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BPH-RELATED VOIDING DYSFUNCTION (R LEE, SECTION EDITOR)

BPH-Related Voiding Dysfunction—i-Tind

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Abstract

Purpose of Review Benign prostatic hyperplasia (BPH) is a common condition that affects a majority of the aging male population. The majority of aging male population was afflicted with lower urinary tract symptoms (LUTS). Over the past several years, there has been an armamentarium of advances in the treatment of this condition to improve a patient's quality of life (QoL). A new treatment that shows promising results is the i-TIND system, an implantable device.

Recent Findings We present the most current literature on this therapy. There are ongoing trials evaluating the use of the newer second-generation i-Tind, although there are currently no functional differences from the first-generation device. The pilot study of the first-generation device was shown to improve both IPSS score and Q_{max} over the course of 12 months with a trend to benefit in the 24 to 36-month period. The i-Tind represents another attempt to introduce an office-based procedure for the treatment of BPH. The preliminary results seem to indicate that this device shows efficacy in improving urinary symptoms.

Summary There is promising evidence for the use of i-Tind as an office-based treatment for BPH. An important consideration, however, will center on patient selection. There will be a cohort of men who elect to undergo this minimally invasive procedure over the gold standard TURP. However, this will not be a viable treatment option for men with particularly large prostate volumes.

Keywords BPH · LUTS · QoL · i-TIND

Introduction

Benign prostatic hyperplasia (BPH) affects nearly 10 million men in the USA, with about 30% suffering from moderate to severe lower urinary tract symptoms (LUTS) [1••, 2••]. The standard of medical treatment for BPH has been alpha-blockers, 5-alpha-reductase, and PDE5. The gold standard of surgical treatment to date has been transurethral resection of prostate (TURP), offering a documented decreased IPSS of 70% and increased maximum urinary flow rate (Q_{max}) of 150% [3]. However, the primary disadvantage of TURP has been the complication rate and high perioperative morbidity.

To reduce perioperative morbidity, novel alternatives to TURP have been introduced. While multiple options exist, many patients still experience similar complications from these newer techniques as they do from TURP, with some patients unable to pursue surgical treatment simply due to chronic medical conditions.

One novel treatment is the Tind® (Israel) device, which is a 50-mm implantable device with preloaded elongated struts and an anchoring leaflet made of nitinol, an elastic shape-memory alloy. In the expanded configuration, the Tind exerts a radial force outwardly on the prostatic urethra and bladder neck to direct tissue away from obstructing the urinary path [3–5]. This force causes ischemic necrosis of the hyperplastic prostatic tissue, leading to the formation of incisions of the bladder neck and prostatic urethra, thereby reshaping the region and reducing urinary flow obstruction [3, 4]. The i-Tind is the second-generation design of the temporary implantable nitinol device (TIND), which has recently been introduced to offer patients a minimally invasive means of relieving LUTS due to outflow tract obstruction secondary to BPH by increasing prostatic urethral patency.

The device is implanted under light I.V. sedation, with the patient in lithotomy position. A rigid cystoscope is inserted at

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the urethral meatus, and the Tind is advanced into the bladder through the cystoscope sheath. The device is deployed inside the bladder and adjusted until the anchoring leaflet is positioned distal to the bladder neck, and the device is secured within the bladder neck and prostatic urethra. To confirm correct placement, the device is visualized by cystoscopy [3, 4].

The device remains in place for 5 days during which time the nitinol wires continue to apply force, reducing tension at the bladder neck and relieving outlet obstruction. After 5 days, the device is removed either using a cystoscope under sedation or with a 22 Fr catheter with topical anesthesia. The former technique is performed with the aid of a SNARE, a metallic double wire, and involves the insertion of a nylon wire into the sheath, followed by a rigid cystoscope, which allows for direct visualization of the nylon wire until the TIND device is closed into the sheath. The latter technique can be done in the outpatient setting, in which a SNARE captures the nylon wire into the lumen of the catheter, while the catheter is pushed into the urethra. As the catheter approaches the distal portion of the TIND device, the wire is pulled and the device is retracted into the lumen of the catheter [3].

This newer device is used in Italy, Switzerland, Spain, the UK, Austria, Greece, and Canada, and contains only a few differences from the original model [3]. The second-generation device contains the same anchoring leaflet and distal nylon wire but has three struts placed at the 12, 5, and 7 o'clock positions, instead of four elongated struts at the 5 and 7 o'clock positions. Additionally, there are double intertwined nitinol wires that connect at the top of the device to exert force on the urethral mucosa at the bladder neck. This newer design eliminates the risk of bladder mucosal injury via use of a plastic cover. Devoid of major surgical risk, the device in its first- and second-generation forms offer faster and symptomatic relief, as well as lower risks of sexual dysfunction. The purpose of the present review is to provide an up-to-date discussion of the literature on the use of the i-Tind system [3, 4].

