Review Article

Bladder Innervation and Types of Neurogenic Bladder

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Bladder innervation is a complex network integrating the activation of Autonomic Nervous System and somatic Nervous System controlled by Central Nervous System. Due to the intricacies of the Neural mechanisms involved, this whole process of Bladder control and Micturition is subject to varied pathological insults at various levels. Neurogenic Bladder is classified depending on the location of the lesion. Only a clear understanding of these mechanisms will allow us to obtain a detailed history and thus initiate appropriate treatment strategies. This review highlights the Anatomy and Physiology of various Neural Networks regulating the Bladder function and also the variedmanifestations of Neurogenic Bladder, which will guide us in successful therapeutic interventions.

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Bladder Innervation :

The Central Nervous System (CNS) plays a major role in coordinating the activation of Autonomic Nervous System (ANS) with the Somatic Nervous System (SNS) in the process of micturition. The Lower Urinary Tract comprising of Bladder and Urethra is innervated by the Sympathetic, Parasympathetic and SNS; which contain both afferent sensory and efferent motor axons.

Parasympathetic preganglionic innervation to Lower Urinary Tract arises from the sacral parasympathetic or Detrusor nucleus located in the lateral part of sacral intermediate gray matter at S2-S4 cord level (spinal micturition centre)[1]. These Preganglionic Parasympathetic Neurons travel through the Pelvic Nerves to reach the peripheral ganglia in the Pelvic Plexus and Detrusor wall layer. Parasympathetic Postganglionic Nerve terminals induce Detrusor contraction by releasing acetylcholine. Nitric Oxide is released and Detrusor contraction and Proximal Urethral Relaxation occurs as a consequence of the activation of the Sacral Parasympathetic Outflow.

Sympathetic preganglionic outflow from T11 to L2 cord level travel through the inferior mesenteric and hypogastric plexuses and via the Hypogastric Nerves to innervate the α-adrenergic receptors in proximal Urethra and the Bladder neck. Sympathetic Nerve fibers also innervate and have an inhibitory effect on Parasympathetic Ganglia in the Detrusor wall.

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Editor's Comment :

- Understanding Bladder Anatomy and Physiology will help us in localisation of various Neurological Diseases. A thorough knowledge of the various types of Neurogenic Bladder is essential for clinical reasoning, diagnosis and therapy.

Activation of the Thoracolumbar Sympathetic Outflow results in Detrusor relaxation and Bladder neck (internal sphincter) contraction mediated by the release of norepinephrine at their postganglionic terminals.

The external Urethral Striated Sphincter Muscle is innervated by Pudendal Nerve which receives its somatic efferents from Pudendal Nucleus (Onuf's nucleus)[2] at the S2-S4 cord level. Activation of Pudendal Nucleus which is under the voluntary control of supraspinal centers, results in sphincter muscle contraction through the release of acetyl choline which acts on Nicotinic receptors.

Afferent sensory information from the Bladder is conveyed through sensory fibres in the suburothelial and muscular plexuses to Lumbosacral Spinal Cord through Pelvic, Hypogastric and Pudendal Nerves[3]. The pelvic sensory afferents predominantly consist of small myelinated Aδ fibers and unmyelinated C fibers which respond to bladder wall distension and painful stimuli respectively.

Supraspinal input influences the voluntary control of micturition, which is needed to preserve continence and to postpone Bladder emptying until an appropriate time and place to void are chosen. Most afferent fibers do not just terminate in the sacral levels of the Spinal Cord but ascend further to synapse on relay cells located in the dorsal Pontine Micturition Center (PMC or Barrington's nucleus). PMC is located in the locus ceruleus, pontomesencephalic gray matter and nucleus tegmentolateralis dorsalis. It is vital for the process of

