REVIEW ARTICLES

COMMON NEUROGENIC BLADDER DISORDER DUE TO SPINAL CORD INJURIES- A REVIEW

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Introduction:

The term neurourology used to describe the study of the interaction between the nervous and genitourinary systems. Indeed, neurourology includes the study of nervous system interactions with the upper urinary tract, lower urinary tract (LUT), as well as its impact on sexual function, which also is frequently affected by neurologic disease.' Neurogenic bladder (NGB) is a term used frequently to refer to bladders that have become dysfunctional from a variety of sources (such as long-term obstruction). For the purposes of this review, Neurogenic bladder refers only to conditions where a known neurological disease has affected bladder function, a systemic disease that has resulted in neuropathy causing bladder dysfunction, or abnormal urodynamic findings suggestive of neurological disease. In 2002, the International Continence Society (ICS) redefined the terminology of the lower urinary tract, with regards to both symptoms and urodynamic findings. Many of the commonly used terms were replaced such as detrusor instability (idiopathic detrusor overactivity) and detrusor hyperreflexia (neurogenic detrusor overactivity).. In this review article, we will focus on the neurovesical dysfunction in spinal cord injury (SCI) are chronic pain, muscular atrophy, loss of voluntary control over bladder, inability to produce erection, ejaculation, infertility and autonomic dysreflexia.

Anatomy:

The LUT is comprised of the bladder, which acts as the urinary reservoir, the outlet, which includes the bladder neck, the prostatic urethra, the external urethral sphincter, and remainder of the urethra (bulbar and penile urethra). The LUT serves two main functions: storage and emptying of urine. To store urine, it requires a number of conditions to be met. The bladder outlet must be closed at rest, and the bladder body must be able to accommodate increasing volumes of be able to inhibit

involuntary contraction ndication. These functions are controlled by a series of highly coordinated neural circuit.

The peripheral efferent innervation is provided by three sets of nerves: the sacral parasympathetics (pelvic nerves), thoracolumbar sympathetic (hypogastric nerves), and somatic nerves (pudendal nerve)[3]. The pelvic nerves, with orgins from the S2-S4 spinal cord, are plexiform-type nerves that are primarily responsible for innervation of the detrusor muscle and smooth muscle of the external sphincter. Stimulation of pelvic nerves results in activation of muscarinic receptors and resultant detrusor contraction. The pelvic nerves are also responsible for noncholinergic activation of the detrusor muscle. The hypogastric nerves, on the other hand, functions mainly to relax the detrusor (adrenergic effect) and contract the bladder neck and external urethral sphincter (a adrenergic).

The innervation of the external urethral sphincter is complex and thought to be regulated by a number of different nerves. Primarily, the external urethral sphincter is controlled by somatic nerves, with nerve roots emanating from S2-S4 (Onuf's Nucleus in the ventral horn). Stimulation, or activation of somatic nerves will allow the external urethra to relax. Continence is mediated through sympathetic stimulation via hypogastric nerves, which contract the sphincter. Afferent innervation of the bladder is complex, but essentially is comprised of two fiber types. The Aö fibers are myelinated axons located in the detrusor muscle, which transmit information about passive distension (bladder filling) and active contraction via their ability to detect stretch and tension of the bladder wall. In contrast, the C-fibers are unmyelinated fibers located in the urothelium of the bladder that detect noxious or thermal stimuli and are activated in times of filling during distention of the bladder as well as in pathological states. It has been demonstrated in cats with spinal cord injuries, for example, that bladder contractions are mediated by C-fibers. Similarly, patients with interstitial cystitis, have been shown to have an upregulation of nerve growth factor (NGF), which has been shown to play a role in the development of peripheral neurons, particularly C-fibers. Both fibers have cell bodies located in the dorsal

root ganglia of the sacral and thoracolumbar spinal cords. Their afferent activity plays a crucial role in the spinal reflexes[3].

Bladder filling and voiding are regulated by a number of complex reflex pathways including the guarding reflex and the micturition reflex. These reflexes are mediated by central nervous system (CNS) pathways involving the aforementioned nerves, and an understanding of these pathways is dysfunction. as the bladder starts to fill, low level afferent activity from the bladder causes inhibition of parasympathetic stimulation to the bladder body with simultaneous activation of the external urethral sphincter. This inhibition allows the bladder to fill passively, without reflex contractions, with the bladder outlet to remaining closed. The guarding reflex refers to the collective group of urethral reflexes that increases sphincteric activity up until the point of micturition.

