

Is there a place for surgical treatment of premature ejaculation?

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Abstract: Management of premature ejaculation (PE) has evolved tremendously over the last 20 years. Selective serotonin reuptake inhibitor (SSRI) antidepressants and local anesthetics are the most and best studied treatments. This evidence has led to the establishment of an evidence-based definition of PE and the International Society for Sexual Medicine (ISSM) guidelines for the diagnosis and treatment of PE. The current treatment of choice for PE according to the ISSM guidelines is a centrally acting SSRI or peripherally acting topical anesthetics. Despite the progress in treating PE, the drawbacks of these medical treatments are controversial. Before the ISSM guidelines were established, selective dorsal neurectomy (SDN) and glans penis augmentation (GPA) using a hyaluronic acid (HA) gel were developed to decrease sensitivity of the glans penis but later ISSM guidelines do not recommend surgical treatment because of possible permanent loss of sexual function and insufficient reliable data. Despite the drawbacks of medical treatments and debates about the ISSM guideline, surgical treatment for PE has increased continuously in Asian countries for non-responders to medical treatment. In contrast to the concerns outlined in the ISSM guidelines, SDN has been reported as effective and safe with rare sensory loss. Percutaneous computed tomography-guided cryoablation of the dorsal penile nerve and neuromodulation of the dorsal penile nerve by pulsed radiofrequency are reported as effective and safe for PE. It is time to re-evaluate rather than ignore surgical treatments for PE because doctors and patients need surgical alternatives for patients with PE who are not satisfied with medical treatment. SDN has a definite role in the efficacy but needs more safety data to be used as standard surgical treatment for PE. SDN must be performed carefully and more well-designed studies are needed. GPA with a HA gel does not induce serious sensory loss in patients with ED erectile dysfunction and the recommendation should be re-evaluated by the ISSM after additional reliable studies are performed.

Keywords: Premature ejaculation (PE); surgical treatment; selective dorsal nerve neurectomy; glans penis; augmentation

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Premature ejaculation (PE) is one of the most common male sexual dysfunctions with a prevalence of 20–30% in adults (1-3). An evolution has occurred in the management of male sexual dysfunction in the last 20 years. Many advances have been made in our understanding of the epidemiology, pathophysiology, and management of PE as a result of studies that have reported high prevalence rates, detrimental psychosocial consequences, and possible pharmacological management options (4,5). Many treatment options are available for patients with PE, such as psychological

education, behavioral therapy; selective-serotonin reuptake inhibitors (SSRIs), phosphodiesterase type 5 (PDE5) inhibitors, topical anesthetics, selective dorsal neurectomy (SDN), and glans penis augmentation (GPA) by injecting hyaluronic acid (HA) gel (6-8). The 2010 International Society for Sexual Medicine (ISSM) Guidelines for the diagnosis and treatment of PE were released and were updated in 2014 (5,9). The ISSM guidelines recommend pharmacotherapy as the main treatment. Shindel *et al.* (10) performed a nationwide survey based on the 2004 American

Urological Association (AUA) guidelines for treatment of PE to determine contemporary urologists' practice patterns for managing PE. In the survey, 71% of US urologists prescribed an SSRI as initial PE management. However, 35% of urologists used other treatment options as the initial treatment and 50% used other treatments as second-line. Although SSRIs are effective oral medications, their main drawback is recurrence after stopping treatment and a lack of efficacy in all patients. Topical local anesthetics diminish sensitivity of the glans penis and are the oldest known pharmacological treatments for PE (11). Although not approved by the FDA, topical desensitizing agents, such as lidocaine and/or prilocaine, in the form of a cream, gel, or spray, are moderately effective for delaying ejaculation, without adversely affecting the sensation of ejaculation (5). Local anesthetics do not have general side effects but they can cause local irritation, penile hypoesthesia, transvaginal contamination and female genital anesthesia, and erectile dysfunction (12). Moreover, a local anesthetic is inconvenient and messy to use and can interfere with arousal and spontaneity. The 2010 ISSM guidelines do not recommend surgical treatment for PE because it may be associated with permanent loss of sexual function (5,9). Despite the new definitions, evolved treatment options, and updated guidelines for diagnosing and treating PE, they all remain controversial because many patients still suffer from PE due to a lack of definitive treatment and many doctors are not satisfied with the current practice guidelines. Interestingly, the frequency of surgical treatments for PE, such as SDN and GPA with HA, has increased for many years in Asian countries after development of dapoxetine (8,13). In this chapter, the surgical treatments for PE will be reviewed based on technical developments, recent reports, and guidelines. The discrepancies between physicians treating PE with surgery and guideline committees will hopefully be resolved in the near future.

