The aging bladder

O envelhecimento vesical

Homero Bruschini

ABSTRACT: The aging of the population is exposing patients and physicians to new challenging urological conditions. The prevalence of lower urinary tract symptoms (LUTS) increases significantly over the age of 65 in both sexes and severely impairs patients’ quality of life (QOL). A better understanding of the possible causes involved in this process will clarify some forms of treatment and stimulate new researches on this matter. The purpose of this review is to better describe the pathophysiological implications related to the aging bladder, allowing a more accurate management of this specific entity.

Keywords: Urinary bladder; Lower urinary tract symptoms; Aging.

INTRODUCTION

Urinary problems mean a number of symptoms, occurring since childhood to senility. It include all types of incontinence, limitations to the urinary storage as urgency, frequency and nocturia, voiding problems as intermittency, slow stream and straining, post micturition symptoms as incomplete voiding and post micturition dribbling, and all combinations of these symptoms. Lower urinary tract symptoms (LUTS) were introduced by Paul Abrams to replace the term “prostatism”, which implied that the prostate was responsible for most (or all) symptomatic voiding complaints in men. LUTS with its subdivisions, filling/storage symptoms and voiding/emptying symptoms, have replaced the terminology of “irritative” and “obstructive” symptoms, both rather imprecise terms that imply an etiology that may be incorrect. The prevalence of both storage and voiding lower urinary tract symptoms increases significantly over the age of 65 years in patients of both sexes. Also, it is well recognized that overactive bladder (OAB) symptom syndrome and urodynamic evidence of bladder overactivity which is seen in a proportion of these patients increases in both sexes with increasing age as does detrusor underactivity and indeed both can co-exist in the same patient. Furthermore there is a clear increasing prevalence of bladder outflow obstruction in the aging male population and of other disorders such as diabetes, cerebrovascular accidents and neurological
disease, all exerting an accumulative influence in the bladder with increasing age. Therefore, a number of causes seem to affect the normal bladder/sphincter function in the aging process. Although LUTS cause limited risks to life expectancy, they severely impair patients’ quality of life, leading to depression, sleep deprivation, embarrassment and fatigue, causing a huge impact on global healthcare resources. The underlying pathophysiological processes are poorly understood, although there is an increasing emphasis on the importance of both peripheral afferent mechanisms in the lower urinary tract as well as altered central transmission and processing of neural information from the bladder and lower urinary tract. The purpose of this review is to better describe the pathophysiological implications related to the aging bladder, allowing a more accurate management of this specific entity.

**Bladder wall structural changes**

Structural changes in the bladder wall, including widespread degeneration of muscle cells and axons and decrease in the area density of smooth muscle to connective tissue ratio, indicate that fibrosis develops in aged human bladder. Similarly, in aged rodents fibrosis (increased collagen deposition) was reported in various studies, and was to some extent alleviated by caloric restriction. Obesity is a known risk factor for LUTS. Hypercholesterolemic diet and obesity also influence adhesion molecules of detrusor muscle cells, potentially disturbing the spread of electrical signal between cells, compromising contraction. Urinary obstruction also promotes bladder fibrosis, leading to poor compliance and impaired bladder contraction. Impaired blood supply causing ischemia and reperfusion injury is absolutely accepted now as a neglected cause of bladder alterations but not yet fully understood. Gross anatomical observations have shown axonal degeneration in human bladders and bladder from rats with induced ischemia. A systematic study in rats with induced bladder ischemia (a risk factor in aging) has shown differential expression pattern for different subtypes of muscarinic receptors depending on the time and age after inducing ischemia. Ischemia in young individuals seems to promote overactivity and in oldies, underactivity.

**Changes in bladder afferent system**

The peripheral afferent limb of the micturition includes the urothelium and afferent nerves. Although the urothelial functions and urothelial-afferent nerve interactions play an important role in bladder sensations, little is known about the influence of aging on these components. The oxidative stress and altered mitochondrial function seems to be the cause of structural studies as urothelial thinning, granular appearance of umbrella cell layer, discoidal vesicles, electron dense bodies and vacuoles in umbrella layer, often containing what appears to be cellular debris in all layers. Changes in the urothelium can affect afferent neuronal input. Experiments in mice showed increase in the activity of afferent nerves during bladder filling with age, possibly consequence to increase of stretch-induced release of acetylcholine from non-neuronal cells from the urothelium. A correlation with humans can explain the mechanism for bladder overactivity in the elderly.

It has been shown that in aged mice the activity of afferent nerves is augmented during bladder filling (3-4 vs. 24 months). This could be due to increased stretch-induced release of acetylcholine (ACh) from non-neuronal cells, possibly from the urothelium and/or increased adenosine 5’-triphosphate (ATP) and ACh bioavailability in the urothelium, as inferred from measurements of transmitter levels in the lumen. If these findings are similar in humans, they could represent underlying mechanisms for bladder overactivity in the elderly.

Finally, there was a reduction in the number of small diameter fibers, predominantly unmyelinated. These changes, if occurring in humans, may account for alterations in bladder sensations in the elderly.

**Changes in central micturition pathways**

The fact that voiding and continence are under forebrain control is now well established by multiple lines of evidence. Some of the brain regions involved are known with reasonable certainty, although further investigations are needed. A series of diseases affecting the neurological system may alter this control as seen in Parkinson disease, dementia and other situations. The aging of the population even in Brazil, is exposing patients and physicians to new conditions that still deserve further studies and a special complete report.

**Changes in the efferent system**

The efferent system includes the sympathetic and parasympathetic nerves and the smooth muscle. The sympathetic system is thought to be tonically active during filling phase, releasing Norepinephrine (NE) to relax the bladder smooth muscle. The parasympathetic system is active during voiding and releases ACh to contract the bladder and nitric oxide (NO) to relax the urethra. Histological studies have found a reduction of the sympathetic fibers in the aging rat bladder body. Cystometry studies reported variable changes in micturition pressure, which is a measure of the efferent parasympathetic nerves and smooth muscle contractility, suggesting changes in more than one component of the efferent system. A decrease (~40%) in the number of acetylcholinesterase (AChE)-positive neurons in the intramural plexus in older guinea pigs may impact the strength of the contraction and may lead to changes in voiding function that could account...
for the underactive bladder condition\textsuperscript{15}.

The purinergic component of the efferent transmission has been shown to be up regulated in conditions like aging. Decreased P2X1 mRNA expression in the smooth muscle in human tissue or overexpression of P2X3 receptor in the urothelium in male mice suggest the need of further detailed studies of the purinergic component in the process of aging.

Changes in the immune system

Very few is known about the influence of immune system in the aging bladder, but it is conceivable that with age there is a decrease in the ability of the immune system to react to insults (e.g., urinary tract infections)\textsuperscript{4}. This raises the possibility that voiding dysfunctions may be associated with immune and inflammatory related responses in the bladder and afferent system\textsuperscript{4}.

CONCLUSION

The aging bladder is still a condition that deserves further investigation, though the knowledge we have so far allows us to better understand and manage elderly patients with lower urinary tract symptoms. It is imperative that we dedicate time and resources to elucidate all aspects of this entity, as the population gets older worldwide.

REFERENCES


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