Surgery is not indicated for the treatment of premature ejaculation

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Abstract: Premature ejaculation (PE) is considered the most common male sexual disorder, affecting up to 75% of men at some point in their lives. While medical management is the mainstay of therapy, surgical options such as dorsal nerve neurectomy (DNN), hyaluronic acid (HA) gel glans penis augmentation, and circumcision have been studied as alternative forms of treatment. Preliminary studies have suggested that DNN and HA gel glans penis augmentation are relatively safe and effective, but due to a lack of large, multicenter, randomized-control trials with long-term follow-up, the International Society of Sexual Medicine (ISSM) has been unable to endorse DNN or HA gel glans penis augmentation as options in the treatment of PE. Conflicting data regarding the efficacy and safety of circumcision has similarly led to its exclusion from ISSM recommendations for the treatment of PE. Ethical concerns, particularly the fundamental concept of non-maleficence, are also barriers to the implementation of surgery for PE.

Keywords: Premature ejaculation (PE); neurectomy; penis augmentation; circumcision; erectile dysfunction (ED)

Introduction

There is no debate about the impact premature ejaculation (PE) has on the quality of life of a man (1). Ejaculatory control issues are not a novel concept, having been documented for more than 1,500 years. Today, PE is considered the most common male sexual disorder, affecting as many as 75% of men at some point in their lives (1). A variety of medical options are used to treat PE, and recently various surgical solutions have been introduced (2-10). In this review article, surgical therapy for PE will be closely analyzed in order to determine whether it deserves a place in the treatment of PE.

Medical therapy

There are currently four key treatments (or therapies) in the pharmacological treatment of PE: topical local anesthetics (LA), selective serotonin reuptake inhibitors (SSRIs), phosphodiesterase type 5 inhibitors (PDE5-I), and tramadol (11-16). The published literature shows topical LA to be moderately effective, increasing intravaginal

ejaculatory latency time (IELT) up to 6.3 times (11), but also possibly causing penile hypoesthesia and/or transvaginal absorption, resulting in female anorgasmia. Daily SSRI therapy generates up to an 11.6-fold increase in IELT (12). Dapoxetine, an on-demand, rapid-acting SSRI, approved in 80 countries worldwide but not in the US, leads to a 2.5–3-fold increase in IELT and an overall patient satisfaction of 43% (13). These drugs can have a moderate side-effect profile, including nausea, diarrhea, headache, dizziness, and somnolence, and are seen in up to 60% of patients using dapoxetine as needed (13). Patients are advised not to suddenly halt use of daily SSRIs in order to avoid SSRI discontinuation syndrome (13). Due to the high odds of concomitant erectile dysfunction (ED), many physicians use PDE5-I monotherapy to treat PE, although studies have thus far been equivocal (14). Lastly, tramadol has been shown to effectively delay ejaculation in some men, but has a risk of addiction and other side effects, which are seen in 5% of patients (15). Adherence to medical therapy for PE varies, reaching 70% for dapoxetine, while 30% of patients refused use of off-label SSRI's, and 30% of those that started discontinued (16). A summary of the

Table 1 Recommended pharmacologic treatments for premature ejaculation

Drug	Dose	IELT increase	Side effects	References
Dapoxetine	30–60 mg OD	2.5-3×	Nausea, diarrhea, headache, dizziness, somnolence, decreased sexual desire	(13)
SSRIs (off-label)				
Paroxetine	10–40 mg daily/OD	11.6×/1.4×		(12)
Sertraline	50–200 mg daily	5×		(17)
Fluoxetine	20–40 mg daily	5×		(18)
Clomipramine	12.5–50 mg daily/OD	4×/6×		(19)
Lidocaine/prilocaine (local anesthetic)	25 mg/g OD	4–6.3×	Penile numbness, partner genital numbness, local erythema	(11)

OD, on demand; IELT, intravaginal ejaculatory latency time.

recommended pharmacologic treatments for PE is seen in *Table 1*. Ongoing research is attempting to uncover new techniques for medical management. Patients with PE are currently being recruited in an ongoing clinical study examining the role of onabotulinumtoxinA in the treatment of PE (Allergan, 2015, unpublished data). Current pharmacotherapy has demonstrated efficacy, but additional research is needed to further optimize the management of PE.

Surgical therapy overview

To date, three surgical approaches have been described: (I) dorsal nerve neurectomy (DNN); (II) hyaluronic acid (HA) gel glans penis augmentation; and (III) circumcision (2-10). These techniques have acquired some popularity in Asia, but have failed to gain acceptance in the rest of the world, in part due to the small number of randomized controlled trials (RCTs), methodological issues such as small sample size, and lack of long-term efficacy and safety data. Key trials in DNN and HA gel glans penis augmentation literature is summarized in *Table 2*.

