The effects of experimental unilateral vasectomy on testicular structure in the rat

Saifzadeh, S.¹ and Derakhshanfar, A.²

¹Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Urmia, Urmia, Iran
²Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Kerman, Iran

Correspondence: S. Saifzadeh, Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Urmia, Urmia, Iran. E-mail: s.safizadeh@mail.urmia.ac.ir

Summary

In order to find out the effects of vasectomy on testicular structure, twelve mature male Dawley rats were undergone left vasectomy. Sixty-two days after the surgery, all rats were euthanized and both the testes of each rat were examined at the level of light microscope. Formation of spermatic granuloma (7/12, 58.3%) and atrophy of seminiferous tubular epithelium (6/12, 50%) were the most prominent microscopic changes. These findings were probably attributed to the hydrostatic pressure caused by semen retention as well as pressure caused by granuloma produced. The authors suggest that failure to regain fertility following vasectomy-reversal was probably related to the detrimental changes in testicular structure.

Key words: Vasectomy, Testicular structure, Dawley rats

Introduction

Vasectomy is a popular male contraception method that its side effects and reversibility rate are still controversial (Basimoglu et al., 1998). Since the introduction of microsurgical techniques for the treatment for male infertility, the success rate of seminal tract reanastomosis has markedly improved. A patency rate of 86% was reported following vasectomy reversal. However, not all patients have restored fertility even when the anastomosis is patent (Jarow et al., 1994; Matsuda et al., 1994). The reason for this apparent reduction of fertility following a successful vasectomy reversal remains unclear but has been attributed to immunologic effects (Linnet et al., 1981; Fuchs and Alexander, 1983), secondary obstruction of the epididymis (Silber, 1989), endocrinologic changes (Fisch et al., 1989), injured deferential nerves (Esk and Pbsi, 1981; Dixon et al., 1987), impairment of spermatogenesis (Matsuda et al., 1994) caused by seminal tract obstruction, and deteriorating effects of vasectomy on testicular histology (Bedford, 1976; Jenkins et al., 1979; Jarow et al., 1985; Flickinger et al., 1987).

The purpose of the present study was to illustrate the testicular histopathological changes following unilateral vasectomy by creating an experimental vasectomy model using mature rats.

Materials and Methods

Twelve native male Sprague-Dawley derived rats (Rattus norvegicus); Razi Institute, Tehran, Iran weighing 180 to 200 grams and ranging in age from 2 to 2.5 months, were used in this study. All rats were quarantined for 5 days and acclimated to environmental conditions of 21°C± 0.5°C with 50% ± 20% relative humidity and a 100% fresh air exchange rate of 15 complete changes per hour. The manually controlled photoperiod was 14 hours light (0700-2100) and 10 hours of dark (2100-0700) without twilight. Water and food (Dry commercial rat pellets-Pars Co., Tehran, Iran) were available ad libitum. Water was not withheld prior to experimental study to avoid dehydration. The rats were housed in groups of

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four animals per stainless steel wire bottom laboratory cages (60 × 40 cm floor space × 20 cm high). All animals were placed in cloth handmade restraint device during the induction of anaesthesia.

**Induction of anaesthesia**

The three drugs used in this study for induction of general anaesthesia in the rats, were atropine sulphate (Darou Pakhsh, Iran; 0.05 mg/kg), xylazine Hcl (Rompun®, Bayer, Leverkussen, Germany; 5 mg/kg) and ketamin Hcl (aescocet®, Gent, Belgium; 50 mg/kg). The drugs were injected by the intramuscular route into the thigh muscles, using 25-gauge needle and insulin syringes, with dosages based on data obtained from other study (Erhardt et al., 1984). Induction of general anaesthesia was determined by the loss of corneal and palpebral reflexes, reaction to sound and web pinch.

**Surgical procedure**

After induction of general anaesthesia, rats were positioned in dorsal recumbency on the operating table. Scrotal skin was prepared presurgically with antiseptic scrub solution (Betadine® scrub), then painted with povidone-iodine solution and allowed to dry. Finally, the scrotum was draped by 20×20 cm fenestrated drape. Vasectomy was performed for left testicle of each rat. Right testicle in each animal saved as control. Thus, each rat served as its own control. A 12 mm-long incision was made by No. 3 scalp knife parallel to and 3 mm beside the scrotal median raphe. The parietal layer of tunica vaginalis was grasped and incised by tissue thumb forceps and scissors. At the same time, pressure exerted by the thumb and index fingers, caused the left testicle to be extruded. Since the vas deferens was released from within the common tunic, two pairs of simple ligation, about 1 cm apart, using 5/0 Polyamide (Supa Co., Iran) suture material, were applied near the epididymis. The latter structure was severed between the far ligations, with attention to prevent escape of spermatozoa and then examined histologically. The exposed testicular structures pushed back into the scrotum after irrigating the ends of severed vas deferens with sterile warm saline solution. Closure of the scrotal skin wound was performed with simple interrupted pattern using the same material.

