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The Effects of the Autonomic Nervous System on Urogenital Disorders

Otonom Sinir Sisteminin Ürogenital Hastalıklar Üzerindeki Etkileri

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Abstract

The possible effect or activity of the autonomic nervous system (ANS) in urogenital disorders is still controversial. Day by day, further studies that have proved the association between chronic urological situations like chronic pelvic pain, premature ejaculation, etc., and autonomic dysfunction have been published. Understanding the actual role of the autonomic nervous system on chronic pelvic disorders will be of interest soon.

Keywords: autonomic nervous system, chronic pelvic disorder, urogenital disorders

Öz

Otonomik Sinir Sistemi'nin (OSS) ürogenital hastalıklardaki olası etkisi ve aktivitesi hala tartışmalıdır. Gün geçtikçe, kronik pelvik ağrı, prematüre ejakülasyon gibi kronik ürolojik durumlar ve otonomik disfonksiyon arasındaki ilişkiyi kanıtlayan çalışmalar yayınlanmaktadır. Otonomik sinir sisteminin kronik pelvik hastalıklardaki gerçek rolü, yakın gelecekteki ilgi alanlarından biri olacaktır.

Anahtar kelimeler: otonom sinir sistemi, kronik pelvik hastalık, ürogenital hastalıklar

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Introduction

Autonomic nervous system (ANS) consists of the sympathetic, parasympathetic, and enteric nervous systems. Despite the well-understood vital properties like energy storage and consumption, reproduction, and excretion, the possible effect or activity level in pathologic circumstances are still under investigation and have not been completely defined.

In this review article, the effects of ANS dysfunction on urogynecological problems like urinary incontinence, interstitial cystitis, infertility, premenstrual syndrome, pelvic pain, polycystic ovary syndrome (PCOS) were investigated. Also, the relationship between ANS and erectile dysfunction and premature ejaculation was discussed briefly. The issue of this review article was related to disorders that are mainly attributed as idiopathic disorders and/or those within physiologic limits. Pathologies like mechanical, anatomical, infectious, neuronal, or vascular damage were excluded.

Estrogen

Estrogen leads to vasodilatation in both arteries and veins. The levels of circulating estrogen may not reflect the total activity because their levels in the tissue and their intracellular activities are influenced by concentrations of enzymes like aromatases. The reduction in the estrogen levels causes sympathetic overactivity and an increase in norepinephrine levels in the blood [1]. It controls sympathovagal balance centrally and prevents sympathoexcitation. Estrogen receptors are localized on autonomic neurons from the spinal cord to the brain. The injection of estrogen to the rats increases vagal parasympathetic activity and decreases renal sympathetic activity [2].

However, there are still questions about the effects of estrogens on ANS and the cardiovascular system [3]. Sympathetic nerve activity does not change during the menstrual cycle in young eumenorrheic women but orthostatic stress causes different sympathetic responses in the early follicular and mid-luteal phases. Although the sympathetic baroreflex sensitivity remains stable, the sympathetic response increases during the mid-luteal phase [4]. This may due to vasodilatation in the mid-luteal phase as a result of elevated estrogen or regression of estrogen dominance by progesterone. Consequently, estrogen seems to have an impression on ANS but the accurate measurement and the way of affection are still undefined.

PCOS and Infertility

Polycystic ovary syndrome (PCOS) is a metabolic disorder with oligo/anovulation and hyperandrogenism [5]. Obesity, hyperinsulinemia, obstructive sleep apnoea are frequently associated with sympathetic nervous system (SNS) hyperactivity which can be an etiologic precipitant or a result. The local or widespread sympathetic predominance in ovary is correlated with testosterone levels. Weight loss, insulin sensitizers, electroacupuncture, continuous positive airway pressure can decrease sympathetic hyperactivity and are beneficial in the treatment of PCOS [5]. Tekin et al. found that PCOS patients have reduced vagal activity through decreased heart rate variability, impaired heart rate, and recovery of systolic blood pressure after exercise [6]. Yildirir et al. also showed similar results in the same patient group [7]. High sympathetic activity is strongly associated with testosterone level and in combination, they enhance vascular problems in PCOS [8].

Stener-Victorin et al. hypothesized that impaired β-endorphin function, its increased production, and release have a role in the PCOS process. Low-frequency electro-acupuncture (1-15 Hz) decreases central β-endorphin concentration and sympathetic tone [9]. This possibly regulates the secretion of gonadotropin-releasing and gonadotropin hormones in addition to the decline in ovarian androgen production [9,10]. Low-frequency electro-acupuncture and physical exercise exert similar effects on disease behavior in long-term follow-up, and partial healing with the decrement in the activity of the sympathetic nervous occurs [11].

