RECENT ADVANCES IN MANAGEMENT OF NEUROGENIC BLADDER

Essay

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List of abbreviations

LUT	Lower urinary tract
OAB	Overactive Bladder
CIC	Clean intermittent self-catheterization
SNS	Sacral nerve stimulation
SPN	Sacral parasympathetic nucleus
NANC	Nonadrenergic, Noncholinergic
ATP	Adenosine triphosphate
VIP	Vasoactive intestinal polypeptide
IMF	Inferior mesenteric ganglia
DRG	Dorsal root ganglia
PAG	Periaqueductal gray
PMC	Pontine micturition center
CAP	Capsaicin
NVD	Neurogenic voiding dysfunction
DSD	Detrusor sphincter dyssynergia
ICS	International Continence Society
VV	Voided volume
P**abd**	abdominal
P**ves**	bladder pressures
P**det**	detrusor pressure
DLPP	Detrusor leak-point pressure
ALPP	Abdominal leak-point pressure
SUI	Stress urinary incontinence
EMG	electromyograph
IDC	Involuntary detrusor contraction
NDO	Neurogenic Detrusor Overactivity
VR1	Vanilloid-receptor subtype 1
BOO	Bladder outlet obstruction
DUA	Detrusor underactivity
PVR	Post-void residual urine
BTX	Botulinum toxin
PTNS	Posterior Tibial Nerve stimulation
SPAIRS	Sacral posterior and anterior intrathecal root stimulator

PNE	Percutaneous nerve evaluation
IPG	Implantable Pulse Generator
ECM	Extracellular matrix
GAGs	Glycosaminoglycans
FACIT	Fibril-associated collagen with interrupted triple helices
SIS	Small intestinal submucosa
PGA	Polyglycolic acid
PLA	Polylactic acid
PLGA	Polylactic coglycolic acid
NGF	Nerve growth factor
STZ	Streptozotocin
HSV	Herpes simplex virus

Introduction

The bladder, in coordination with the urethra and the pelvic floor is responsible for storage and periodic expulsion of urine. The integrated function of these components of the lower urinary tract (LUT) is dependent on a complex control system in the brain, spinal cord and peripheral ganglia, and on local regulatory factors ***(de Groat, 2006)***.

Injuries or diseases of the nervous system in adults can disrupt the voluntary control of micturition, causing disturbance of urine storage or voiding, resulting in detrusor overactivity and urge incontinence (***Yoshimura and de Groat, 1997).***

Overactive Bladder (OAB)

Overactive bladder is a condition resulting in a disruption to the normal micturition process. It is a syndrome complex characterized by urinary urgency, frequency and may or may not be accompanied by incontinence. Incontinence is due to involuntary contraction of the detrusor muscle during bladder filling (detrusor overactivity).

Neurogenic Detrusor Overactivity

Neurological disease involving the spinal cord can result in incontinence secondary to a loss of inhibitory input from the micturition center and from interruption of the spinobulbospinal pathways which normally control bladder behavior. In the event of a spinal cord lesion, a change of balance of the effects of the afferent fibers, located between the muscle and submucosa of the bladder, is seen. The unmyelinated C fibers become functionally dominant and the neurogenic detrusor overactivity described in such patients is considered due to the reflex mediated by these unmyelinated C fibers.

(Foley et al., 1997)

Currently Available Treatments of neurogenic bladder

Clean intermittent self-catheterization (CIC) is commonly used to drain the bladder and manage neurogenic incontinence. However, CIC can be associated with infection. Common pharmacologic treatments to reduce bladder contractility include anticholinergics, antispasmodics and tricyclic antidepressants. However, these therapies are associated with a high incidence of side effects including dry mouth, constipation and blurred vision ***(Ouslander, 2004)***.

