Dysfunctional Voiding in Adults

Miki Haifler MD[1] and Kobi Stav MD[2]

[1]Department of Urology, Sheba Medical Center, Tel Hashomer, Israel
[2]Department of Urology, Assaf Harofeh Medical Center, Zerifin, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: Dysfunctional voiding is characterized by an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated or levator muscles during voiding in neurologically normal women (International Continence Society definition). Due to the variable etiology, the diagnosis and treatment of DV is problematic. Frequently, the diagnosis is done at a late stage mainly due to non-specific symptoms and lack of awareness. The objectives of treatment are to normalize micturition patterns and prevent complications such as renal failure and recurrent infections. Treatment should be started as early as possible and a multidisciplinary approach is beneficial.

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KEY WORDS: dysfunctional voiding, "lazy bladder," Hinman syndrome, Fowler syndrome

Normal bladder function consists of two main phases: storage and emptying. These phases are controlled by higher micturition centers in the brain: the sacral reflex arc and the innervations of the detrusor and sphincter muscles. Three mechanisms govern female voiding: detrusor muscle contraction, rise in abdominal pressure, and relaxation of the urethra and pelvic musculature. Failure of any of these mechanisms leads to voiding dysfunction [1].

Urinary retention may be caused by bladder outlet obstruction or detrusor acontractility. Etiologies for urinary retention are summarized in Table 1. One of the causes of urinary retention is detrusor-sphincter dyssynergy. Normal micturition requires complete synergy between the detrusor muscle and the urethral sphincter. This synergy is controlled by the micturition center located in the pons. With neural breakdown of the synergic pathways of the detrusor and external sphincter, these two muscles contract synchronously. This condition is defined as detrusor-sphincter dyssynergy. Neural damage is mandatory for this diagnosis and usually occurs in patients with suprasacral lesions [2].

However, in some cases of voiding dysfunction no neurological damage is found. According to the ICS (International Continence Society), dysfunctional voiding is characterized by an intermittent and/or fluctuating flow rate due to involuntary intermittent contractions of the periurethral striated or levator muscles during voiding in neurologically normal women [3]. In these cases the external sphincter, bladder neck, or all the pelvic floor muscles are contracted concomitantly with the detrusor muscle. Akikwala et al. [4] prospectively evaluated different criteria of bladder outlet obstruction in women with no neurological disease. The authors found that bladder outlet obstruction with no anatomic etiology occurred in 39.5% of the women [4]. In a prospective study of 1193 women with lower urinary tract symptoms, 165 patients (13.8%) were diagnosed with dysfunctional voiding. Twenty percent of the patients in this group had no apparent cause for their voiding difficulties. The incidence of voiding dysfunction with no apparent etiology is probably higher than reported [5].

In order to characterize dysfunctional voiding, we performed a Medline search for articles published before August 2011 using the following terms: urinary retention, voiding dysfunction, dysfunctional voiding, detrusor sphincter dyssynergy, bladder outlet obstruction, "lazy bladder" syndrome, primary bladder neck obstruction, Hinman syndrome, Fowler syndrome, and postoperative urinary retention.

ENTITIES AND SYNDROMES

"Lazy bladder" syndrome occurs twice as common in females as in males and mainly concerns young girls. It is one of the common causes of recurrent urinary tract infections in chil-

Table 1. Etiologies for urinary retention

Dysfunctional detrusor contraction		Obstructive
Myogenic	**Neurogenic**	
Aging	Peripheral neuropathy	Prostate enlargement (benign/malignant)
Radiation	Spinal injury – lower motor neuron	Anti-incontinence surgery
Metabolic disorders		Vaginal prolapse
Fibrosis		Urethral stricture
Inflammation	Pelvic surgery	Urethral diverticulum
Drugs		Urethral prolapse
Myopathies		Urethral tumor
		Detrusor-sphincter dyssynergy
		Dysfunctional voiding

Figure 1. [A] Normal voiding cystography. Arrows indicate normal funneling of the bladder neck and proximal urethra

