REVIEW

Post-vasectomy pain syndrome: clinical features and treatment options

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Introduction: *Post-vasectomy pain syndrome (PVPS), defined as chronic epididymal pain that is continuous or recurrent in the absence of proven epididymal or testicular infection, has become more common as the number of vasectomies performed rises. With more than four million vasectomies performed annually, the prevention and treatment of this condition becomes more important. Multiple theories have been proposed as a potential etiology of this condition, and along with this have come multiple modalities of treatment. With the uncertainty surrounding the etiology of this syndrome, the aims of treatment are varied and are described and analyzed in this review.*

Materials and methods: *A literature review was conducted to ascertain the various theories explaining the source of the discomfort in this syndrome, along with several treatment modalities, both medical and surgical.*

Conclusions: *Options for the management of PVPS are rapidly expanding. Among the existing surgical options that include spermatic cord denervation and vasovasostomies, testosterone has emerged as a potential medical therapy with some promising results. Our review of the literature reveals the etiology of PVPS is still uncertain, as multiple theories still prevail. However, progress has been made in the development of additional medical therapies that could provide some relief for patients who are unwilling to accept the risks of surgery. Nevertheless, the importance of counseling patients of the risks of PVPS with vasectomy cannot be overstated. Through review of the pathophysiology of this condition and treatment options including conservative approaches, topical therapies, denervation of the spermatic cord, and surgical approaches, a comprehensive therapeutic approach can be offered to affected patients.*

Key Words: vasectomy, chronic pain, post-vasectomy pain syndrome

Introduction

Vasectomy is the most effective form of male contraception and is chosen annually by more than 4 million men worldwide. The procedure has numerous advantages, which is why it is chosen by so many men. It can be performed in office or in the operating room, under local or general anesthesia, and can be performed by a wide array of physicians, including urologists, general surgeons, and family practitioners. The complication rate has always been considered to be low and much less than the female counterpart, tubal ligation. In the 1980s, post-vasectomy pain syndrome (PVPS), was not even considered, but it has evolved into an important but poorly understood complication

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of the procedure.[1] PVPS has been defined by the European Association of Urology as chronic epididymal pain that is continuous or recurrent episodic pain of ≥ 3 months' duration that is associated with lower urinary tract symptoms or sexual dysfunction in the absence of proven epididymo-orchitis or other obvious pathologic features.[2] It was not until 1996, when Choe and Kirkemo noted that chronic scrotal pain was a common complication of vasectomy and suggested inclusion on the procedure consent form, as the pain became a litigious issue.[2] They concluded that 18.7% of men have post-vasectomy scrotal pain, and of them, 2.2% said the pain adversely affected their lives.[3] This, like many studies had a low response rate of under 50%, which has lead to incidences of PVPS ranging from 0.1%-54%. Leading urologic textbook-based literature currently states the incidence rate of PVPS at ≤ 1 in 1000 vasectomized men, with the exact cause of the pain unknown.[4] Nevertheless, prevention and treatment of the PVPS needs to be a high priority. With the uncertainty surrounding the etiology, the aims of treatment are varied and are described and analyzed in this review.

Pathophysiology of PVPS

Like the incidence of PVPS, the determination of the etiology of PVPS has been an area of debate as well. Multiple theories have been proposed, such as long standing obstruction of the epididymal ducts, extravasation of sperm and sperm granuloma with an inflammatory reaction, and nerve entrapment at the vasectomy site.[5] However, the most accepted theory appears to be chronic congestive epididymitis due to continued sperm production.[5,6]