Methods

Search Strategy

Comprehensive searches to identify studies related to i-Tind, Tind, and BPH were conducted until October 2018 in the following databases: Pubmed, OVIDMED, and EMBASE. Studies were identified and selected according to PRISMA guidelines. Searches included the combination of terms "i-TIND" and "BPH." There were no language restrictions, publication date restrictions, or article type restrictions on the search strategy. Systematic search identified only eight studies, with six used for the present review. Titles and abstracts were reviewed using a protocol of predefined inclusion and exclusion criteria.

Study Selection

Studies chosen for inclusion were a prospective single-arm trial and second 3-year follow-up to the initial pilot study. These studies were conducted on male humans with BPH and LUTS undergoing Tind. Excluded studies included either comments on the selected studies or a review of the Tind method.

Results

The first-generation Tind was reported in a pilot study by Porpiglia et al. in 2015 that included 32 patients with LUTS and a mean age of 69.4 years, mean prostate volume of 29.5 mL, and mean Q_{max} of 7.9 mL/s. Of the 32 successfully completed operations, four postoperative complications were observed, including one case of urinary retention, one of transient incontinence, one of prostatic abscess, and one urinary tract infection. A comparison of pre- and postoperative measures after 12 months showed significant improvements in IPSS score (− 10) and quality of life (QoL) score (+ 1). A mean increase of Q_{max} was documented to be 12 mL/s. Most importantly, at 12 months post-treatment, none of the patients in the pilot study required medical therapy or further surgical procedures [1••].

In July of 2018, Porpiglia et al. reported a second study on the efficacy of Tind on a 3-year follow-up of the original 32-patient cohort from the group's pilot study in 2015. This study noted that of the 32 patients initially enrolled in the study, there was a mean of 41% rise in Q_{max}, with an overall decline noted during a 24-month to 36-month time period. The median IPSS score at 36 months was reported to be 12 and QoL was reported to be 2, from a baseline of 19 and 3, respectively. In addition, while none of the patients resumed BPH medications at 12 months of follow-up, three patients resumed therapy between 12 to 24 months of Tind treatment. Overall, this follow-up study concluded that the overall improvement of IPSS and Q_{max} values was significant and superior when compared to alternative minimally invasive techniques. Additionally, none of the patients required invasive surgeries to treat BPH during the course of the study. However, the study identifies limitations such as a small sample size, a small initial mean prostate size, as well as a limited duration of follow-up [2, 4].

A one-arm, multicenter, international prospective study conducted by Porpiglia et al. in October of 2014 reported on the efficacy of the second generation of the i-Tind. This study followed 40 patients with LUTS with a mean age of 65.7 years, mean prostate volume of 35.3 mL, IPSS score of 25, Q_{max} of 7.5 mL/s, and QoL score of 4. None of the patients in this study suffered intraoperative complications. Six months following implantation, the study reported mean

IPSS score, QoL score, and Q_{max} values of 7, 2, 14 ml/s, respectively, which were statistically significant changes when compared with the preoperative values. Notably, none of the patients in this study experienced sexual dysfunction or needed medical or surgical treatment for BPH on follow-up evaluation.

In November of 2018, Porpiglia et al. reported again on the efficacy of i-Tind in a new trial. This study followed 81 patients with LUTS with a mean age of 65 years, mean prostate volume of 40.5 mL, IPSS score of 22.5, Q_{max} of 7.3 mL/s, and QoL score of 4 [6••]. There were, again, no intraoperative complications. At the 1-year follow-up of the study, the study reported mean IPSS score, QoL score, and Q_{max} values of 8.8, 2.4, and 14.7 mL/s, respectively. These changes were noted to be statistically significant improvements from the preoperative values. No patients in this study experienced sexual dysfunction, demonstrating again that i-Tind is able to spare sexual function. However, four patients required medical ($n = 2$) or surgical ($n = 2$) treatment for BPH on follow-up.

A trial completed in September of 2016 assessed the efficacy of Medi-Tate TIND in the alleviation of symptoms of bladder outlet obstruction (BOO) secondary to BPH. This trial (ClinicalTrials.gov identifier: NCT01436877) was a one-arm feasibility and prospective study whose primary outcome was device-related and unanticipated serious adverse events. The secondary outcomes were the reduction of IPSS by at least 3 points and increase of Q_{max} by at least 3 mL/s [7].

