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Physiology of Urethral Muscles

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Abstract: ***The urethra is a channel that connects the bladder to the outside of the body, and in both sexes, the urethra has an excretory function. In males, it also performs a reproductive function by allowing the passage of the ejaculate. The urethra plays a role in keeping the urine in the bladder during the filling of the bladder with urine. Two sphincters perform this function. The internal sphincter is not a true sphincter. It is a functional structure formed as a result of the condensation of the circular fibers of the bladder in the bladder neck. The external urethral sphincter is a true sphincter of striated muscle. It is located in the membranous urethra and is under the control of the somatic pudendal nerve. Muscle physiology of the urethra shows a complex structure, neural, cellular, and physical. In this review, urethral muscle physiology will be evaluated in light of the literature.***

Keywords: Muscle, Physiology, Sphincter, Urethra

1. Introduction

The urethra is composed of striated and smooth muscles. Contraction of the longitudinal smooth muscles may play a role in stabilizing the urethra and helping the force of the circular muscle elements to close the lumen or to help open the bladder neck during voiding. There is debate over the relative roles of urethral smooth muscle, striated muscle, and lamina propria in creating a urethral pressure profile, but all seem to play a role.[1]

Blocking striated sphincter activity with nicotinic neuromuscular blocking drugs has many effects. it can rarely decrease urethral tone by more than 40%, indicating the importance of smooth muscle. By blocking the sympathetic tone with α - adrenoreceptor blockers, a reduction in urethral pressure of approximately 30% is achieved.[2]

There is little evidence on the role of cholinergic innervation in generating urethral pressure. In this review, urethra muscle physiology will be discussed.

2. Materials and Methods

Search strategy

We searched the following electronic databases from 1980 to 2022: PubMed, Medline, Excerpta Medica Database (Embase), and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The following search term strategy was modified for the various databases and search engines: “urethra”, “muscle”, “physiology”, “sphincter”. We also searched amongst the references of the identified articles. If it was not clear from the abstract whether the paper contained relevant data, the full paper was assessed. Along with Medical Subject Headings (MeSH) terms and relevant keywords, we used the Cochrane Highly Sensitive Search Strategy to identify articles in PubMed. We restricted the search to articles published in the English language that reported on “urethra”, “muscle”, “physiology’ “sphincter”. A total of 25 original articles, systematic reviews, and meta - analyses were included in this review.

Data extraction and management

Based on the pre - determined selection criteria, one author (LOS) independently selected all trials retrieved from the databases and bibliographies. Disagreements between evaluators were resolved via discussion. Studies were reviewed to determine their relevance to “urethra”, “muscle”, “physiology’ their outcome measures. We retrieved full - text copies of the articles identified as potentially relevant by either one or both review authors.

Urethral Muscles

Smooth muscle cells in the urethra are arranged in small fibers and are joined by adhesion - type junctions rather than gap junctions. Smooth muscle fibers in the urethral wall are arranged in thinner and more prominent folds than in the detrusor. Humans and advanced mammals have a relatively thin inner layer, predominantly in longitudinal arrangement, with a thinner circular muscle layer outside. In the lamina propria of the urethra, small fibers consisting of several cells are dispersed. The striated muscle is located in the wall of the male and female urethra where it forms the rhabdosphincter separate from the pelvic wall. In men, the striated muscle extends from the bladder neck and the anterior aspect of the prostate along the entire membranous urethra; in women, the striated muscle is located proximal to the proximal urethra. The striated sphincter is horseshoe - shaped, and the muscle cells are smaller than normal skeletal muscle, 15 - 20 μm in diameter.

Morphology

The urethral stroma has been less studied than the bladder stroma, but is known to consist mainly of longitudinally arranged collagen and elastin fibers.[3]

The vascular structure of the urethral lamina propria is known to be important in urinary continence, although its contribution to the continence mechanism is not fully understood.[4]

Estrogen is known to increase urethral blood flow, resulting in the dilation of lamina propria blood vessels. Impaired urethral blood flow reduces intraluminal pressure, but it is

currently unknown whether a decrease in vascular filling or urethral hypoxia lowers urethral pressure.[3, 4]

Both mechanisms are thought to be involved, as the initial decrease in urethral pressure is caused by a decrease in vascular flow, while subsequent stages are due to hypoxic effects on urethral smooth muscle.[5]