Multiple histologic changes consistent with long standing obstruction have been found to be attributed to PVPS, as suggested by the literature. In fact, the common presenting symptom of painful ejaculation in patients with the syndrome suggests that obstruction or congestion of the vas or epididymis may be the cause of the pain.[7] Multiple studies have documented the changes in histology of the epididymis and testis following vasectomy. These studies have demonstrated a chronic inflammatory process that begins to explain the development of PVPS.[8] This inflammatory process appears to be triggered initially by the increase in intraluminal fluid pressure that results from transaction of the vas deferens. This increase in pressure is transmitted to the source of the fluid, namely the efferent ductules and the head of the epididymis. These structures become markedly distended and then adapt to reabsorb large volumes of testicular fluid and sperm products.[9] In 1972, Alexander found that the diameter of the ducts increases 2 to 4 times its original size to counteract the increase in fluid pressure.[10] Interestingly, the effect of obstruction on spermatogenesis seems to be minimal. Previous studies have reported that after vasectomy, spermatogenesis continues unabated with increasing fluid pressure, forcing sperm into the dilated, congested epididymis.[11,12]

At some point in time, the absorptive capacity of the epithelial cells in the epididymis and efferent ducts becomes overwhelmed. In response, macrophages are recruited from the circulation to aid in the digestion and clearance of sperm products.[8] During this period of time, there is thought to be concurrent breakdown of epithelial tight junctions with subsequent leakage of sperm into the interstitium.[13] As a result of this disruption in the blood-testes barrier, detectable levels of anti-sperm antibodies are found in 60% to 80% of men.[4] It has been suggested that these antibodies may play an important role in the pathology of PVPS.

Multiple lesions within the vasa and testes, namely vasitis nodosa and sperm granulomas, occur as a result of more long standing damage secondary to increasing pressures within the vasa and epididymis. The first lesion to develop is vasitis nodosa, which is formed by the proliferation of vassal epithelial cells within the adventitia and surrounding interstitium in response to fluid and sperm dissection into the vasal wall. Lesions tend to be located at the ligation site of the proximal vas deferens.[14] Over time, once the sperm have dissected through the muscular wall of the vas deferens, they ultimately extravasate into the interstitium. As these sperm are broken down by macrophages and lymphocytes, they begin to stimulate antigen presenting cells which initiates the release of cytokines that activate branches of the chronic inflammatory pathway. Activation of fibroblasts via cytokine release stimulates fibrosis, and the subsequent development of a sperm granuloma.[8]

The formation of sperm granuloma post vasectomy is well documented. Sperm are highly antigenic and stimulate a significant inflammatory reaction. A sperm granuloma may form when sperm leaks from the testicular side of an open-ended vas deferens following vasectomy. Less commonly, they may form with extravasation from a cauterized or fulgurated vas.[15] Whether this entity has a protective versus causative role has been controversial. According to multiple studies, sperm granulomas occur frequently. Nangia et al reported that they occur in 4%-60% of patients undergoing closed-ended vasectomy.[16] The large range in percentages is likely due to the discrepancy among physicians and researchers in describing the lesions.

According to Christiansen and Sandlow, the sperm granuloma is clinically seen as a nodule (tender or non-tender), present on the epididymis or at the end of the proximal vas deferens. Histologically, they are characterized as a chronic inflammatory infiltrate surrounding a site of sperm extravasation and are mostly asymptomatic.[8] Recent research has suggested that the formation of a sperm granuloma at the vasectomy site allows decompression of the vas and epididymis without causing discomfort to the patient.[17] These findings suggest that an open ended vasectomy procedure could reduce the incidence of post-vasectomy pain, but possibly at the price of a higher incidence of recanalization.[7]

On the other hand, a contradictory report suggested that sperm granulomas at the vasectomy site were intensely painful in 40% of cases.[18] The authors of this study hypothesized that a branch of the nerve (internal spermatic, external spermatic or vas deferens) becomes incorporated within the wall of the granuloma. Thus, any stimulation of the nerve, such as compression due to touch or the cremasteric reflex, distention from ejaculation or inflammatory responses, may cause acute pain at that site. The symptoms would be relieved after excision of the granuloma. Overall, most recent studies report that patients with PVPS generally do not have sperm granulomas, suggesting that PVPS is caused in part by the lack of pressure vent on the epididymis.[16,19]

Treatment options

Many treatment options have been used to cure PVPS. As with most medical problems the treatment begins with conservative medical management prior to exploring surgical options. The procedures include denervation of the spermatic cord, epididectomy, vasectomy reversal, and orchiectomy. These will be discussed in detail in the following sections, Table 1.