Dorsal nerve neurectomy (DNN)

Some urologists abroad have added DNN to their arsenal in the treatment of PE. According to a nationwide survey of Korean urologists, 73% of urologists reported experience in performing DNN, and almost all private clinicians (94%) felt they were capable of performing the operation (20). Upon review of the existing literature, one might understand why the procedure is gaining popularity. In a Korean RCT in 2012, 78 patients were randomized to either DNN or circumcision and followed for up to

6 months (2). Results showed a 2.7-fold increase in IELT from 1.1 min at baseline to 3.8 min and an increase in perceived control in the DNN group, without any recorded complications. Circumcised patients showed no significant changes in IELT or perceived control after surgery. Similar results have been produced by studies analyzing the effects of pulsed radiofrequency on the dorsal nerve, as well as computed tomography (CT)-guided cryoablation (3,4).

The obvious question is if these studies have been so successful, why have similar procedures not been recommended as treatment for PE in the rest of the world?

First, the literature is lacking long-term data on the safety and efficacy of DNN in the treatment of PE. DNN is an invasive and irreversible procedure, and, to date, the longest studied time point is 6 months after surgery and 1 year after CT-guided cryoablation (2,4). One week after CT-guided cryoablation, the IELT jumped from 55 s at baseline to 256 s, but was only 56% of that value (146 s) after 1 year, demonstrating the importance of long-term follow-up (4). Pulsed radiofrequency neuroablation showed promising results, but patient outcomes were not monitored past 3 weeks of treatment (3). While not detected in the previously described RCT, literature has shown that DNN may lead to certain complications (5). In the previously mentioned Korean national survey, urologists reported that the most common complication of DNN was the recurrence of PE, which they reported to be at approximately 10% (20). Also reported was pain or paresthesia of the glans, penile curvature, ED, and psychotic episodes, amongst others. These significant side effects and complications warrant long-term follow-up before this procedure can be safely recommended.

Another concern with the available DNN literature is the limited sample size of the published studies.

Table 2 Predominating literature on new surgical options for premature ejaculation

Modality	Study	Design	Sample size	Outcomes	Complications	Study drawbacks
Dorsal nerve neurectomy	Zhang et al., 2012	RCT	32 DNN; 46 Circ	DNN [2.7× increase in IELT (1.1 to 3.8 min)]; Circ [0.3× increase in IELT (1.2 to 1.5 min)]	None reported	No long-term data; small sample size; unequal allocation of resources; single-center study
Hyaluronic acid augmentation	Kwak et al., 2004	Prospective observational study	25 - DNN; 49 DNN + HA; 65 HA	DNN [2.7× increase in IELT (1.5 to 4.0 min)]; DNN+HA [3.4× increase in IELT (1.7 to 5.4 min)]; HA [2.9× increase in IELT (1.6 to 4.7 min)]	5 patients in DNN, 9 patients in DNN+HA: numbness [6], paresthesia [4], pain [3], Peyronie's disease [1]; no complications reported in HA group	Not a RCT; small sample size; single-center study
	Kwak et al., 2008	Observational study	58 HA (5 years post-op)	6 months post-op [4.5× increase in IELT (1.4 to 6.3 min)]; 5 years post-op [4.2× increase in IELT (1.4 to 5.9 min)]; decrease in IELT from 6 months to 5 years	None reported	Not a RCT; small sample size; single-center study
	Abdallah, et al., 2012	Pilot study	49 HA	1 month post-op [3.7× increase in IELT (2.1 to 7.7 min)]; 3 months post-op [2.5× increase in IELT (2.1 to 5.3 min)]	Complication rate of 30.4%: pain and bullae at injection site	Not a RCT; small sample size; single-center study
Circumcision	Tian et al., 2014	Systemic review and meta analysis	10 studies	No difference in IELT between circumcision and controls	No difference in adverse effects between circumcision and controls	Low quality studies

RCT, randomized controlled trial; DNN, dorsal nerve neurectomy; Circ, circumcision; IELT, intravaginal ejaculatory latency time; HA, hyaluronic acid augmentation.

The aforementioned RCT did not detail sample size calculations, a requirement for identifying a clinically relevant treatment effect (21). In this study, the small sample size—78 subjects only—undermines the reliability of the findings, particularly that randomization did not perform well, with significant differences in the allocation of study participants to treatment arms; 32 patients (41%) and 46 (59%) for DNN and circumcision, respectively (2). This risk is understandably much more common in studies with a small sample size. This may have drastically reduced the power to detect changes in the IELT in both groups, and limits the application of DNN's effect to the population at large. On a similar note, the single-center design of this study limits its generalizability. Indeed, practice guidelines should rarely, if ever, be solely based on evidence from single-center trials (22). Because DNN is an invasive and irreversible procedure, urologists and patients can only be convinced of its role in the treatment of PE if favorable results emerge from multicenter, RCTs with large sample sizes and long-term follow-up. Due to these limitations, the International Society of Sexual Medicine (ISSM) has been unable to endorse DNN as an option in the treatment of PE (23). Practicing urologists need to be certain DNN is not only effective, but also safe.