Recent advances in management of neurogenic bladder

Intravesical injection of botulinum toxin A into the detrusor muscle is great therapy for overactive detrusor and this treatment may be recommended when standard pharmacotherapy using bladder relaxant drugs fails ***(Schurch, et al., 2000).***

Sacral nerve stimulation (SNS) offers an alternative state-of-the-art, minimally invasive treatment for patients with voiding dysfunction for whom conservative therapies have failed and who are being considered for irreversible major surgery, such as augmentation enterocystoplasty or urinary diversion ***(Das, et al.,2000).***

Sacral root neuromodulation for voiding and storage problems is becoming increasingly an acceptable concept for therapy. It has shown its efficacy in patients who failed much other conservative management ***(Elabbady, et al. 1994).***

In recent advances, a new therapeutic strategy in neurourology, that will change how we practice urology:

Gene therapy; In Diabetic neurogenic bladder may be cured with one or more injections of a gene vector that the physician will inject into the bladder or urethra. Injection of

a nerve growth factor via a herpes virus vector into the bladder of a diabetic may restore bladder sensation and innervations ***(yoo, et al., 2008).***

Tissue engineering; Rapid advances are being made in tissue and organ reconstruction using autologous tissue and stem cells. In recent years, attention has turned to tissue engineering as an alternative to free tissue grafts for bladder augmentation ***(Atala, et al., 2006).***

Aim of the work:

Due to the inherent progressive nature of many neurologic disorders causing bladder dysfunction and lack of targeted medical therapy, much work has been done to advance the management of this often-difficult patient population. This study reviews the latest advances in managing the neurogenic bladder.

Simplified anatomy of the vesico–urethral functional unit

The bladder:

The bladder is a hollow muscular organ that serves as a reservoir and excretion of urine (Figures 1-1a, b), located in the pelvis behind the pubic bone, can be divided into two portions:

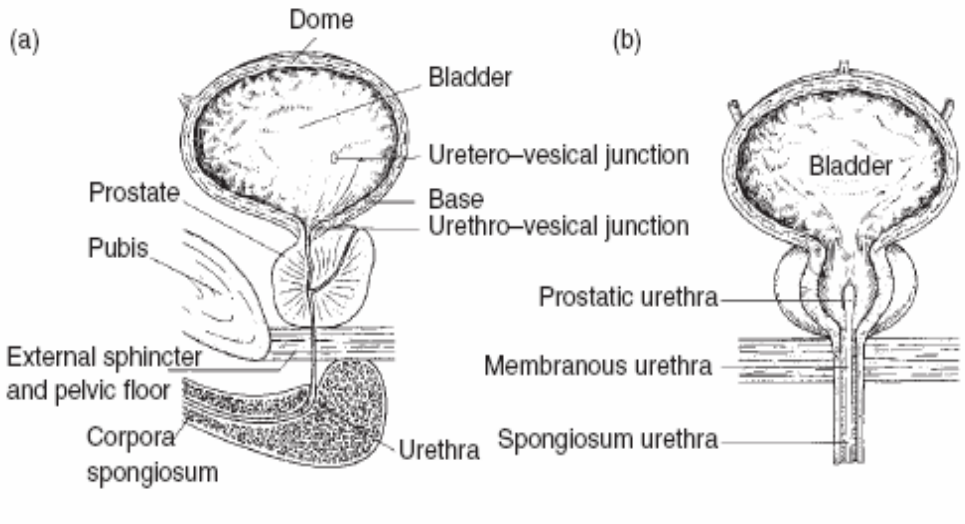

Figure 1-1

Anatomy of the vesicosphincteric unit in man.
(a) Sagittal view. (b) Frontal view.

(Quoted by Aldousari and Corcos, 2008)

(1) ***The dome***, the upper part of the bladder is spherical, extensible, and mobile. The median umbilical ligament (urachus) ascends from its apex behind the anterior abdominal wall to the umbilicus, and the peritoneum behind it creates the median umbilical fold. In males, the superior surface of the dome is completely covered by the peritoneum extending slightly to the base. It is in close contact with the sigmoid colon and the terminal coils of the ileum. In females, the difference arises from the posterior reflection of the peritoneum on the anterior face of the uterus, forming the vesico–uterine pouch. In both sexes, the inferolateral part of the bladder is not covered by the peritoneum. In adults, the bladder is completely retropubic and can be palpated only if it is in overdistention.

(2)*The base* of the bladder, i.e. the lower part, is fixed. The trigone is a part of the base, triangular between three orifices – two ureteral orifices and the urethral orifice or bladder neck. At the level of the vesico–ureteral junction the ureters cross the bladder wall obliquely in a length of 1–2 cm (intramural ureter).

The bladder mucosa:

The bladder mucosa is composed of transitional epithelium, folded when the bladder is empty, is loosely adherent to the submucosal tissue and the detrusor. Over