Current PE guideline and recommendation status for surgical treatment of PE

The penile dorsal nerve is the sensory nerve for the glans and penis. Patients with primary PE have penile hypersensitivity, which provides further evidence for an organic basis of PE (14). Based on the neurobiological pathophysiology of PE, the principle of current surgical treatments is to decrease sensitivity of the glans penis. SDN was first suggested for selective patients resistant to conventional PE treatments (15), and GPA using HA was

developed as a less invasive surgical treatment to avoid possible permanent sensory loss due to SDN (16). The AUA released the first guidelines in 2004 on the pharmacological management of PE (17) and the European Association of Urologists (EAU) released separate guidelines on ejaculatory dysfunction in 2004, which were updated in 2009 (18,19). These guidelines mainly focused on medical treatments and did not consider surgical treatments. Based on the 2004 AUA guidelines for treatment of PE, Shindel *et al.* (10) performed a nationwide survey to determine contemporary urologists' practice patterns for managing PE and reported no definitive treatment for PE.

In 2008, the ISSM (20) proposed a comprehensive evidence-based definition of lifelong PE and released PE guidelines in 2010, which were updated with a definition in 2014 (5,9,21). The 2010 ISSM guidelines stated that the existing guidelines were insufficiently comprehensive, failed to adequately address psychological and medical interventions for PE, and that essential new evidence was not included. Therefore, they developed a contemporary set of practical guidelines primarily targeting front-line clinicians and secondarily sexual medicine specialists. The ISSM guidelines graded local anesthetics as level 1 but do not recommend SDN or GPA with HA because of possible permanent loss of sexual function after SDN and insufficient reliable data (9). This statement caused confusion among physicians and legal problems for unsatisfied patients after SDN in Korea. A 2013 Korean survey (13) reported that 91.5% of Korean urologists consider SSRIs the primary treatment choice and 53.7% use local anesthetics, whereas 72.9% had prior experience with SDN for patients who benefitted from local anesthetics or who suffered from penile hypersensitivity.

The development of guidelines is an evolutionary process that continually reviews data and incorporates the best new research. As recommended by the ISSM guidelines, SSRIs and topical anesthetics are insufficient but the guidelines do not recommend surgical therapy. As described in the 2010 ISSM guidelines, the aim of the ISSM guidelines is to develop clearly worded, practical, evidenced-based recommendations for the diagnosis and treatment of PE by family practice clinicians and sexual medicine experts. The AUA and EAU guidelines do not consider surgical treatment because of the possible sensory loss and inadequate data for a recommendation.

Reported efficacy of SDN

SDN was first suggested for selective patients resistant to

conventional PE treatments (15). Despite its possible side effects, such as numbness, paresthesia, pain from neuroma, and erectile dysfunction, SDN has been performed continuously in Korea (13,16,22). You (22) reported his private Korean clinic results of SDN. In 143 patients with primary PE and penile hypersensitivity, 81.8% were satisfied with increased ejaculatory latency time and a decrease in vibration threshold, and complications occurred in 11.8% of patients, such as glans pain or discomfort (4.9%), penile edema (4.2%), wound dehiscence (2.1%) and delayed ejaculation (0.6%). Kim *et al.* (16) reported a 3-fold increase in intravaginal ejaculatory latency time (IELT) and a 2-fold decrease in vibratory threshold. Patient's satisfaction was around 70% and numbness occurred in 8.1% of patients. In 2012, the Korean Society for Sexual Medicine and Andrology (KSSMA) conducted a nationwide survey of 527 urologists and reported the efficacy and complications of SDN in 4,400 cases (13). In this survey, SDN was one of the most popular surgical procedures performed by private Korean clinical urologists for selected patients who had an effect from local anesthetics or who had penile hypersensitivity. Urologists answered that 56% of patients with PE were satisfied after SDN, and only 3.4% were dissatisfied. Although recurrence was observed in 10% of patients, other complications were very rare. The main complication of SDN is recurrence of PE (10.2%), pain or paresthesia on the glans (3.8%), and erectile dysfunction (0.4%).

