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Article in *Journal of clinical psychopharmacology* · August 2012

DOI: 10.1097/JCP.0b013e318266c6f5 · Source: PubMed

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This case demonstrates the risk for abuse/dependence from ramelteon use in a patient who has previously abused other sedative-hypnotics. Although devoid of abuse liability, it should be used with caution, especially in patients with a history of substance abuse. The neurobiological basis for the abuse of ramelteon is still not known.⁴ Whether neurobiological changes due to chronic mood disorders and substance abuse play a role is an area that needs further research.

AUTHOR DISCLOSURE INFORMATION

The author declares no conflicts of interest.

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Treatment With Triptorelin in Mentally Disordered Sex Offenders: Experience From a Maximum-Security Hospital

To the Editors:

The management of sex offenders with mental disorders is a complex, sensitive, and evolving subject. Treatment encompasses both addressing the patients' disorder and reducing future risk of reoffending. Current treatment involves a combination of pharmacological agents and psychological therapies.^{1,2} However, treatment is often complicated by poor compliance due to undesirable side effects of medication³ and low patient motivation to participate in psychological therapy.⁴ Adding to these woes are that current treatment regimens lack robust evidence showing a significant

reduction in recidivism rates of "treated" patients.^{5,6}

We describe the benefits of using triptorelin, a gonadotropin-releasing hormone (GnRH) analog in seven patients who were treated in a maximum-security psychiatric hospital in England. This case series was a retrospective review of medical case notes and interviews with treating clinicians. All patients received a long-acting depot injection of triptorelin commencing between 2003 and 2009 on a voluntary basis. They also provided written consent for the purposes of this report. In conjunction with triptorelin, they received psychological therapy including offense-related work and participated in rehabilitation programs such as occupational therapy and education.

Triptorelin lowers serum testosterone by replacing the natural pulsatile secretion of gonadotropins with a continuous secretion. This results in a down-regulation of GnRH receptors leading to a significantly lowered serum luteinizing hormone and testosterone levels. Testosterone has been well documented to have a significant role in the maintenance of sexually driven behavior, aggression, and the intensity of sexually deviant thoughts.⁷ Past research has found that testosterone-lowering medication, including triptorelin, can reduce sexual arousal and urges in patients as well as their reoffending rates.⁸ A small double-blind study further reported the reduction of deviant and nondeviant sexual activity with leuprorelin (GnRH analog) when compared with the patients solely receiving cognitive-behavioral therapy.⁹ This report aimed to illustrate the therapeutic gains of triptorelin in patients who are difficult to treat and pose a significant risk to the public.

The improvements noted in these seven patients were recorded in objective measures comprising plasma testosterone levels, the number of aggressive and sexual incidents, and penile plethysmography, where available. The subjective measures of improvements were also noted in the following categories: the patient's self-reported levels of sexual urges and arousal, the patient's perspective of the medication, the patient's general behavior, compliance with psychological and rehabilitation therapy, and progression toward treatment in lower levels of security.

Triptorelin has been reported to give rise to several adverse effects such as a decrease in bone mineral density, hepatotoxicity, gynecomastia, weight gain, and impaired glucose tolerance.¹⁰ However, in comparison with other antitestosterone medication used to treat sexual offenders such as cyproterone acetate and medroxyprogesterone

acetate, triptorelin is thought to cause less severe adverse effects. Monitoring of the above adverse effects was reported.

The mean age of the seven patients at the time of writing was 42 years old. Five of the seven patients had a diagnosis of dissociative personality disorder with psychopathy (PCL-R > 25). The other two patients were diagnosed with dissociative personality disorder with obsessive-compulsive disorder and generalized anxiety disorder, and dissociative, paranoid and borderline personality disorder, respectively. All of the patients were sentenced and received either mental health disposals (Section 37 of the Mental Health Act 1983, England and Wales) or were transferred from prison under a mental health order (Section 47). They all received a restriction order (Section 41 or 49) by the Ministry of Justice for public protection. Of seven patients, three were convicted of indecent assault on children, one was convicted of malicious wounding of a child, one was convicted of indecent assault on young women, one was convicted of hostage taking and indecent assault, and one was convicted of arson. The last patient had been cautioned for "interfering" with a child aged 11 years. Three of seven patients continued to display sexually inappropriate behavior while in secure care including one patient seriously sexually assaulting a female staff member. Three patients received triptorelin depot injection of 11.25 mg every three months and four received a monthly dose of 4.2 mg. Three patients had previously been treated with cyproterone acetate as an antiandrogenic medication with suboptimal therapeutic benefits.