Early during bladder filling, afferent nerves carry signals to periacquaductal gray area (PAG) that acts to stimulate sympathetic outflow to the bladder and urethra, causing bladder relaxation and increased tone of the urethral sphincter. Later, after increased afferent activity is sensed, the act of voiding is initiated in the prefrontal cortex that has direct projections periacquaductal gray area. Through its communication with the pontine micturition centre, the periacquaductal gray area removes tonic inhibition of parasympathetics and inhibition of sympathetic outflow occurs. impulses traveling in the spinobulbospinal pathway result in contraction of the bladder and relaxation of the urethral spincter and the micturition reflex is initiated.

Spinal Cord Injury:

For long years, death as a result of genitourinary disease was common among SCI patients. However over the past 50 years, there has been a dramatic reduction in urological causes of death in SC! patients. This is due largely to our understanding, diagnosis, and treatment of neurogenic bladder dysfunction from S . Lower urinary tract symptoms (LUTS) resulting from SC! will vary depending on the level and completeness of injury. The completeness of injury is determined by the American Spinal Injury Association (ASIA A-E) impairment scale, with ASIA A referring to patients with a complete and total paralysis below the injury level and ASIA E being patients who are normal. After spinal shock resolves and, if the distal autonomic segments remain viable, injuries rostra! to the suprasacral spinal cord will result in neurogenic detrusor overactivity (NDO) with or without detrusor-sphincter dyssynergia (DSD). The precise mechanism by which neurogenic detrusor overactivity (with or without DSD) develops has yet to be determined. De Groat and Yoshimura recently proposed that the CNS damage induces changes of the C-fiber afferents. They claimed that the injured spinal neurons may release neurotrophic factors, specifically NGF that remodel C-fiber afferents, rather than direct injury to the C-fibers themselves. The SCI patients who develop neurogenic detrusor over activity ± - DSD are exposed to high bladder storage pressures, reflex voiding and, potentially, increased detrusor leak point pressures (DLPP) when compliance is altered, which can result in upper tract damage if not adequately managed[7]. with that in mind, urodynamics (UDS) have become a mainstay in evaluation of lower urinary tract dysfunction.

Recent literature has sought to determine if ASIA classification may impact UDS findings. In 2008 Moslavac Ct a! compared UDS findings in patients with incomplete and complete SCI in order to determine if there was a difference in DLPP and cystometric capacities between groups. Fifty ASIA A patients and 30 ASIA B-E patients who had neurogenic detrusor overactivity were included in the analysis. No significant difference was noted in mean DLPP between groups (79±30 cm 1120 vs 70±29 cm H p.234, respectively). Similarly, with regards to cystometric capacities the two groups did not demonstrate any significant difference (239± 107 ml vs 227±125 ml, p=.655). These findings suggest that clinical mechanisms to stratify the injury do not predict urodynamic findings or appropriately stratify urological risk.

Treatment options and strategies for patients with neurogenic bladder dysfunction secondary to SCI have evolved a great deal over the past 50 years. This evolution and trend was captured by Cameron et a! in their large analysis of treatment trends in SC! patients. Study group investigated bladder management over a 33-year period (1972-2005) by using the National Spinal Cord Injury Database. Bladder management on discharge from rehabilitation, for 24762 patients at 5-year intervals was recorded. Over the course of the study period, the proportion of patients who managed their bladder with an indwelling catheter decreased from 33.1% in 1972 to 23.1% in 2005, at least 165% from 1986 to 1995. Condom catheter usage steadily decreased over the study period from 34.6% to 1.5%. Their explanation for the drop off is based on a 2009 study by Pan et al and is centered around the need for a high level of patient and physician compliance following sphincterotomy, since repeat procedures are often necessary. Clean intermittent

catheterization (CIC) usage increased dramatically from 12.6% at study in 1972 to 56.2% in 1995, which was essentially maintained until study end. They also investigated bladder management as a function of years after injury and concluded that indwelling catheter usage increased steadily from zero years after injury (23.2%) to 30 years after injury (45.1%). Conversely, use of CIC decreased as a function of years postinjury, with CIC rates being 45% at zero years and 43.3% at 30 years postinjury[9].

Pharmacotherapy has become a cornerstone in treatment of patients with neurogenic bladder dysfunction fr0m SCI. medical therapy is useful in trying to minimize the Impact of complications associated with neurogenic detrusor overactivity such as urinary tract infection (UTI), bladder calculi, incontinence, vesicoureteral reflux, and upper tract damage. Antimuscarinics increase bladder capacity and compliance, recuing intravesical pressures. the use of antimuscarinics and their role in increasing MCC and improving compliance in Neurogenic bladder dysfunction has been well documented.