In December 2017, a one-arm, multicenter, international prospective trial assessing the efficacy of Medi-Tate TIND (TINDTM) in 75 patients with BPH was completed (ClinicalTrials.gov identifier: NCT02145208). The study's primary outcomes were to assess reduction of IPSS score by at least 3 points in at least 75% of patients at 6-month follow-up and to report on the incidence of serious adverse events related to Medi-Tate TIND implantation or retrieval procedures. The secondary outcome of the study was to increase maximal urinary peak flow over 12 months [7].

Currently, there is a one-arm, multicenter, international prospective study that is recruiting to assess the efficacy of i-Tind subjects with symptomatic BPH (ClinicalTrials.gov identifier: NCT03395522). This trial will include up to 200 subjects with a duration of 12 months post-implantation and a follow-up of 24 and 36 months. The objective of the study will be to assess the efficacy of the second-generation i-Tind measured by reduction of the International Prostate Symptoms Score (IPSS). The secondary objectives will be to further evaluate efficacy by determining an increase in maximal urinary peak flow, satisfaction from the device, sexual function and ejaculation, and assessing safety by complication rates. Table 1 shows a summary of all the studies involved in the review.

Conclusion

There is promising evidence for the use of i-Tind as the second-generation Tind device. The limitations of the

Table 1 Summary of studies

Name of study	Authors	Study design	Follow-up	Patient number	Outcomes
"Follow-up of Temporary Implantable Nitinol Device (TIND) Implantation for the Treatment of BPH: a Systematic Review"	Bertolo et al.	Review	–	–	–
"Update on minimally invasive surgery and benign prostatic hyperplasia."	Chung et al.	Review	–	–	–
"What's New in TIND?"	Marcon et al.	Review	–	–	–
"Temporary implantable nitinol device (TIND): a novel, minimally invasive treatment for relief of lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH): feasibility, safety and functional results at 1 year of follow-up."	Porpiglia et al.	Single-arm, prospective study	1 year	32	Pre vs postoperative % change in IPSS, QoL score and Q_{max}
"3-Year follow-up of temporary implantable nitinol device implantation for benign prostatic obstruction."	Porpiglia et al.	Single-arm, prospective study	3, 6 weeks; 3, 6, 12, 24, and 36 months	32	Pre vs postoperative % change in IPSS, QoL score and Q_{max}
"The New Meditate® Temporary Implantable Nitinol Device (I-Tind) in the Treatment of Bladder Outlet Obstruction Due to BPH: Results of One Arm, Multi-Center Prospective Study."	Porpiglia et al.	Multicenter prospective study	3, 6 months	40	Pre vs post-operative % change in IPSS, QoL score and Q_{max}
"Second-Generation of Temporary Implantable Nitinol Device (i-TIND) for the Relief of Lower Urinary Tract Symptoms Due to BPH: Results of a Prospective, Multi-Center Study at 1 Year of Follow-Up."	Porpiglia et al.	Multicenter prospective study	12 months	81	Pre vs postoperative % change in IPSS, QoL score and Q_{max}

review include a limited number of studies that fit the inclusion and exclusion criteria, a small patient sample size in each study and limited duration of follow-up in each study. There are ongoing trials evaluating the use of the newer second-generation i-Tind, and that there are currently no functional differences from the first-generation device. The pilot study of the first-generation device was shown to improve both IPSS score and Q_{max} over the course of 12 months with a trend to benefit in the 24 to 36-month period. Furthermore, the i-Tind is another attempt to introduce an office-based procedure. The preliminary results seem to indicate this device shows efficacy in improving urinary symptoms. A caveat to this is patient selection. There will be a cohort of men who elect to undergo this minimally invasive procedure over the gold standard TURP. However, this will not be a viable treatment option for men with particularly large prostate volumes.

Compliance with Ethical Standards

Conflict of Interest Dominique Guelce declares that he has no conflict of interest.

Mitali Kini declares that she has no conflict of interest.

Dominique Thomas declares that she has no conflict of interest.

Bilal Chughtai declares that he is an investigator for Medi-Tate, Astellas, and Ipsen. He is also a speaker for Boston Scientific.

References

Papers of particular interest, published recently, have been highlighted as:
•• Of major importance

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2.•• Porpiglia F, et al. 3-year follow-up of temporary implantable nitinol device implantation for the treatment of benign prostatic obstruction. BJU Int. 2018;122(1):106–12 **Offered 3-years follow-up of the durability of i-TIND device. Showed device was able to improve urinary symptoms such as Qmax as well as IPSS and QoL**.

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