[B] Voiding cystography of a woman with primary bladder neck obstruction. Black arrows indicate non-funneling bladder neck; white arrow indicates small bladder diverticulum
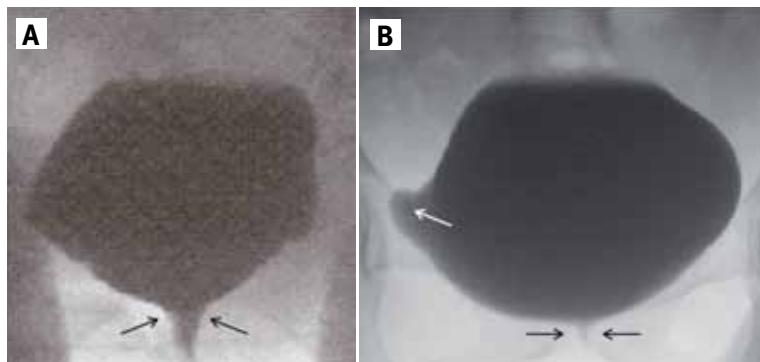
dren [6]. Symptoms usually appear at age 5–10 years. These children are usually excessively clean. They avoid urination in public toilets and frequently urinate only in the morning and afternoon to avoid school toilets [6]. The prevalent symptoms are those of a UTI, urinary overflow incontinence and residual volume [7]. On cystography the bladder appears smooth and enlarged and ureteral reflux may be seen. Cystoscopy may demonstrate trabeculations in rare cases but is usually normal [6]. Urodynamic studies demonstrate detrusor hypocontractility and the need for significant abdominal straining [7]. The pathophysiology of this syndrome is unknown. One theory hypothesizes that detrusor overactivity triggers pelvic floor muscle contractions, leading to bladder outflow obstruction. This, in turn, decompensates the bladder and leads to a non-contractile bladder. Other theories concern UTIs, sexual abuse and behavioral causes (e.g. too-early toilet training) [7].

Primary bladder neck obstruction is characterized by failure of the bladder neck to open during voiding. It has also been referred to as smooth sphincter dyssynergia, proximal urethral obstruction, and dysfunctional bladder neck. A prerequisite of primary bladder neck obstruction is the absence of anatomic obstruction or increased striated sphincter activity. The exact cause of this problem is unknown. Three hypotheses exist: a) abnormal arrangement of musculature in the bladder neck region so that coordinated detrusor contractions cause bladder neck narrowing instead of the normal funneling, b) sympathetic flow hyperactivity, and c) increased or aberrant adrenergic receptor density in the smooth muscle of the proximal urethra. The true prevalence of primary bladder neck obstruction

Dysfunctional voiding is complex, not well understood and under-diagnosed. A high index of suspicion is extremely important

is unknown and ranges from 33% to 54% [8,9] and 4.6% to 8.7% in males and females, respectively, with voiding difficulties [4,10,11]. Presenting symptoms are varied and include obstructive symptoms (decreased force of stream, intermittency, incomplete voiding, hesitancy), irritative symptoms (dysuria, frequency, urgency, nocturia), urinary retention, and pain. The diagnosis is difficult due to the non-specific symptoms and lack of awareness among physicians. The time lag to diagnosis may be several years [12]. The diagnosis is made by video-urodynamic study, which demonstrates high pressure, low flow voiding, lack of significant electromyographic activity, and a non-funnelling appearance of the bladder neck on fluoroscopy [Figure 1].

Hinman and Baumann [13], in 1973, described a series of 14 children with dysfunctional voiding pattern. The characteristics of the patients were day and night wetting, encopresis, recurrent urinary tract infections, vesical trabeculation and hydroureteronephrosis. The hallmark of these patients was the lack of neurologic insult, hence the authors coined the term "non-neurogenic neurogenic bladder" syndrome, later called Hinman syndrome [14]. Video-urodynamics of these patients demonstrate detrusor-sphincter dyssynergy and uninhibited detrusor contractions [15]. In all cases, a psychosocial background was found, represented by depression and anxiety disorders [13]. The natural pathway in which detrusor contractions induce relaxation of the sphincter is disrupted in this syndrome. The elevated pressure in the bladder causes irreversible structural damage such as thickening of the bladder wall, urine reflux, hydroureteronephrosis and renal parenchymal damage. Urinary stasis favors bacterial growth and causes recurrent UTIs. Extreme cases may reach end-stage renal disease and the need for replacement therapy. The treatment is more effective if started as early as possible [13,16].