All seven patients experienced a substantial reduction in plasma testosterone levels, ranging from 0.1 to 1.8 nM. These levels are consistent with levels reported in surgical castration. It was also observed that all of the seven patients experienced a decrease in sexual and aggressive incidents on the unit. Two patients consented to penile plethysmography testing for levels of arousal. Both displayed significantly reduced levels of arousal.

The clinical impression from the treating team after the commencement of triptorelin was recorded as positive. The general demeanor of the patients was improved with a decrease in hostility and aggression. As a consequence, they were reported to have participated more readily in psychological therapy and rehabilitation activities. The patients themselves reported a reduction in sexual fantasy, desire, and arousal. These self-reports were not measured using rating scales; however, it is noted that had it been used, the possible accompanying bias of self-reporting would still be present.

The adverse effects of triptorelin were recorded. One patient experienced gynecomastia and a decrease in bone mineral density, confirmed through a dual-energy x-ray absorptiometry of the bone. He was treated with calcium supplements and has remained compliant with triptorelin. There were also no reports of any pathological fractures or functional limitations experienced by this patient. Two other patients experienced minor adverse effects. One patient complained of gynecomastia and transient hot flushes, and the second complained of testicular atrophy. All of the seven patients, however, were satisfied with the triptorelin treatment and were willing to comply with it. One patient even expressed his desire to be considered for surgical castration.

The treatment of mentally disordered sex offenders is still evolving, and large-scale research providing clinical guidelines for treatment is scarce. The challenges in producing level A evidence for treatment are evident, not least because of small participant numbers, diagnostic, and methodological heterogeneity.² This report, albeit a retrospective case series, highlights the benefits of triptorelin treatment in a group of patients who are difficult to treat and pose a significant risk of reoffending. All seven patients experienced a significantly lowered serum testosterone after treatment, in keeping with other published studies of GnRH analog treatment used in sex offenders.^{3,9,10} Concurrently, all seven patients reported a significant reduction in sexual arousal, deviant fantasies, and masturbation. This, too, was consistent with the findings of the previously mentioned studies, although different GnRH analogs (leuprorelin and goserelin) were used.

All seven patients in our report experienced lower levels of aggression and sexual violence. This was derived through the recorded number of incidents reported (Broadmoor Security Incident Reporting). Although this did not equate to a criminal record, incidents of sufficient concern are reported to the police department and could potentially lead to charges within the criminal justice system. In addition, the number and severity of incidents within secure psychiatric care is often deemed to be a marker

of the patient's progress. Indeed, four of the seven patients reported had improved sufficiently and were either referred or transferred to less secure units after triptorelin treatment. The decrease in incidents reported in our patients is encouraging and may provide an indication of future recidivism. Other authors have demonstrated reduction in recidivism in patients treated with antilibidinal medication in the community.¹¹

Medication compliance is widely known to be variable, especially with psychiatric or antilibidinal medication.¹² Triptorelin has the benefit of a simple dosing regimen; a depot injection either monthly or every three months. This infrequent administration is likely to improve adherence and the depot preparation, likely to provide reassurance regarding medication compliance.

In sum, this report suggests that triptorelin should be more widely considered in patients who are challenging to treat and present a high risk of reoffending. It has the potential to enable these patients to progress and experience continued rehabilitation within conditions of lesser security. Further controlled studies are required to establish clinical efficacy and long-term recidivism rates. Its benefits, however, are difficult to ignore when treating this complex patient group.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

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