Hyaluronic acid (HA) gel glans penis augmentation

HA gel glans penis augmentation to treat PE has also gained popularity in Asia, albeit at a slower rate than DNN. A survey of Korean urologists predicted that HA gel glans penis augmentation is administered by up to 17% of practicing physicians (20). The principle behind this approach is the injection of a HA gel into the glans penis in order to create a permanent physical barrier between hypersensitive dorsal nerve receptors and the outside environment. As with DNN, initial studies with HA gel glans penis augmentation revealed efficacy, resulting in a 2.9-fold increase in IELT (1.6 to 4.7 min) at 6 months after the procedure, which was maintained when studied 5 and then 10 years later (5,6). When HA gel therapy was compared to DNN, similar delays in IELT were reported, but a higher incidence of complications were seen with DNN or a combination of DNN and HA gel therapy, further detailed in *Table 2* (5). Newer reports indicate possible complications including granulomatous foreign body reactions by contaminants and ischemic necrosis due to improper injection technique (7). While somewhat positive, the literature surrounding HA gel glans

penis augmentation does not support incorporation into treatment guidelines.

There is a fundamental issue with HA gel therapy being included in the management of PE: there is not a single double-blind RCT in the literature. All trials up to this point have been pilot or prospective observational studies (5,6). Four key factors for associations are at the heart of any clinical study: bias, confounding, chance, and cause (22). With an adequate sample size, a double-blind RCT has the advantage of drastically minimizing the first three variables, making it the best method to determine causality. If the outcome is solely based on the results of observational studies, as observed in the HA gel literature to date, a vulnerable methodology makes it difficult to decipher between what is the result of treatment, and the result of faulty associations. As an example, while the previously described HA gel treatment 5-year follow-up study showed no difference in IELT when compared to immediate post-op IELTs, a more recent pilot study from 2012 documented that the IELT had dropped from 7.71 min post-op to 5.32 min after just three months, demonstrating need for follow-up (8). Additionally, similar to the previous argument against the results with DNN, all studies for HA gel augmentation was conducted in single center institutions, and with a relatively small sample size. If the use of HA gel glans penis augmentation is to be seriously considered as a therapeutic option for PE, then large, multicenter, double-blind RCTs are needed to ensure its safety and efficacy.

Circumcision

The final suggested surgical treatment for PE is actually one of the most commonly performed surgical procedures in the world: circumcision. The prepuce (foreskin) is richly innervated with sensory neurons, explaining the high sensitivity of the human foreskin (24). The precept behind circumcision to treat PE is that the surgical removal of the prepuce also ablates many of these sensory receptors, thus decreasing glans sensitivity. In a systematic meta-analysis exploring the effects of circumcision on male sexual function, the majority of trials showed no improvement in sexual function after the procedure, and it was shown that circumcision may adversely affect sexual function (25). Overall, there were no differences between circumcised and uncircumcised men regarding PE, IELT, ED, low or absent sexual desire, orgasm difficulties and dyspareunia. While some studies showed an IELT delay from 64 to 731 s and reductions in PE frequency from 32% to 14% after circumcision, newer data have discounted these

results (9,26). The preponderance of the evidence reveals that there is no significant relationship between post-circumcision mucosal cuff-length and IELT, or brief male sexual function inventory (BMSFI), with some studies even showing a worsening of PE, as well as significant scarring (9). Furthermore, circumcision has been shown to lead to decreased masturbatory pleasure and sexual enjoyment, leading many authors to believe circumcision adversely affects sexual function in a significant number of men (9). While circumcision is commonly performed, the large amount of conflicting data has created widespread skepticism about its role in the treatment of PE.

Of note, some physicians have suggested that a shortened frenulum, which is an elastic band of tissue under the glans, may be linked to PE in up to 43% of patients (10). Surgical lengthening of the frenulum (frenulectomy) has been shown to lead to an average increase in IELT of 2.5 min and improvements in sexual function, but similar to the aforementioned surgical methods, lack of substantial evidence demonstrating safety and efficacy makes it impossible to recommend this surgical treatment for PE (10).

Ethics

The argument against surgical treatment for PE also takes on an ethical context. As medical professionals, one of the maxims of our practice is the principle of non-maleficence. The cornerstone of this concept is to "first, do no harm," and to avoid even the risk of harm, if at all possible. As we consider invasive and irreversible procedures for a medically manageable condition, it is important to keep this fundamental principle in mind. This discussion applies to the use of DNN for the treatment of PE, as it is already prevalent in Asia. According to a Korean survey of urologists, up to 73% of private clinicians believed that DNN is necessary for the management of patients with PE (20), a disturbing number, considering that the majority of patients do respond to medical management. While not sufficiently studied, DNN can lead to potential complications, thus posing an ethical dilemma. Data on surgical management is limited, and it is difficult, if not impossible, to provide the patient with a "truly informed" consent, when we don't fully understand the potential risks and benefits of the procedure.

Conclusions

Surgical treatment does not currently have a role in the

management of PE. There is a lack of large, multicenter, double-blind RCTs and long-term data to support the safety and efficacy of surgical treatment of PE. With improving medical management, we need to be absolutely convinced that surgery is at least as effective and safe as current medical treatments before we recommend it to patients. As the Dalai Lama wisely stated, "*Our prime purpose in this life is to help others. And if you can't help them, at least don't hurt them.*"

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Footnote

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