Recently SDN has been continuously studied and reported from China. Zhang *et al.* (23) suggested that SDN of the dorsal penile nerve is safe and effective for treating primary PE because of the underlying abnormal increase in the dorsal penile nerve at the bottom of the pathogenesis of primary PE. In his study, SDN increased the IELT from 1.1 to 3.8 min and improved ejaculation control. Except for postoperative wound pain, no other complications were noted. Zhang *et al.* (8) and Shi *et al.* (24) also reported that SDN effectively increases IELT without complications in a Chinese report. In contrast to the worries conveyed by the ISSM guidelines, SDN has not induced permanent sensory loss in these Chinese reports. However, they did not assess changes in sensory function. David Prologo *et al.* (25) reported that transient computed tomography-guided cryoablation of the dorsal penile nerve increases IELT but induces temporary flaccidity in four of 24 patients. The flaccidity improved after treatment with phosphodiesterase 5 inhibitors and over time.

SDN seems to definitely decrease IELT and improve patient satisfaction but can induce evident sensory loss

and rare erectile dysfunction. The prevalence of erectile dysfunction complications may vary with different procedures, number of patients, assessment tools, follow-up periods, and operator. Considering the KSSMA survey, insufficient evidence for SDN is due to the limited number of peer-reviewed publications in international journals. SDN results have been presented continuously at international symposia but have not been published. A well-designed study performed in a private clinic is often negatively criticized by reviewers because of the ISSM guidelines.

Establishment of a standard SDN procedure

The dorsal nerve is the sensory nerve of the glans penis and is necessary for a normal erection. Resecting the nerve can decrease sensory of the glans and may increase IELT in patients with PE but could induce erectile dysfunction due to a lack of sensory. It is very important to cut the relevant number of dorsal nerve branches to induce optimal prolongation of IELT. Resecting too many nerve branches may cause sensory loss and erectile dysfunction. There is no established number of branches that should be cut but many authors have cut as few as possible to prevent sensory loss.

Korean doctors usually cut lateral branches and evaluate the vibratory threshold, IELT, and patient's satisfaction. You (22) resected 2–3 lateral branches on both sides in 143 patients, and 81.8% were satisfied with the increased IELT and decreased vibratory threshold but no sensory loss. Kim *et al.* (16) resected the dorsal branch on one side and lateral and ventral branches on the other side of 74 patients and reported a 3-fold increase IELT and a 2-fold decrease in vibratory threshold. Patient satisfaction was about 70%, and numbness occurred in 8.1% of patients.

Chinese doctors tend to resect more branches at the coronal sulcus level. Shi *et al.* (24) resected 3–10 branches and reserved only two main branches in 483 patients with PE. Zhang *et al.* (23) suggested that resecting extra dorsal penile nerves may increase sensitivity. They found a mean number of 3.55 dorsal nerves in 38 cadaveric adult penis' dissected and abnormal increase of 7.16 in 128 patients with primary PE treated with SDN. Thereafter, Zhang *et al.* (8) resected every other nerve segment near the level of the coronary ditch (roughly 0.5 cm in length) and roughly half of the distributed dorsal nerve branches after surgery. They reported a 2.5-fold increase in IELT, improved control, and no changes in sexual function as measured by the Brief Male Sexual Function Inventory.

A recent Korean nationwide survey reported that 54.3% of 4,400 patient respondents underwent SDN and that SDN was one of the most popular surgical procedures for private clinical urologists in Korea for selected patients who had effect local anesthetics or who had penile hypersensitivity. Urologists answered that 56% of patients with PE were satisfied after SDN, and only 3.4% were dissatisfied. Although recurrence was observed in 10% of patients, other complications were very rare.

