Sexual Dysfunction Associated With Intrathecal Baclofen Use: A Report of Two Cases

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Abstract

Background/Objective: Intrathecal baclofen is considered standard treatment for severe spasticity of spinal cord and cerebral origin. Recognized side effects include fatigue and constipation. There are few reported findings of sexual dysfunction in men and none in women.

Methods: Two case reports.

Results: A male and a female patient with spasticity treated with intrathecal baclofen were recognized to have sexual dysfunction side effects from treatment. On reduction of the intrathecal baclofen dose, complete return to baseline sexual function was achieved for both subjects.

Conclusions: Intrathecal baclofen can impair sexual function and ejaculation in some patients. Clinicians should be aware of this risk and ask about it during routine clinic follow-up for spasticity. Dosing adjustments need to be considered in these patients.

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Key Words: Baclofen; Intrathecal; Spinal cord injuries; Cerebral palsy; Sexual dysfunction; Spasticity; Gamma-aminobutyric acid-B receptors

INTRODUCTION

Baclofen is a centrally acting gamma-amino-butyric acid B (GABA_B) agonist used to treat spasticity in patients with upper motor neuron syndromes such as spinal cord injuries and spasticity of cerebral origin such as cerebral palsy. Intrathecal baclofen (ITB) has been used as part of the standard treatment of intractable spasticity for well over a decade (1,2). More commonly known side effects of this treatment are weakness, fatigue, nausea, urinary retention, and constipation (1). Less noted have been the sexual side effects of ITB, including the decrease or loss of penile erections (1,3,4) and the inability to ejaculate and obtain an orgasm through impaired ejaculation reflexogenic activity (4). This was most pronounced with dosages greater than 350 µg/d (4). Other researchers have found a dose-related inhibitory effect of ITB injections of the lumbosacral cord on penile sexual function in male rats but not on ejaculatory behavior (5). There has been no literature to date on the effects of ITB on sexual dysfunction in women, although case

studies have found evidence for decreased sexual function in women with use of oral baclofen (6).

CASE REPORT 1

A 41-year-old man presented with a C6 American Spinal Injury Association Level D spinal cord injury secondary to a motorcycle collision in 1999. His medical history was negative up to the time of his injury, with no prior sexual dysfunction. From the injury, he was left with a neurogenic bladder, spasticity, lower extremity weakness, and neurogenic erectile dysfunction. He was able to obtain manual and psychogenic erections, ejaculate, and experience orgasms during sexual intercourse with pharmacologic medication without the need for an assistive device. He was followed for ongoing management of his SynchroMed II 40-mL ITB pump (Medtronic Inc, Minneapolis, MN) with catheter tip placed in the midthoracic region. Recent magnetic resonance imaging showed a stable spinal cord.

At his initial visit, he was on ITB 76 µg/d at a simple continuous rate, with a 500-µg/mL concentration. He received physical therapy initially to help with his gait and strengthening of his lower extremities, and no changes were made to his pump. After 1 month, his ITB pump rate was decreased by 5% to determine whether increased strength could be augmented with increase in tone. The patient stated that he felt “too tight,” and

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the 76- $\mu\text{g}/\text{d}$ rate was resumed. One month later, his dosage was increased by 5 $\mu\text{g}/\text{d}$, because he was having difficulty with a spastic catch at his right knee. Within 1 week of his dosage increase, he noted minor improvement of his tone at his right hamstring and plantar flexor; however, he reported difficulty ejaculating and experiencing an orgasm. He was able to maintain his erection and reported no loss of libido. He was taking tadalafil 20 mg as needed for erectile dysfunction. He also noted increased urinary retention and the need to catheterize more often. He continued on the current regimen for another 2 weeks with no improvement in his symptoms. He returned to the clinic, where his ITB pump dosage was reset to his original dosage of 76 $\mu\text{g}/\text{d}$ and noted complete return to baseline sexual function within 1 week.

The patient had reported this happening after initially receiving his ITB pump 1 year previously. He also noted worsened urinary retention with increases of the ITB and has had to start periodic straight catheterization since having his pump placed. He did not remember any sexual dysfunction with the use of oral baclofen; however, he was only able to tolerate dosages up to 20 mg 4 times a day because of the side effect of fatigue.

CASE REPORT 2

A 42-year-old woman with diplegic, spastic cerebral palsy diagnosed in early adulthood presented with a spastic gait. She had no significant medical history. Before her initial ITB pump placement in 1999, she noted difficulty with gait and activities of daily living secondary to spasticity in upper and lower extremities but no problems with sexual dysfunction. She did not use any pharmacologic medications to enhance sexual function.