**Post-operative management**

Upon completion of the experiment, rats were kept in warm environment and each animal was given 2 ml normal saline intraperitoneally. After 3 to 5 hours, the rats were become conscious and aroused. To minimize the possibility of post-operative infection, the wounds were cleaned once daily with antiseptic solution and dressed by topical antiseptic ointment at the same time. Skin sutures were removed in 10 days.

**Euthanasia and sampling**

Sixty-two days post-vasectomy at the completion of the study, all rats were euthanized by decapitation using a sharp scissors (Poole 1999). Both testicles of each rat were removed and fixed in 10% buffered formalin, trimmed, embedded in paraffin wax, sectioned at 5 μ, stained with haematoxylin and eosin and microscopically examined.

**Results**

The most frequent microscopic changes were spermatic granuloma (7/12, 58.3%) and atrophy of seminiferous tubular epithelium (6/12, 50%), respectively (Figs. 1 and 2). The seminiferous tubular epithelium showed microscopic changes indicative of detachment and denudation with an incidence of 33.3% (4/12). Dilatation of epididymis was observed in 33.3% (4/12) of the vasectomised rats (Fig. 3). Mixed histopathological changes were noted in 41.6% (5/12) of the rats, as well.

**Discussion**

The most frequent histopathological change within the vasectomised testes, at the light microscopic level, was the formation of spermatic granuloma. Following vasectomy,
Fig. 1: Multiple spermatic granulomas surrounded by dilated epididymal tubules (H & E, original magnification, × 40)

Fig. 2: Atrophy, denudation and detachment of the epithelium of seminiferous tubules (H & E, original magnification, × 40)
epithelial rupture at locations above the point of surgery occurs as a result of increased hydrostatic pressure and directly correlates with excessive accumulation of intraductal spermatozoa within the occluded vas deferens and cauda epididymis. Such exposure of whole sperm and degenerated sperm fragments to immunocompetent cells and other antigen presenting cells within the interstitium of the epididymis and the peripheral smooth muscle layers of the vas deferens resulted in the formation of spermatic granuloma (Silber, 1977; Tung and Alexander, 1977; Saravananamuthu et al., 1991; Matsuda et al., 1994; Flickinger et al., 1995; Jessop and Ladds, 1995).

Whyte and co-workers reported severe tubular atrophy following closed technique of vasectomy in dogs, which finally destroyed the architecture of the testis (Sarrat et al., 1996; Whyte et al., 1998). Our results also demonstrated atrophy of seminiferous tubular epithelium (50%), detachment and denudation of tubular epithelium (33.3%).

By comparing the testicular histology of vasectomy and control cases, we also detected dilatation of epididymis (33.3%). This is in agreement with the findings of Chiang et al., (1998).

There are several possible explanations for the changes in testicular histology in patients with seminal tract obstruction, including an autoimmune reaction and hydrostatic pressure in the seminal tracts. Hargrave et al., (1982) reported no association between damage to the seminiferous tubule and the presence of agglutinating or immobilizing antisperm antibodies. Jarow et al., (1985) did not detect a direct association between histological changes after vasectomy and antisperm antibody status. These findings suggest that the autoimmune reaction may have a minimal role in the histological changes to the testis caused by seminal tract obstruction. Another possible explanation for the changes in testicular histology after vassal obstruction is the hydrostatic pressure in the seminal tract (Antypas et al., 1994; Jarow et al., 1994; Matsuda et al., 1994). Vasectomy suddenly blocks the flow of sperm and seminal fluids, resulting in a sudden increase in pressure in the seminiferous tubules. Silber (1977) reported that sperm granulomas were involved in pressure release in vasectomy patients. Jarow et al., (1985) reported a 50%
increase in the cross sectional tubular area in the vasectomy patients compared to the normal controls.

This study confirms previously reported vasectomy-related testicular histological changes. Although it is not easy to extrapolate conclusions drawn from animal studies to humans, we recommend to family physicians and urologic surgeons involving in vasectomy-reversal surgical techniques to be aware of the potential post-vasectomy detrimental changes in testicular seminiferous structures.

References

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