $15.1 \pm 1.6 \text{ mm Hg}$ ) and 1 mg/kg silodosin ( $12.9 \pm 2.2 \text{ mm Hg}$ ) were significantly lower than that in control rats ( $61.4 \pm 13.4 \text{ mm Hg}$ , P < 0.05). The AUC values in rats receiving  $3 \mu g/kg$  ( $72.7 \pm 18.9 \text{ mm Hg} \times s$ ) and  $10 \mu g/kg$  tamsulosin ( $23.5 \pm 6.1 \text{ mm Hg}$ ) and 1 mg/kg silodosin ( $23.9 \pm 8.0 \text{ mm Hg}$ ) were also lower than that of control rats ( $162.6 \pm 34.3 \text{ mm Hg}$ , P < 0.05).

*Conclusions.* Telemetric ISVP assessment is reliable and feasible for investigating apomorphine-induced ejaculation in rats. Tamsulosin (3 µg/kg and 10 µg/kg) and silodosin 1 mg/kg decreased the ISVP during ejaculation. **Sung HH**, **Kim JJ**, **Han DH**, **Kang SJ**, **Chae MR**, **Kim CY**, **Park JK**, **and Lee SW**. **New methodology for investigating ejaculation dysfunction: measuring intraluminal seminal vesicle pressure in rats with a telemetric device. J Sex Med 2015;12:2134–2140.** 

Key Words. Ejaculation Dysfunction; Telemetry; Telemetry Monitoring; Apomorphine

#### Introduction

jaculation dysfunction is one of the most Common male sexual disorders [1,2]. This disorder encompasses various types of ejaculatory problem such as premature ejaculation (PE), delayed ejaculation, and inability to ejaculate. Among these, PE is the most prevalent, accounting for approximately 20-30% of cases, depending on the definition for this condition [1-3]. PE has been clearly shown to exert a significant negative impact on the psychological statuses of patients with PE and their partners [4]. Medical conditions, including depression, anxiety, psychological distress, relationship problems, and general confidence, may be affected by PE [5-7]. In addition, many patients with PE suffer from concomitant sexual disorders. PE correlates with erectile dysfunction (ED) and coexists in approximately onethird of patients complaining of ED [8]. However, investigations of male sexual dysfunction have predominantly focused on ED, rather than ejaculation dysfunction. Accordingly, comprehensive research is essential to a better understanding of ejaculatory dysfunction.

In vivo experimental studies of ejaculation physiology and PE have introduced procedures in which the intra-seminal vesicle pressure (ISVP) of an animal is measured [9-12]. Specifically, in rats, the intraluminal pressure of the seminal vesicle in response to electrical nerve stimulation was recorded to investigate the effects of particular drugs. This technique is usually performed under anesthesia in rats fixed on a surgical plate. However, this research has been limited by the unnatural characteristics of sexual behaviors in response to anesthesia and electrical stimulation [13,14]. Copulatory behavior, matched ejaculation, and confirmation of increased ISVP cannot be simultaneously obtained. Additionally, the animals must be sacrificed after the experiments, thus restricting repeated trials with different drugs.

In a previous study, a telemetric device was introduced to measure the intra-cavernosal pressure (ICP), thus overcome the limitations associated with in vivo studies of ED [15]. In our previous studies, we successfully determined that ICP could be feasibly and reproducibly measured in rats using a telemetric device under minimally affected or unaffected conditions [16,17]. However, to our knowledge, no studies concerning ejaculation dysfunction have utilized a telemetric device. Therefore, the current study aimed to introduce new methodology with which evaluate the ISVP in rats with a telemetric device.

#### Materials and Methods

#### Animals

Seven-week-old male Sprague–Dawley (SD) rats (Orient Bio, Seoul, Korea) were housed 1 per cage at 22.8°C under 12-h light/12-h dark photoperiodic conditions (lights-off at 8:00 PM). Rats were fed a standard, fat-free pellet diet and water ad libitum throughout the experimental period. The rats were divided into four groups: tamsulosin (3  $\mu$ g/kg or 10  $\mu$ g/kg; Sigma-Aldrich Chemical Co, St. Louis, MO, USA), silodosin (1 mg/kg; JW Pharmaceutical, Seoul, Korea), and normal saline (control). A total of 15 rats were used. All animal experiments were conducted under the approval of the Institute for Animal Care and Use Committee of Samsung Medical Center.

#### Telemetric Device Implantation

Surgical implantation of the telemetric device was similar to the previously described technique used for telemetric ICP measurement [15,16]. The rats were anesthetized with an intraperitoneal injection of ketamine (80 mg/kg; Yuhan Co, Seoul, Korea). A sterile telemetric sensor device (PA-C40; Data Sciences International, St Paul, MN, USA) was implanted as follows. A mid-abdominal incision was made to expose the seminal vesicle. The tip of a recording catheter was carefully inserted into the body of the right seminal vesicle. This tube was tightly secured to prevent seminal vesicle pressure leakage. A pressure transducer was placed subcutaneously at the lateral aspect of the abdominal wall (Figure 1). All telemetric devices were calibrated and zeroed before and after implantation. After surgery, rats were housed in cages in the animal facility for 7 days before the ISVP recordings were performed. No obvious immediate adverse events were observed in any rats. All rats exhibited spontaneous movement and eating behaviors immediately after implantation. After completing the experiments, the rats were killed with an intracardiac injection of air. The insertion site was then evaluated for displacement of the catheter tip and any damage to the catheter or obstructions.

#### ISVP Measurements in Apomorphine-Induced Rats

One week after surgery, experiments were performed between 1:00 and 6:00 pm. Each rat was Download English Version:

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