TABLE 1. **Treatment options for post-vasectomy pain syndrome**

Conservative
Non-steroidal anti-inflammatory agents
Antidepressants
Alpha-blockers
Narcotic analgesics
Testosterone crème
Denervation of the spermatic cord
Epididymectomy
Vasovasostomy
Orchiectomy

Conservative management of PVPS

Conservative medical management includes the use of antibiotics, NSAIDs, anti-depressants, α-blockers, narcotic analgesics, warm baths, and scrotal support.[20] Other alternative methods have been tried, including regional nerve blocks, physical therapy, myofascial release, biofeedback, psychotherapy or acupuncture.[21] Data on the effectiveness of these conservative measures is lacking in the literature. However, a study in Switzerland was performed for chronic scrotal pain, not necessarily due to PVPS. The results showed the mean estimated recurrence rate after conservative treatment was 48%, versus 18% when invasive surgical techniques were used, mainly epididectomy or ochiectomy.[22] The most common methods of treatment were with NSAIDs, followed next by antibiotics. Conservative medical management should remain the first line treatment, but the actual effectiveness at this time is unknown.

Proposal of medical management with testosterone

The use of testosterone in the treatment of PVPS has not undergone a large a clinical trial, but a case report and proposal was made by Pienkos.[23] Monthly intramuscular injections of testosterone cypionate are used to induce azoospermia by feedback inhibition on the hypothalamic-pituitary axis. In animal models, a decrease in 20% of normal intratesticular testosterone was effective in causing azoospermia.[24,25] Additionally, exogenous testosterone has been used in two studies by the World Health Organization as a hormonal male contraceptive. Results showed testosterone injections produced azoospermia in 60%-70% of Caucasians and 95% of Asian men, with oligospermia occurring in the remaining men.[23] Halting spermatogenesis may improve symptoms of PVPS through the absence of antigenic sperm being produced after the testis-blood barrier is destroyed from vasectomy. This can decrease the incidence of sperm granulomas and pressure in the epididymal end of the vas deferens, and therefore, is proposed to eliminate pain in men without the need for invasive procedures.[23] At this time, being only a case report, we cannot endorse testosterone injections as an acceptable and effective treatment. However, it will be important to follow this method of treatment to see if it may receive consideration in the future.

Microsurgical denervation of the spermatic cord

Testicular pain following vasectomy may be due to nerve damage innervating the testes and scrotum, particularly

branches of the genitofemoral traveling in the spermatic cord and illioinguinal nerves. During chronic pain, sensitization of nociceptors and their neurons in the peripheral nervous system and changes in the central nervous system occur from repeated stimulation leading to a decreased threshold for depolarization, increased frequency of response, and a decreased response latency time. Eventually, neurons will fire spontaneously.[26,27] Therefore, microsurgical denervation of the spermatic cord is used to remove the afferent nerve stimulus, and down-regulate the neurologic changes.[21] The procedure outlined by Levine and Strom was only performed in those men who reported at least a temporary 50% reduction in pain following a spermatic cord block using 0.5% bupivacaine. Through a low inguinal incision a 2 cm-3 cm segment of the illioinguinal nerve is excised and ligated. The spermatic cord is then dissected leaving only the testicular, cremasteric, and differential arteries and lymphatics intact. Finally, the vas is divided and all neuronal fibers are destroyed. Results of the technique in patients with PVPS, after 20.3 months of follow up showed a complete relief in 67%, partial relief in 17%, and no change in pain in 12%.[21] Further, Ahmed et al evaluated microsurgical denervation of the spermatic cord performed on 17 patients resulted in complete pain relief in 13 (76%) men with the remain having partial relief.[28] Results of this procedure are encouraging and should be considered prior to more extensive procedures.