Fowler syndrome was first described in 1986 [17]. Patients with this syndrome are in their twenties and thirties. Most describe suprapubic pain only when the bladder is full. Upon catheterization the residual volume is often more that 1 L. Polycystic ovaries are found in 50% [18]. Electromyelographic scan of the sphincter shows complex repetitive discharges and decelerating bursts. The decelerating bursts resemble the EMG pattern of mytonia, characterized by failure of muscle relaxation. The above mentioned bursts coincide with poor urinary stream which supports the hypothesis that impaired relaxation is involved [19]. Cystometry shows a prolonged filling phase with reduced sensation. Kavia et al. [20] showed in a retrospective analysis that Fowler syndrome is the most common cause of urinary retention in women. This can also be explained by over-activity of the sphincter and its inhibitory

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UTI = urinary tract infections

EMG = electromyography

effect on sensation. Because of the association with polycystic ovaries, an underlying hormonal sensitive channelopathy has been suggested [21].

Postoperative urinary retention is quite common. The incidence ranges from 4% to 29%. Male gender and advanced age are known risk factors. The risk of a male patient older than 50 years developing postoperative urinary retention is 2.4 times higher than a patient under age 50. Men develop POUR more frequently than women (4.7% and 2.9% respectively) [22]. Another risk factor is the type of surgery: 17% of patients undergoing hernia repair or anal surgery develop POUR compared with 0–0.8% for other types of surgery [23]. The incidence of POUR after anorectal surgery and after herniorrhaphy ranges from 1% to 52% [24] and 5.9% to 38% [25], respectively. POUR is the most common complication after benign anorectal surgery and the mean incidence is 15% [22]. The mechanism of POUR is uncertain. Adrenergic stimulation may cause reflex inhibition of the detrusor muscle and bladder outlet contraction [28]. Such adrenergic stimulation may be precipitated by anal distension and sympathomimetic or anticholinergic drugs used for anesthesia. Pain caused by the surgical procedure itself can increase adrenergic tone and induce the same effect.

The most useful tool is video-urodynamics with pelvic floor electromyography

Another possible mechanism is increase in the tone of the internal sphincter caused by injury to the pelvic nerves [27].

DIAGNOSIS

Diagnosis of the precise causes of dysfunctional voiding is difficult due to their non-specific symptoms and signs. Another reason is the lack of awareness on the part of caregivers. Several diagnostic tools (e.g., cystography, cystoscopy) may help to differentiate between different syndromes. However, the most useful tool is video-urodynamics with pelvic floor EMG. The combination of functional test (urodynamics and EMG) with anatomic display (cystography) makes the test the gold standard for complex problems and diseases of the lower urinary tract. In most cases, location of the obstruction can be demonstrated (bladder neck, proximal, mid-urethra). Complications of high pressure storage such as hydroureteronephrosis and bladder diverticuli may be seen as well [Figure 1].

TREATMENT

The objectives of treatment are to normalize micturition patterns and prevent complications such as renal failure and recurrent infections. All etiologies of dysfunctional voiding lead to a common pathway of upper tract deterioration due to

high bladder pressure and high residual volumes. Therefore, treatment should be started as early as possible.

For patients with "lazy bladder" syndrome who have minimal residual urine without recurrent infections the treatment is conservative. They are instructed to void regularly every 3 to 4 hours in order to establish voiding urge at low threshold stimulus and to lower the bladder capacity. Recurrent UTIs are managed with prophylactic antibiotics. If the above mentioned treatment is ineffective after 6 months, then clean intermittent catheterization or surgical intervention may be warranted (e.g., Y-V plasty of the bladder neck) [11].