For infertility, despite opposite results [4], we can accept a sympathetic tendency or mild elevation during the second half of normal menstrual cycles as Yuna et al. mentioned. They also declare that this tendency is essential for T helper balance for fertility. Sympathetic and T helper-2 activity-related disorders mostly worsen in the luteal phase [12]. Although ovarian hormones are accounted for this process, autonomic dysfunction also must be kept in mind. T helper-2 cells and related cytokines allow the development of allograft tolerance [12]. Smoking is a well-known risk factor for infertility [13,14]. Park et al. found that sympathetic nerve activity does not decline in the early follicular phase compared with the mid-luteal phase in premenopausal smokers which may be crucial for fertility. Smoking exerts its effects on the cardiovascular and reproductive system also via impaired SNS activity [15].

Urinary Incontinence and Interstitial Cystitis

ANS function is essential for normal urinary system functioning. The parasympathetic nervous system regulates bladder contraction, sphincter relaxation, and SNS does the opposite. Idiopathic overactive bladder syndrome (IOBS) causes urgency with or without incontinence. Both sympathetic and parasympathetic activity is attenuated in the overactive bladder and autonomic imbalance exists [16-19]. Hubeaux et al. declared a sympathetic ANS dysfunction especially in IOBS patients without detrusor overactivity [20]. However, Sauver et al. stated that men with lower urinary tract symptoms do not have a high sympathetic tone or ANS dysfunction [21].

Hyperthyroidism can cause increased sympathetic and decreased parasympathetic activity. The imbalanced ANS in hyperthyroidism may also cause lower urinary tract symptoms and in patients with hyperthyroidism urinary incontinence risk increases [22]. Hyperthyroid women have lower peak flow rates of micturition and this resolves in the euthyroid state [23].

Interstitial cystitis is an idiopathic illness with visceral sensory hypersensitivity characterized by increased urinary frequency/urgency and pelvic pain [24]. Pelvic pain worsens as the bladder fills and resolves with emptying. Interstitial cystitis or painful bladder syndrome coexists with other central

and autonomic nervous system disorders like irritable bowel syndrome, fibromyalgia, chronic pain, migraine, syncope, and functional dyspepsia so it is like a part of systemic disorder or syndrome, and does not affect only bladder [25]. SNS dysfunction or predominance could be the underlying pathology of these disorders [26]. An extra information we can say about the urinary system and ANS is that the impairment of parasympathetic nerve function is associated with asymptomatic leukocyturia [27].

Evidence generally supports ANS dysfunction in IOBS, interstitial cystitis, etc. but possibly because of its nature we find sometimes contradictory results related to functions of ANS.

Pelvic Pain

Pelvic pain seems mostly a gynecologic complaint but it can emerge from pelvic floor muscle and viscera or surrounding structures like lumbosacral, hip, and sacroiliac joints [28]. There is limited, insufficient but supporting evidence about the existence of autonomic dysfunction in chronic pelvic pain. Dysmenorrhea, dyspareunia, pain with bowel movements accompany this prevalent disorder [29]. Baker et al. found that parasympathetic activity during sleep is decreased in premenstrual syndrome patients when they are symptomatic in the late luteal phase of the cycle [30]. Spinal cord stimulation seems an effective way of treatment in chronic intractable pelvic pain. One possible mechanism is the downregulation of the sympathetic outflow to the pelvis [31].

Yilmaz et al. found that ANS dysfunction exists in men with chronic prostatitis/chronic pelvic pain syndrome. They found findings related to heart rate variability similar to fibromyalgia [32]. Cho et al. also supported this information by pointing out that autonomic dysfunction may be one of the underlying mechanisms in the development of chronic pelvic pain [33].

Erectile Dysfunction and Premature Ejaculation

The parasympathetic nervous system causes penile arterial dilatation and relaxation of the smooth muscles of the corpora cavernosa [34]. Pelvic diseases like erectile dysfunction, premature ejaculation, benign prostatic hyperplasia, incontinence, overactive bladder, pelvic pain, colorectal motility disorders seem to have a connection with each other possibly via the ANS network. The deterioration of the function of a structure also leads to the inevitable impairment of the adjacent structures [35]. Erectile dysfunction is characterized by ANS imbalance/dysfunction and SNS hyperactivity [36-38]. In normal conditions, ejaculation is maintained by SNS, however premature ejaculation is also associated with SNS hyperactivity like erectile dysfunction [39].

Conclusion

The role of ANS dysfunction for all of the aforementioned disorders is still unclear. In general, we can not directly measure the status of ANS so we based our findings on only the clues we gathered. Studies have conflicting results which compel us to reconsider this issue. Rather than dysautonomia, autonomic dysfunction is mainly a disorder behind the mirror. However, there is still a question that needs to be answered about ANS dysfunction; "Is it a result or a cause of all these aforementioned disorders?"

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