Sphincter shapes

A confusing issue in the literature is what the external sphincter consists of and which of the terms rhabdosphincter and external striated sphincter are correct. In the membranous urethra, a thin layer of smooth muscle runs along the entire urethra in women, and the prostate and its capsule in men.[6, 7]The outer layer of circularly located striated muscle takes a horseshoe - shaped form on the anterior surface of the male urethra near the apex of the prostate in adults. This striated muscle forms a complete ring in the fetus and neonatal period and forms the external urethral sphincter or rhabdosphincter. The periurethral striated muscles of the pelvic floor lie outside the rhabdosphincter. Despite its horseshoe shape, the urethral pressure at the external sphincter, measured during bladder filling, increases steadily along the entire circumference of the sphincter, like an iris.[8] Norepinephrine or hypogastric nerve stimulation further increases this pressure, suggesting a role for adrenergic receptors and sympathetic nerves in external urethral sphincter function.[9]

The arrangement of the muscles forming the distal sphincter in women is different from that in men. In women, apart from the weak striated muscle sphincter mechanism, the urethra has additional muscle structures called the suppressor and urethrovaginal sphincter. If there is sufficient pelvic support from the muscles and connective tissue, the posterior wall remains stable. As in men, the striated elements are weak posteriorly. The relative weakness of this periurethral striated musculature creates difficulties in obtaining external sphincter electromyography during urodynamic studies in women.

Weakness in these distal sphincter muscles may contribute to the incontinence that can occur in women after bladder neck resection. Urinary continence in women is achieved by three mechanisms that occur during increased intra - abdominal pressure. The first is the passive transmission of abdominal pressure to the proximal urethra. The protective reflex, which includes active contraction of the striated muscles of the external urethral sphincter, may temporarily aid continence. However, the increase in urethral pressure cannot be entirely attributed to the transmission of abdominal pressure to the proximal urethra. Urethral pressure rises before the cough is transmitted. These findings suggest that there is an active urethral continence (neural) mechanism in women.[10]

"DeLancey claimed in the "hammock hypothesis" that abdominal pressure transmitted along the proximal urethra sticks the anterior wall to the posterior wall.[11]If there is sufficient support from the muscle and connective tissue, the posterior wall will remain stationary. More distally, based on morphological information, they argued that the urethral connections to the pubis (pubourethral) and the connections of the vagina to the pelvic muscles and fascia actively change the position of the bladder neck and proximal urethra with voiding. These connections compress the urethra towards the pubis during bladder filling and tension. These connections contain both fascia and smooth muscles.1[1] As a result, urinary continence is achieved by a mixture of active muscle tone and passive anatomical compression.

Types of Urethral Striped Muscle Fibers

Striated muscles are characterized as the slow type or the trembling type. Twitch - type myofibrils are divided into slow and fast according to their functional and metabolic properties.[12] While slow - twitch fibers have ideal properties to maintain sphincter tone for a long time, fast - twitch fibers are needed when the intra - abdominal pressure is too high to increase sphincter tone rapidly to maintain continence. As with smooth muscle, skeletal muscle contractions depend on the interaction of intracellular calcium with troponin. Fast - twitch fibers contract quickly, tire, and generally have anaerobic metabolism.[13] Fast - twitch fibers show sudden bursts of contraction and are rich in ATPase, which catalyzes the actin - myosin interaction. The rate of contractions is related to the histochemical reactions of ATP'ases and alkaline pH. In addition, fast - twitch muscles also contain fast isotypes of Ca2+ ATPase, which introduces cytosolic calcium into the sarcoplasmic reticulum to induce rapid contractions.

In contrast, slow - twitch fibers are largely found in muscles that require constant prolonged contractions, such as the pelvic levators, and urethral sphincter. These muscle fibers contract, tire slowly and are capable of highly oxidative metabolism. Because they contain less myosin ATPase activity and predominantly contain the slow isotype of Ca 2+ ATPase.[13]These fibers form the background electromyographic activity during urodynamic examination.