The mainstay therapy for Hinman syndrome is behavioral change of voiding habits by means of hypnosis and biofeedback. Another option is a combination of anti-adrenergic and anticholinergic drugs to improve voiding functions and inhibit uncontrolled detrusor contractions. Treatment of fecal accumulation by adjusting the diet is helpful. The treatment may last for several weeks or months and, subject to the patient's total compliance, the success rate can reach 80% [19]. In long-lasting cases with irreversible bladder damage, clean intermittent catheterization with or without enterocystoplasty may be the only option to prevent end-stage renal disease. When self-catheterization cannot be performed, urinary diversion (e.g., ileal conduit) is another option [17].

The main goal in patients with Fowler syndrome is to achieve adequate bladder emptying. Clean intermittent catheterization is offered as an alternative to continuous urethral or suprapubic catheterization. Sphincter relaxation was attempted using oral agents (alpha-blockers, beta-agonists, bethanecol) with no proven effect [26]. Botulinum toxin was also administered to relax the external urethral sphincter, but the results were conflicting [28,29].

Sacral neuromodulation was shown to restore voiding function in these women. Abosief and co-workers [30] reported that of 20 patients with-non obstructive urinary retention, 18 were able to void with SNM. Furthermore, Shaker et al. [31] reported significant improvement in voiding function in patients with non-obstructive urinary retention in whom SNM was applied. These studies examined the effect of SNM on female patients with urinary retention not specifically caused by Fowler syndrome. In their prospective analysis of 82 female patients with urinary retention who underwent SNM, De Ridder et al. [32] classified 30 women as having Fowler's syndrome based on the EMG of the external urethral sphincter that showed complex repetitive discharges and decelerating bursts. The authors defined failure of SNM as the recurrence of urinary retention or resistance to eventual technical revision of the SNM device. Nine patients with Fowler syndrome pre-

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POUR = postoperative urinary retention

SNM = sacral neuromodulation

sented with failure compared to 19 in the idiopathic retention group ($P = 0.04$). There was a significant difference in time to failure between the two groups in favor of patients with Fowler syndrome ($P = 0.005$). The presence of Fowler's syndrome was shown to have a 62% positive predictive value for success and a 68% negative predictive value ($P = 0.02$). The authors conclude that the presence of complex repetitive discharges and decelerating bursts on concentric needle EMG of the external urethral sphincter of women is a predictive factor for the success of sacral nerve stimulation [32].

Optional treatments for PBNO include watchful waiting, medical treatment, and surgery. For patients with mild symptoms and no evidence of urinary tract decompensation (either clinical or urodynamic), surveillance may be offered. Alpha-blockers are the mainstay medical treatment of PBNO. Cisternino et al. [33] conducted a prospective analysis of 41 male patients aged 31–49 diagnosed with PBNO and treated for a mean time of 16 months with $\alpha 1$-blockers (alfuzocin and tamsulosin). Twenty-nine patients reported symptomatic improvement. In these patients prior to treatment the average Q_{max} and post-void volume were 8.5 ml/sec and 63.5 ml compared with 14 ml/sec and 40 ml respectively at 12 months follow-up ($P > 0.05$) [33]. Kessler and colleagues [34] described 15 women with PBNO treated with terazocin, 67% of whom showed significant improvement in symptoms and urodynamic parameters. P_{det} declined from 45 to 35 cmH$_2$O, post-void volume decreased from 120 to 40 ml, and Q_{max} increased from 9 to 20 ml/sec after 2 weeks of treatment [34]. Transurethral incision of bladder neck is the surgical treatment of choice for PBNO. Kaplan and team [35] performed a retrospective study on 34 patients aged 26–51 years with the misdiagnosis of chronic non-bacterial prostatitis. Thirty-one patients had urodynamic evidence of bladder outlet obstruction (Q_{max} 9.2 ml/sec, detrusor pressure 76.6 cmH$_2$O). These patients underwent TUIBN performed at the 5 o'clock position from the bladder neck to the verumontanum. Thirty patients reported significant symptomatic improvement; 24 (77%) had perineal pain as part of the presentation which resolved within 3 months of the operation in 22 patients. Furthermore, an increase in mean Q_{max} was demonstrated after surgery (16.4, 15.7, 16.8 ml/sec at 3, 6 and 12 months respectively) [35]. Goldman et al. [36] performed TUIBN in 11 women with PBNO of whom 10 had complete resolution or major amelioration of symptoms.