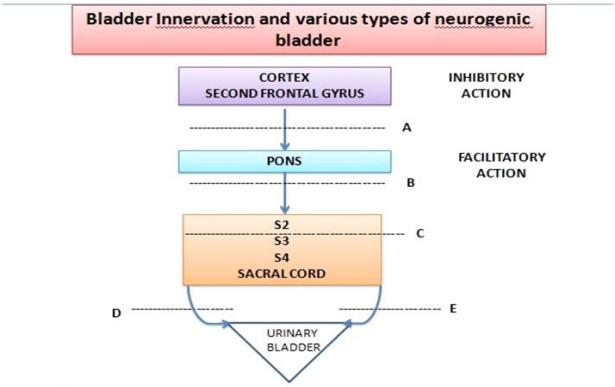
micturition by coordinating the antagonizing effects of the Sympathetic and Parasympathetic Nervous Systems on the Urinary Tract.The subcortical centers are located in multiple sites including Thalamic Nuclei, Subthalamic Nuclei, Limbic System, Substantia Nigra, Hypothalamus and the Red Nucleus.

The Filling Phase and the Emptying Phase are the two phases occurring in a normal Urinary Bladder. To maintain urinary continence,they both work together as a coordinated unit to store and empty urine. An increase in Bladder pressure due to raised intra abdominal pressure is counteracted by a rise in urethral pressure.

During storage phase, there is a passive low pressure filling of Bladder while the urinary sphincter maintains high resistance to the urine flow. Whereas during the emptying phase, there is Detrusor contraction to void urine along with relaxation of external and internal urinary sphincter which allows un-interrupted urinary outflow. The Neural Circuits in Brain and Spinal Cord coordinates this whole process of micturition by acting as on-off switches (phasic patterns of activity) to alternate the lower Urinary Tract between storage and voiding of urine[4]. Micturition process is under voluntary control and it depends on a learned behaviour[5].

During the filling phase, the Detrusor is inhibited and the Urethral sphincter is contracted to prevent involuntary emptying of Bladder via the activation of parasympathetic outflow. This whole process is organized by a group of urethral reflexes termed as guarding reflex, which are activated by Bladder afferent activity relayed through the Pelvic Nerves, and organized further by interneuronal circuitry located in the Spinal Cord. During the filling phase, supraspinal centres inhibit the pontine micturition center resulting in an enhanced thoracolumbar sympathetic outflow along with parallel suppression of sacral parasympathetic supply to the Lower Urinary Tract. In addition, supraspinal centers also send excitatory signals to external urethral sphincter via the Pudendal Nerve resulting in sphincter contraction.

During the voiding phase of Bladder, inhibitory effect of supraspinal centers on the pontine micturition center is suppressed. The PMC gets activated and conveys its inhibitory influence to Thoracic sympathetic outflow along with an enhanced sacral parasympathetic outflow to the Lower Urinary Tract. The excitatory output of supraspinal centers through the Pudendal Nerve is also suppressed, producing external urethral sphincter relaxation. Net effect is detrusor smooth muscle contraction, Bladder Neck smooth muscle relaxation, and external Urinary Sphincter Skeletal Muscle



A) Uninhibited bladder B) Automatic bladder C) Autonomous bladder D) Motor paralytic bladder E)Sensory paralytic bladder

relaxation allowing evacuation of stored urine from the Bladder.

Though micturition reflex is essentially the basis of micturition process, the voluntary or conscious control of urination is controlled by supraspinal centers. Afferent sensory information to the Anterior Cingulate Cortex, Prefrontal Cortex and Insula send inhibitory action on the PAG, whereas the Hypothalamus has an excitatory action on it. Whenever a conscious decision to void is made, there occurs an interruption of prefrontal Cortex's inhibitory influence on the PAG and a simultaneous hypothalamic stimulation of the PAG. This finally leads to excitation of the PMC (due to the excitatory input from PAG) thereby voiding takes place.

Thus, a person voluntarily contracts the abdominal muscles during the initiation of Voluntary Urination, thereby Bladder pressure is increased. The stimulation of stretch receptors results in generation of the Micturition Reflex[6].