Her second pump, a Medtronic Synchromed II 40-mL ITB pump with catheter tip at T11, was implanted 3 years ago. After placement, ongoing issues with fine-tuning of her ITB dosage occurred, characterized by symptoms of feeling “too tight” vs “too loose,” affecting her ability to ambulate with the use of an assistive device. Dosing varied from a high of 650 $\mu\text{g}/\text{d}$ to a low of 400 $\mu\text{g}/\text{d}$, with an ITB concentration of 2000 $\mu\text{g}/\text{mL}$. Her course was complicated by lower extremity cellulitis, which occurred several months after having the pump placed, and this worsened her spasticity. The patient was given a bolus of 30 μg of ITB at 8:00 PM at night over a half hour to improve night-time spasticity. This bolus dose was decreased to 25 μg 1 week later after her pump refill, secondary to a complaint of low muscle tone. Approximately 3 weeks later, she expressed difficulty achieving orgasm, which she noted had been occurring since her pump refill 1 month earlier. She had had no problems during the first several months after receiving the pump or with her prior SynchroMed EL ITB pump (Medtronic Inc, Minneapolis, MN). Her decreased sexual function affected her quality of life, and she was uncertain whether this problem was a side effect of the ITB. Her bolus dose

was decreased from 25 to 17 μg , with resolution of the sexual dysfunction and mild increase in night-time spasticity. She continued to receive the nightly bolus of 21 μg with a daily dose of 480 μg , which has changed little in the last several months, with no further problems with sexual dysfunction and stable spasticity.

DISCUSSION

Several authors have purported that the mechanism of action behind decreased sexual function and ejaculation may be the inhibitory effect of GABA_B receptors at the spinal level (6), and more specifically, at the lumbosacral spinal cord on presynaptic sacral afferent reflexes (4,5). As baclofen acts on these receptors, penile reflex responses are inhibited. This inhibitory relationship between GABA and sexual behavior in male rats may be explained through the dramatic concentration increases (1,000%) of GABA in the cerebral spinal fluid (CSF) noted immediately after ejaculation when the male rat was unresponsive to sexual stimulation (7). However, on studying the actual copulatory behavior of male rats, ITB was noted to have much less of an inhibitory effect than presumed based on the high levels of GABA noted above in the CSF after copulation (5). Additionally, the inhibitory effects of ITB on penile reflexes in male rats seen after injection in the lumbosacral subarachnoid space were not observed with injection into the thoracic space and ejaculation still occurred, although the rats studied did not have a spinal cord lesion (5). Our male patient and several of the male patients cited by Denys et al (4) were able to gain an erection but unable to ejaculate; our patient had his pump catheter tip placed at the midthoracic level. These discrepancies in sexual function and administration of ITB may support additional mechanisms of action.

There have been no case reports to our knowledge on the effects of ITB on sexual function in women; however, researchers have noted an inhibitory effect of GABA in regulating sexual behavior in female rats (8). In female rats with dorsal raphe nucleus lesions, baclofen decreased lordotic (sexual) behavior, suggesting that GABA_B receptors may be involved in the inhibitory mechanism regulating sexual behaviors (8). This is an issue that will need further research and inquiry as more ITB pumps are placed in women.

Bitran et al (5) postulated 2 other theories to understand the deficits in erectile responses seen after administration of ITB on the lumbosacral spinal cord.

One hypothesis postulated by Bitran et al (5) involved the inhibition of motor efferents, which control contractions of perineal muscles by means of baclofen engaging the GABA_B binding sites found in the ventral horn. This may play a role in the difficulty our 2 patients had with experiencing an orgasm, and in 1 patient, his difficulty with ejaculation. The second mechanism of action posited by Bitran et al (5) involved GABA-ergic inhibition through baclofen of the visceral efferents that

stimulate the parasympathetic nerves that cause vasodilation of the penis and may interfere with ejaculation.

The loss of orgasm and ability to ejaculate caused our 2 subjects to seek a return visit for pump dosage changes to avoid the sexual side effects and improve quality of life.

Clinicians treating spasticity need to thoroughly examine the effects and side effects of ITB on treated patients. These cases indicate that this inquiry needs to include questions about sexual function. The patient may not experience side effects at a certain dosage; however, as the dosage is titrated up, function may be affected. The male patients in previous reports had been taking larger dosages of ITB at standard concentrations of 500 and 2,000 µg/mL, with those with larger daily doses experiencing more pronounced sexual dysfunction (4). However, our patient was on a very low dose and reported side effects with small changes. For our female patient, several small dosage adjustments were needed before an ideal dosage was achieved that maximized function. Continued study into the role of ITB and sexual dysfunction is needed to elucidate the mechanism of action involved.

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