Recurrent Use of Implantable Buprenorphine

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Buprenorphine implants received US Food and Drug Administration (FDA) approval in May 2016.[1] The implant consists of a set of 4 26-mm implantable rods, which are subdermally placed in the biceptal groove. The implants produce a plasma-level equivalent of up to 8 mg of daily oral buprenorphine for up to 6 months.[2] Peak plasma levels are reached within 12 hours of insertion and stabilize after several weeks. The implants are designed to be removed and either replaced or switched to another form of buprenorphine after 6 months. After implant removal, plasma levels are undetectable after several days.

The FDA has approved buprenorphine implants for 1 year of total use or 2 sets of implants. The ability to prescribe, insert, and remove buprenorphine implants is under the guidance of a FDA Risk Evaluation and Mitigation Strategies (REMS) program. To prescribe buprenorphine implants, a written test must be passed. Privileges to insert and remove the implants involve passing a clinical practicum after a day-long training session. The buprenorphine implants impart significant advantages in compliance, reliable plasma levels of buprenorphine, and low risk of diversion due to surgical placement.[3] Despite these advantages, as an opioid, buprenorphine implants still carry a risk of addiction and are a mere extension of buprenorphine medication-assisted treatment, which was approved by the FDA in 2002. Diversion of oral buprenorphine has become a growing problem.[4] Patients with opioid use disorder often use illicit buprenorphine as a substitute for preferred opioids, to bridge between preferred substances, or to self-taper.[5] Consequently, forms of buprenorphine that ensure compliance like implantable or depot buprenorphine are a natural development. Treatment of opioid use disorders with implantable buprenorphine past 1 year is demonstrated with this case.

Case Report

Mr A is a 55-year-old white man who first sought care in August 2012 for posttraumatic stress disorder (PTSD). He had recently lost both of his parents and was involved in a serious car accident. His primary symptoms of PTSD included significant anxiety, flashbacks, and nightmares involving the accident and subsequent driving. He was treated with a combination of paroxetine and clonazepam. His extreme inability to ride comfortably in a motor vehicle precluded him from driving, and he rarely drove himself in his 10-minute commute to work. The patient has a history of alcohol use disorder in long-term remission, which is maintained with Alcoholics Anonymous meetings. The patient has a comorbid tobacco use disorder but no other reported medical history.

Mr A's PTSD symptoms improved over the course of 2 years with medication management and concurrent cognitive-behavioral therapy. He reported prescription opioid use for chronic pain symptoms but no symptoms of an opioid use disorder. Eventually, his follow-up lapsed, and he was not seen again until 2016.

Mr A returned to the clinic in January 2016 for significant anxiety due to several domestic disputes with his wife and son. The latter resulted from his son's own struggle with opioids. The former was due to relational difficulties that were heavily impacted by his opioid use, which was in prescription medication form. Due to this domestic dispute with his wife, the patient was facing legal charges and possible incarceration. In March 2016, he was started on sublingual buprenorphine/naloxone 8mg/day to aid in discontinuing his opioid medications.

Following his incarceration, the patient returned to the clinic in July 2016 for continued 8-mg sublingual buprenorphine/naloxone treatment as well as concurrent group and individual alcohol and drug counseling. The patient had significant motivation to stay opioid free, as he wanted to mend his marriage and avoid further jail time via parole. The patient did very well on 8 mg of buprenorphine from March 2016 until placement of implantable buprenorphine in the fall of 2016.

In March 2016, the option of buprenorphine implants was discussed with the patient. These discussions continued through the FDA release of buprenorphine implants. After his incarceration, Mr A spoke directly to the pharmaceutical company representatives to assuage his fears of this new buprenorphine modality. Even after he decided to try the buprenorphine implants, there was a considerable delay due to insurance confusion/coverage. Finally, in October 2016, Mr A became the clinic's first patient to receive buprenorphine implants for maintenance buprenorphine. Approximately 1 month after the implants were placed, he required an extra 2 mg of buprenorphine/naloxone sublingual film to maintain adequate control of cravings. This extra dosing continued until December 2018. He has given monthly consecutive negative urine samples (excluding buprenorphine) since

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starting the buprenorphine implants and otherwise leads a productive life with his wife. He is now off parole.

In October 2019, Mr A received his seventh set of consecutive buprenorphine implants. His would be the first documented case of a patient successfully maintained on buprenorphine implants longer than the FDA-approved 1 year of usage. There were no observed complications from placement of buprenorphine implants in previously used sites with the seventh set of implants. Incisions were made at the approximate insertion scars with no complications. Previous explants were completed as expected. The patient experienced no adverse events from consecutive buprenorphine implants. Implants in a stacked position were easier to explant than the standard fan pattern. Mr A continues in treatment to the present day and did not require the resumption of 2-mg buprenorphine/naloxone film in the summer of 2019. The patient reported that he ultimately felt more comfortable on the slightly higher dose and acknowledged that the difference was most likely psychological.

Conclusion

The FDA approval of repeated applications of buprenorphine implants would seem self-evident given the need for more reliable forms of buprenorphine than once-a-day self-dosing. The technology and methods used for buprenorphine implants have been utilized for longer time between implants and overall longer time for usage in implantable birth control.[6] Incidental long-term placement of implantable buprenorphine has also been documented.[7] The lack of FDA approval for buprenorphine implants past 1 year is a stumbling block for health insurance coverage for this modality. As such, this novel modality is limited in its usage in the midst of a national opioid crisis. This case demonstrates the use of implantable buprenorphine past 1 year and suggests further study is needed for extended usage. Further study is also needed for other uses such as long-term placement past 6 months for tapering purposes that has been observed in this clinic but not in this case (currently there is no guidance for use past 6 months other than tapering with oral buprenorphine following explant).

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Additional information: Dr Campbell has served as the behavioral health director of Wayne Memorial Community Health Centers since 2012. Wayne County is a small rural county that has been ravaged by opioid use disorders. Dr Campbell has used medication-assisted treatment with only depot naltrexone, depot buprenorphine, and implantable buprenorphine. He has treated approximately 30 patients with implantable buprenorphine. Dr Campbell is board certified in family medicine, psychiatry, and addiction medicine.

Patient consent: The patient was informed of the use of his medical information and signed release of information, which is available for inspection.

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