POUR is usually managed with temporary urethral catheterization. However, the choice between indwelling catheter or clean intermittent catheterization is not clear. After hip arthroplasty different studies have shown benefit of both methods [37]. Most patients undergoing rectal surgery require only

PBNO = primary bladder neck obstruction
TUIBN = transurethral incision of bladder neck

Early treatment can prevent renal function deterioration

1 day of urinary drainage, but those with low rectal cancer and positive lymph nodes require longer duration. Benoist et al. [38] conducted a prospective randomized controlled trial that compared the effects of 1 day urethral catheterization with those of 5 days catheterization after surgery for rectal disease (carcinoma, inflammatory bowel disease, familial adenomatous polyposis). Twenty patients (31%) in the 1 day group failed to void after catheter removal compared with 6 patients (10%) in the 5 day group ($P < 0.05$). Moreover, the authors performed a multivariate analysis to identify risk factors related to POUR and found that surgery for low rectal carcinoma and lymph node metastases predisposes to POUR [38]. Several alpha-blockers were evaluated in the treatment of post-surgical urinary retention. Phenoxybenzamine was shown to reduce the rates of POUR, the need for catheterization and rates of urinary tract infections after herniorrhaphy, colorectal surgery and other surgeries [39]. However, phenoxybenzamine is rarely used today due to its carcinogenic effect and adverse events. Gonullu et al. [4] have showed that administration of prazosin prior to herniorrhaphy reduced the urinary retention rate and the need for catheterization compared with placebo (10.8% vs. 25% and 3.5% vs. 13.8% respectively). Surprisingly, the literature shows a lack of studies regarding POUR and newer and more selective alpha-blockers such as alfuzosin or tamsulosin.

CONCLUSIONS

Dysfunctional voiding is a complex entity that may cause a variety of symptoms. It is caused by a wide range of etiologies, both neurological and anatomic. Accordingly, the diagnosis is difficult and requires a high index of suspicion. Treatment differs according to the etiology and usually requires a multidisciplinary approach.

Corresponding author:
Dr. M. Haifler
34 Bloch St., Tel Aviv 64161, Israel
Fax: (972-4) 826-2631
email: mikihaifler@gmail.com

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Capsule

The 'obligate diploid' *Candida albicans* forms mating-competent haploids

Candida albicans, the most prevalent human fungal pathogen, is considered to be an obligate diploid that carries recessive lethal mutations throughout the genome. Hickman et al. demonstrate that *C. albicans* has a viable haploid state that can be derived from diploid cells under in vitro and in vivo conditions, and that seems to arise through a concerted chromosome loss mechanism. Haploids undergo morphogenetic changes like those of diploids, including the yeast-hyphal transition, chlamydospore formation and a white-opaque switch that facilitates mating. Haploid opaque cells of opposite mating type mate efficiently to regenerate the diploid form, restoring heterozygosity and fitness. Homozygous diploids arise spontaneously by auto-diploidization, and both haploids and auto-diploids show a similar reduction in fitness, in vitro and in vivo, relative to heterozygous diploids, indicating that homozygous cell types are transient in mixed populations. Finally, the authors constructed stable haploid strains with multiple auxo-trophies that will facilitate molecular and genetic analyses of this important pathogen.

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Eitan Israeli

"We make a living by what we get, but we make a life by what we give"

Winston Churchill (1874-1965), British politician, best known for his leadership of the United Kingdom during the Second World War