Taken together, there is no standard procedure for SDN. As suggested by the ISSM, dorsal nerve neurotomy can induce sensory loss and further erectile dysfunction. It is most important to establish a qualified, standard method to avoid sensory loss after SDN, and it should be done in well selected patients with consent after a full explanation of the complications. A patient with life-long PE who has experienced definite satisfaction from topical anesthetics but no effect from SSRIs should be included as candidates for dorsal nerve surgery. Middle to older aged patients who have mild erectile dysfunction should not be included due to possible aggravation from a minimal loss of penile sensory function. The location of the resection and the number of resected dorsal nerves varies among individual urologists. An assessment tool for sensory and long-term results should be followed in older age patients with PE because SDN can easily cause erectile dysfunction in mid to older age patients who are losing potency. SDN is more commonly practiced in private clinics than in hospitals. Hospital urologists, particularly those in teaching hospitals, have less interest in SDN. Therefore, a well-designed study should be conducted considering both private and hospital urologists.

GPA using HA gel

GPA by subcutaneous injections of HA gel was initially developed to augment a small glans penis (26) and some patients reported improved PE (16). They postulated the theoretical efficacy of GPA in patients with PE. The major factors contributing to the sensory characteristics of the glans penis are distribution of dorsal nerves, number of receptors, receptor threshold, and accessibility of stimuli to the receptor. Considering the studies of Yang (27) and Halata (28), implants can be injected successfully into the dermis of the glans penis just above the nerve terminal. Hence, the principle of GPA with an injectable gel is to form a barrier between tactile stimuli and the dorsal nerve ending receptor and it does not induce permanent sensory

loss or sexual dysfunction (16,26). The efficacy of SDN was compared to treat PE in three group of patients (16), such as SDN alone (n=25), SDN with GPA (n=49), and GPA alone (n=65). Complications, such as numbness, paresthesia, and pain from neuroma, occurred in patients who underwent SDN, but no complications occurred in patients that received GPA. In 2008, available patients PE who received GPA were followed over 5 years to assess long-term efficacy, and no patients complained of sensory loss or erectile dysfunction (7). In the 2010 and 2014 ISSM guidelines, GPA was regarded like SDN and was not recommended due to possible permanent sensory loss. GPA evidently decreased sense of the glans penis and increases IELT. However, it does not completely abolish sense of the glans or penis and does not cause sexual dysfunction because GPA does not affect the dorsal nerve.

The main limitations of GPA are possible long-term volume loss, unnaturally looking surface, expense of filler and lack of multicenter studies. The reported efficacy from a single site is a 3-fold increase in IELT, and 70% of patients were satisfied with no serious complications. In the KSSMA survey, 54.3% of urologists managed patients with PE using SDN and GPA with HA and 16.9% used autologous fat injections. GPA does not induce later sensory loss because the implanted HA gel eventually degrades and an injection of hyaluronidase dissolves the implants in cases of overcorrection even 10 years after the surgery. GPA is less harmful and safer for PE because it is a less invasive treatment that avoids the harmful complications of invasive SDN. Basal *et al.* (29) reported that neuromodulation of the dorsal nerve by pulsed radiofrequency improves IELT, and no patients had any erection problems, penile hypoesthesia, or pain after the procedure. Minimally invasive treatments of the dorsal nerve do not result in permanent sensory loss.

Conclusions

Recent developments in medical treatment of erectile dysfunction and PE have increased more interest for appropriate treatments for PE from physicians and patients. The only approved treatment for PE is dapoxetine, and conventional SSRIs and topical anesthetics are recommended as off-label treatments. Despite possible sensory loss, SDN has increased continuously in Asian countries and has gained interest from Western countries because of the drawbacks of PE recurrence after stopping medical treatment. Surgical treatments to decrease sensation of the glans have demonstrated efficacy for treating PE

but are not recommended due to possible sensory loss and rare erectile dysfunction. The major concern of guideline committees is not efficacy but safety. SDN should be performed carefully in well-selected patients. Development of guidelines is an evolutionary process, and the safety of GPA by using HA should be re-evaluated. SDN must evolve with more reports of a standard technique, scientific assessment, more patients, and long-term follow-up to be recommended as a standard treatment. This review should be helpful for all concerned parties.

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Footnote

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