Epididymectomy

The leading theory in the etiology of PVPS is chronic congestion of the vas and testis due to obstruction after the vasectomy. Therefore, removing the epididymis will remove the source of the pain.[29] It was believed that patients who benefited most from epididymectomy has focal epididymal dilation and tenderness.[30] Further, those inflammatory changes where associated with a poorer prognosis.[30] However, recent studies seem to refute these findings and show that epididymectomy is an effective method to improve PVPS.

Epididymectomy has been found to be more efficacious in the treatment of PVPS versus those with epididymal pain and no history of a vasectomy. Lee et al reported that epididymectomy resulted in complete to marked improvement in pain in 17 of 18 (94.5%) patients.[6] Scrotal ultrasound performed prior to the procedure showed mechanical obstruction. Final pathology reports showed that 44% of the patients treated had chronic epididymitis.[6] Even with the chronic inflammatory changes, significant improvement was seen. Lee et al confirmed the results seen by two other studies performed between 2007 and 2009. Siu et al found that all 25 of the patients with PVPS were satisfied with the results after epididymectomy.[20] Hori et al showed satisfaction in pain relief in 42 out of 45 (93.3%) patients with PVPS.[29] Interestingly, in a retrospective study by Sweeney et al in 2008 showed that in 17 patients with PVPS only 5 (29.4%) were satisfied with their pain afterwards.[31] This presents some controversy as to whether epididymectomy is effective, but the previous study may have be skewed by response bias. It seems as if recent studies show encouraging results for the use of epididymectomy in the treatment of PVPS.

Vasovasostomy

Vasectomy reversal has also been reported in the treatment of the post-vasectomy pain syndrome. Overall, the results of multiple studies have shown promise. Most studies have shown that, in appropriately selected patients, vasovasostomy can produce marked improvement or complete resolution of pain. This form of treatment, however, does have a significant drawback: the restoration of fertility. In 1997, Myers et al reported that 84% of patients with PVPS had complete resolution of pain after vasovasostomy.[32] Nangia et al reported in 2000 that 69% of patients were pain free after reversal. The authors also noted that selection criteria for surgery as an important determinant to the outcome.[16] Most authors agree that careful preoperative evaluation should include serial physical examinations to confirm the site of the persistent pain, consideration of a psychological evaluation to exclude somatization, and a scrotal ultrasound to asses for any occult pathology.[33] Nangia also concluded in the same study that patients with suture granuloma, nerve proliferation and fibrosis develop chronic scrotal pain that does not respond well to vasovasostomy, and patients with sperm granuloma but no nerve proliferation have a higher chance to remain pain free following vasovasostomy.[16]

Orchiectomy

Although there are many options for the treatment of PVPS as discussed previously, some men continue to experience pain. For these men the last option is orchiectomy, however this too has not had complete effectiveness. Orchiectomy can be performed by an inguinal and scrotal technique, which was compared by Davis et al. The results showed inguinal approach was more effective at 73% versus 55% in pain relief.[34] Another study by Yamamoto et al with four patients resulted in 75% relief of pain.[35] Unfortunately, these studies did not

single out results of pain relief in those with PVPS versus other etiologies. With other less invasive procedures that have similar or better outcomes, orchiectomy should only be considered as a last resort.[21]

Conclusion

The concern of PVPS has been rising as it has become a challenge to treat effectively. As more studies are focused towards PVPS the etiology and appropriate management may be discovered. Testosterone use is an intriguing option and it will be interesting if more attention is focused in that direction. At this point treatment should begin with medical options, progress to surgery, and as a last resort orchiectomy. Patients should continue to be counseled on the risk of PVPS with vasectomy. □

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