Types of Neurogenic Bladder :

- An uninhibited type of Neurogenic Bladder Dysfunction occurs with Supra Pontine Neurologic Lesions, in which there is loss of tonic inhibition of pontine micturition center due to cortical or subcortical structural damage. With such Brain Lesions above PMC, particularly with Bilateral Lesions, there is a reduced perception of Bladder fullness and a low capacity Bladder resulting in urinary incontinence[7]. Since the PMC here is intact, the normal oppository effect of Detrusor and internal or external sphincter tone is maintained. So there is no increase in bladder pressure that can lead to upper Urinary Tract Damage. This type of uninhibited Neurogenic Bladder can be seen with various suprapontine Cortical Lesions *including Stroke, Parkinson's disease, Brain tumor and Shy-Drager syndrome. Even though Cerebrovascular accidents are usually associated with urge incontinence and Detrusor overactivity, some*

cases of Detrusor Underactivity have also been reported.

- An upper Motor Neuron type of Automatic Bladder or Hyperreflexic Neurogenic (spastic) Bladder occurs with Spinal Cord Lesions above the level of the sacral micturition center and below the level of the pontine micturition center (associated usually with either paraplegia or quadriplegia). A Detrusor overactivity is seen Loss of the normal inhibition from higher centers results in Detrusor contractions during Bladder filling. Damage to the Spinal Cord causes the Bladder and Sphincters to become spastic and the Bladder capacity is very much reduced, especially if lesions are above the T10 level (above the sympathetic innervation of the Bladder). There can also be a development of characteristic Detrusor Sphincter Dyssynergia (DSD), wherein simultaneous Detrusor and Urinary Sphincter contractions cause high Bladder pressures of up to 80-90 cm H_2O leading to vesicoureteral reflux that can lead to Renal Failure[8]. All this culminate in incomplete emptying. In majority of cases, urinary urgency, urinary frequency, urge urinary incontinence, and intermittent stream or hesitancy is seen. Even small volumes of urine tend to stimulate Detrusor contraction; the Bladder capacity is reduced but the residual urinary volume may be increased (increased post micturition residual volume). Here, the anal and bulbocavernous reflexes usually are preserved.
- An autonomous type of Neurogenic Bladder (Detrusor Areflexia) can be seen with complete cord lesions below the T12 segment involving the Sacral Spinal Cord. This type of Bladder dysfunction can occur with sacral myelomeningocele or sacral level cord injury and also with Conus Medullaris or Cauda Equina Region Tumors. Features suggestive of Autonomic Bladder Dysfunction also occur during the phase of spinal shock following cord injury. There is a weak or absent detrusor contraction (Detrusor underactivity or areflexic/ acontractile Detrusor) and a tonic contraction of the smooth urinary sphincter (non-relaxing urethral sphincter obstruction). The Bladder is paralyzed and sensation of bladder is lost. This results in urinary retention. Ultimately there can be a difficulty in initiation of micturition, overflow incontinence and also elevated residual urinary volume. Patients develop associated saddle anaesthesia with absent superficial anal and bulbocavernous reflexes.
- A sensory Paralytic (de-afferented) Bladder may occur in tabes Dorsalis, Syringomyelia or Diabetes Mellitus. It is caused by the impairment of the afferent pathways to the Bladder or by the damage of the posterior columns or Lateral Spinothalamic Tract at the spinal cord level resulting in prevention of transmission of stretch signals from Bladder. Early symptoms can be retention of Urine or overflow incontinence or a Urinary tract infection. In syphilis, Constrictive fibrosis around the Dorsal nerve fibers destroys them leading to a bladder condition named as Tabetic Bladder.
- A Motor Paralytic (de-efferented) Bladder occurs when the lesions involve the efferent motor fibers to the Detrusor or the Detrusor Motor Neurons in the Sacral Spinal Cord for example Lumbar Spinal Stenosis, Lumbosacral Meningomyelocele, or following Radical Hysterectomy or Abdominoperineal Resection. These patients primarily suffer from painful urinary retention or impaired Bladder emptying with markedly elevated residual urine volume. There is sparing of sacral and bladder sensations, but the anal and bulbocavernous reflexes usually are absent.

Conclusion :

Normal micturition is controlled by Neural Circuits in the Brain and Spinal Cord modulating the activity of smooth muscles in the Bladder and Urethra. Due to the complexity of Neural Networks regulating the Bladder control, it is vulnerable to damage at various levels of the Central Nervous System, Peripheral and Autonomic Nervous Systems resulting in various types of Neurogenic Bladder.

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