Need for Randomized Controlled Trials Studying the Efficacy of Intravaginal Diazepam for the Treatment of Pelvic Floor Hypertonic Disorder in Women

Joyce JS1, Uddin MN2 and Foster RT2*

1Department of Obstetrics and Gynecology, Texas A&M Health Science Center College of Medicine/Scott & White Healthcare, USA
2Department of Obstetrics and Gynecology, Missouri Center for Female Continence and Advanced Pelvic Surgery, USA

INTRODUCTION

Pelvic floor hypertonic disorder, (a.k.a. high-tone pelvic floor dysfunction, levator spasm, pelvic floor muscle spasm, myofascial pelvic pain, etc.) represents a neuromuscular condition characterized by involuntary levator spasm and reproducible pain upon vaginal penetration and internal examination [1]. It may manifest as a primary pain generator, a singular component of chronic pain, or a dysfunction of visceras (bladder or bowel) controlled by the pelvic floor musculature. Clinical syndromes associated with pelvic floor hypertonic dysfunction are numerous and include childhood elimination disorder, idiopathic urinary retention, vaginismus, constipation, pelvic floor dyssynergia, bladder pain syndrome/interstitial cystitis, vulvodynia, colorectal pain, and chronic pelvic myofascial pain syndrome [2]. Although the true prevalence of this condition is unknown, one tertiary care center found that 87% of patients referred for evaluation of interstitial cystitis and pelvic pain had levator pain consistent with pelvic floor dysfunction [3]. In addition, a recent review stated that myofascial pain may be involved in 75-85% of patients with chronic pelvic pain [4]. Clearly, women suffering from this condition represent a significant cohort of patients seen in a urologic and/or gynecologic practice.

A variety of treatment options for pelvic floor hypertonic disorder are described in the literature (pelvic floor physical therapy and rehabilitation, heat therapy, vaginal massage, botulinum toxin injections, oral analgesic therapy, and off-label use of intravaginal diazepam). Unfortunately, data describing their efficacy is limited [2]. A recent retrospective review analyzing the efficacy of a comprehensive pelvic floor rehabilitation program on pelvic floor disorders demonstrated an 80% improvement in urinary, defecatory, and pain disorders throughout a 5-session course of comprehensive pelvic floor rehabilitation (CPFR) [5]. Despite proven benefit, CPFR has limitations due to its cost and accessibility to geographically isolated patients. The data describing the efficacy of botulinum toxin injections is limited as well. A recent systematic review evaluated 5 studies (2 case reports, 1 prospective pilot study, 1 retrospective study and a randomized double-blind controlled trial) and concluded that botulinism toxin has promising potential as a treatment option [4]. These conclusions are in spite of the fact that the only randomized control trial comparing Botulinum Toxin Type A to placebo did not demonstrate any statistically significant improvement in either the Visual Analog Pain Scale or quality of life in patients treated with Botulinum Toxin [6].

Regardless of the benefits of pelvic floor physical therapy and botulinum toxin injections, there remains a need to identify a self-administered treatment modality that is inexpensive and more convenient to the patient. Due to its ability to serve as a muscle relaxer, diazepam is one medication that may be promising for treating pelvic floor hypertonic disorder. For example, a double-blind, placebo-controlled, randomized clinical trial in a population of children with spastic cerebral palsy found a significant reduction of muscle spasm and hypertonia in those allocated to receive oral diazepam at bedtime. The authors concluded that diazepam was an inexpensive and effective method of relieving spasm and stiffness, especially in regions of the world where cost is a significant factor [7].

In a randomized controlled trial that compared biofeedback with oral diazepam for the treatment of pelvic floor dyssynergia-type constipation, biofeedback was found to be superior to
diazepam for relief of constipation and in reducing pelvic floor electromyography during straining [9]. In fact, the patients assigned to placebo had better relief than those who were administered diazepam. Therefore, if diazepam is going to effectively treat pelvic floor hypertonic disorder, an alternative method of administration will have to be sought.

Recently, off-label use of intravaginal diazepam tablets has generated interest as a potential treatment for treating pelvic floor hypertonic disorder. A retrospective study in patients receiving diazepam vaginal suppositories as an adjunct to pelvic floor physical therapy and intramuscular trigger point injections reported a clinically significant, but not statistically significant level of subjective improvement in 25 of 26 patients [9]. Subsequent to that study, a prospective study of 21 patients with levator pain, who were treated with vaginal diazepam, found significant improvements in pain levels measured on a 10-point VAS, with 62% of patients reporting moderate or marked improvement in a global response assessment [10]. The investigators used self-administered doses of 2 to 10 mg every 8 hours as needed for treatment. These authors concluded that vaginal diazepam may be helpful in treating pelvic floor hypertonic disorder, and recommended that larger randomized controlled research trials be conducted to clearly demonstrate the efficacy of vaginal diazepam.

Until now, the only randomized controlled trial studying the efficacy of vaginal diazepam for treating pelvic floor hypertonic disorder was recently reported by Crisp et al. Using a nightly dose of 5 mg of intravaginal diazepam, the investigators failed to demonstrate a significant improvement in resting EMG parameters or subjective outcomes when compared with placebo. However, this study has limitations with sample size, measurement of clinically relevant outcomes, and dosing schedule.

A properly designed randomized controlled trial is needed to clearly determine the effectiveness of off label intravaginal diazepam for treating pelvic floor hypertonic disorder. If vaginal diazepam is found efficacious, it will provide patients with an inexpensive and convenient, self-administered method of treating pelvic floor pain. In contrast, if it fails to be efficacious, it will focus our attention to other treatments that may prove viable options.

REFERENCES