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Recently, the use of intravesical botulinum A toxin (BTX-A) injection has become a primary therapy, albeit still off-label, for patients who have neurogenic detrusor overactivity as a result of SCI. In a study of 214 patients, Wefer Ct al reported on the effect of BTX-A injections on urodynamic parameters. A significant decrease in mean maximal detrusor pressure (45±26 cm H to 30±21 cm H p.OO and increase in maximum cystometric capacity (333±139 ml to 394±124 ml, p=.OO were noted. Compliance was also significantly increased in this study'°. Similar findings were reported by Giannantoni et a! in their 6-year follow-up of patients with repeated (typically at 6-9 months intervals) detrusor injections of BTX-A. There was a significant decrease in number of catheterizations, incontinence episodes, and UTI/year. Maximum cystometric capacity increased significantly from 243±65 cc to 421±56 cc (p.001) at 6 years. DLPP also decreased significantly from 97.6±32.4 cm 1120 at baseline to 23.8±10.8 cm 1120 at 6 years (p=.0l)

Sacral neuromodulation (SNM) has also gained popularity in the treatment of Neurogenic bladder dysfunction in the SCI population. The procedure involves placing leads into the S3 root and connecting it to a generator. Although the exact mechanism of action is unknown it appears to have success. In 2009, Lombardi et al reported their success in 24 patients (11 with neurogenic detrusor overactivity and 13 with retention) at a median of 61 months follow-up. Variables looked at were volume per catheterization, mean number of CIC, mean urinary frequency, and mean voided volume. Across the board, all variables showed a significant improvement in parameters (p<.05). Although this study demonstrated success of sacral neuromodulation in SCI, this is typically not patient population in which neuromodulation is successful. The success may possibly be due to the small sample size, with a large number of incomplete cervical injuries. The Finetech-Brindley stimulator is another neuromodulatory system widely used in Europe. Indicated in SCI patients with areflexic or hypocontractile bladders, the device involves a posterior sacral rhizotomy serving to eliminate any detrusorexternal sphincter dyssynergy (DESD). The Brindley stimulator requires an intact neural pathway between the sacral spinal cord and the pelvic nerve. Long-term results have shown the device to be very effective in the proper patient population[12].

Autonomic dysreflexia (AD) is one of neurogenic bladder dysfunction in the setting of SC!. The autonomic dysreflexia is a sudden and severe sympathetic response to noxious stimuli below the level of a spinal cord lesion. The autonomic dysreflexia can affect patients who have lesions T6 or higher. Generally, symptoms of autonomic dysreflexia include hypertension and headache above the level of the lesion, usually with bradycardia, although tachycardia and arrhythmias are possible. Most commonly, bladder distension is the inciting factor for autonomic dysreflexia, with less common stimuli being fecal impaction, stones, appendicitis, decubitus ulcers, or fractures in long bones. Treatment of autonomic dysrefiexia includes removing the noxious stimuli such as bladder drainage as well as removing all tight clothes, and sitting the patient upright. If conservative measures do not resolve autonomic dysreflexia, pharmacologic treatment can be initiated in the form of oral nifedipine, nitroglycerin paste (above the level of lesion), or a sodium nitroprusside drip. In patients who have a known history of autonomic dysreflexia, medical prophylactic treatment is warranted with alpha blockers or sublingual nifedipine prior to procedure[13].

Conclusion

Management of neurogenic bladder dysfunction is very important for urologists and patients. For the patient it is a tremendous burden, with respect to not only social situations and potential impact on kidney function and recurrent bladder infections, but for the urologist it poses many dilemmas as far as diagnostic and treatment strategies. For the clinician the role of UDS is necessary for diagnosis and treatment of these patients. It is important to understand that symptoms do not always correspond to UDS findings and baseline UDS might be necessary in a select population. Goals of treatment in patients with neurogenic bladder dysfunction should be aimed at reduction of symptoms, improvement of quality of life, preservation of sexual function, avoidance of symptomatic urinary tract infections, and preservation of upper tract function. Last 2 Decades urological care has improved dramatically and, as a result, the morbidity associated with urological conditions in the setting of neurological disease has gradually decreased, We expect that development of less invasive strategies to deal neurogenic bladder conditions to improve the care that we can deliver to our patients.

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