The external urethral sphincter consists of two parts. The periurethral striated muscles of the pelvic floor contain both fast - and slow - twitch fibers. The striated muscles of the distal sphincter mechanism predominantly contain slow - twitch fibers and provide more than 50% constant resistance.[13.14]It has been shown histochemically in humans that the striated muscles of the distal urethra are mainly composed of slow - twitch myofibrils, whereas the periurethral striated muscles of the pelvic floor contain fast - and slow - twitch fibers.[15] In males, the rhabdosphincter consists of 35% fast - twitch fibers and 65% slow - twitch fibers. In women, this ratio is 87% slow twitch, 13% fast twitch fibers.[12]

In the intramural striated muscles of the membranous urethral sphincters of humans, most of the fast - twitch fibers and approximately 25% of the slow - twitch muscles are stained with nitric oxide synthase in their sarcolemma.[16] In addition, the periurethral striated muscles of the pelvic floor can adapt to the fast - twitch motor units needed during increased intra - abdominal pressure. It has been suggested that the successful treatment of stress incontinence with pelvic floor exercises and/or electrostimulation is due to the conversion of fast ones to slow - twitch striated muscle fibers.[14] In addition to striated muscles, the external sphincter also contains smooth muscles with noradrenergic

innervation. Researchers have shown that stimulation of the hypogastric nerve generates a myogenic potential in the external urethral sphincter.[9] It is not known whether this activity originates in smooth or striated muscle.

Lamina Propria and Paraurethral Tissues

The clinical significance of connective tissue outside the urethra is controversial. More than 30% collagen was seen in paraurethral tissue biopsies taken from premenopausal women with stress incontinence, while the diameters of these fibers were larger than in the control group. There was no difference in collagen concentration in women with postmenopausal stress incontinence when compared to their peers. However, other investigators have found that the periurethral collagen concentration is reduced and the ratio of collagen I to collagen III is reduced in patients with stress incontinence.[17 - 19]

Peripheral Nervous System

The lower urinary tract is innervated by three sets of peripheral nerves, the parasympathetic, sympathetic, and somatic systems. Parasympathetic nerves are located at the sacral level, they relax the urethra while contracting the bladder. Lumbar sympathetic nerves relax the bladder and contract the bladder neck and urethra. The Pudendal nerve provides contraction of the urethra. These nerves contain afferent (somatic) and efferent axons.[20]

Parasympathetic Pathways

Parasympathetic preganglionic neurons (PGN) innervating the lower urinary tract are located in a region lateral to the sacral intermediate gray matter known as the sacral parasympathetic nucleus (SPN). Parasympathetic PGN reaches the peripheral ganglia, where the excitatory transporter acetylcholine is secreted via the ventral root.[21]

In humans, parasympathetic postganglionic neurons are located in the pelvic plexus and the detrusor wall. Patients with damage to the cauda equina or pelvic plexus may be neurologically decentralized, but not completely denervated. In damage to the cauda equina, there may be damage to the communication of afferent and efferent neurons at the level of the intramural ganglion.[21, 22]

Sympathetic Ways

Sympathetic flow from the rostral lumbar spinal cord supplies noradrenergic stimulating and inhibitory stimuli to the bladder and urethra. Activation of the sympathetic nerves causes contraction of the bladder outlet and urethra, resulting in relaxation of the bladder body and storage of urine in the bladder. Peripheral sympathetic pathways follow a complicated path from the sympathetic ganglion chain to the inferior mesenteric ganglia and the hypogastric nerves and pelvic ganglia.[23]

Somatic Pathways

The external urethral sphincter (EUS) motoneurons are located lateral to the ventral horn, known as the nucleus of Onuf. Sphincter motor neurons are also found in dendritic bundles located transversely lateral to the lateral funiculus, dorsal to the intermediate gray matter, and dorsomedial to the central canal.[24]

Reflex Control of Urination

There are many reflex pathways in the brain and spinal canal that adjust the coordination between the bladder and the urethra. The main pathways controlling the lower urinary tract function operate on the principle of simple on - off circuits that provide mutual communication between the bladder and the urethral outlet.[21] Some reflexes allow urine to be stored, while others assist in urination. Each reflex can communicate with the other to form complex control mechanisms. Changes in these basic reflexes may contribute to the development of neurogenic bladder dysfunction. Direct activation of these reflexes by electrical stimulation of the sacral spinal roots contributes to the therapeutic effects of sacral nerve root neuromodulation.[21, 25]

3. Conclusion

The urethra muscle physiology has neural and physical complex components. Knowing the urethral muscle physiology will provide a clearer understanding of the pathophysiological processes related to the urethra such as incontinence and obstruction.

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