Full length article

Long-acting intramuscular naltrexone for opioid use disorder: Utilization and association with multi-morbidity nationally in the Veterans Health Administration

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ARTICLE INFO

ABSTRACT

Background: Long acting intramuscular (IM) naltrexone is an effective treatment for opioid use disorder (OUD), but rates and correlates of its use have not been studied.

Methods: National administrative from the Veterans Health Administration (VHA) from Fiscal Year 2012 identified only 16 VHA facilities that prescribed IM naltrexone to 5 or more veterans diagnosed with OUD. Data from these facilities were used to identify sociodemographic, diagnostic, and service use characteristics, including use of psychotropic medication, that were characteristic of veterans who filled prescriptions for IM naltrexone. This was in comparison to users of opiate agonist treatments (methadone or buprenorphine) or veterans with no pharmacologic treatment for OUD. Comparisons were made using both bi-variate analyses and multivariable logistic regression.

Results: Only 179 of 16,402 veterans with OUD (1%) at these 16 facilities filled a prescription for IM naltrexone and only 256 of 99,394 (0.26%) nationally. These veterans were characterized by past homelessness, co-morbid alcohol use disorder, multiple psychiatric disorders, and a greater likelihood of psychiatric hospitalization, as well as mental health outpatient and antidepressant medication use.

Conclusions: IM naltrexone is rarely used for OUD and is primarily used for patients with multiple co-morbidities, especially alcohol use disorder and serious mental illness. The use of this treatment illustrates many of the principles identified by the emerging focus on multi-morbidity as a critical feature of clinical practice.

1. Introduction

Opioid addiction is a serious and growing public health problem in the United States (CDC, 2011; Manchikanti et al., 2012; Martins et al., 2017; Webster et al., 2011). The 12-month prevalence of prescription opioid use disorder (OUD) almost doubled from 2003 to 2013 from 0.6% to about 1% (5–8). Prescription opioids and illicit street heroin pose serious, and not infrequently fatal, health risks (Mars et al., 2014). In addition, there is both a low rate of treatment-seeking among people with OUD and poor treatment adherence (Blanco et al., 2013; Hser et al., 2014; Soeffing et al., 2009; Stein et al., 2005). As a result, OUD is typically chronic and relapsing (Tetrault and Fiellin, 2012). Both the

increase in the prevalence of OUD and the daunting challenges of its treatment are associated with serious societal consequences including crime, homelessness, unemployment, family breakup, and an increase in the rate of deaths due to opioid overdoses (Manchikanti et al., 2012; Mars et al., 2014). The age adjusted death rate from prescription opioids increased almost fourfold between 1999–2009, while heroin-related overdose deaths increased by 36% between 2007–2009 (Calcaterra et al., 2013). Indeed, people with OUD die at nearly 15 times the rate of their age- and sex-matched peers (Degenhardt et al., 2011). Societal costs of OUD have been estimated at a staggering $55.7 billion in 2007 (Birnbaum et al., 2011).

Compared to the general population, veterans have modestly higher

rates of chronic pain, substance use, and mental health disorders (Agha et al., 2000; Clark, 2002; Gironda et al., 2006; Hoglund and Schwartz, 2014; Seal et al., 2011; Toblin et al., 2014), all of which put them at somewhat higher risk of OUD. OUD is approximately seven times more common among veterans enrolled in Veterans Health Administration (VHA) services than adults enrolled in commercial health plans (Baser et al., 2014). The most effective pharmacological treatment for OUD is opioid agonist therapy (OAT), including methadone maintenance and office-based oral buprenorphine therapy. In 2009, VHA established a nationwide mandate to make buprenorphine and methadone treatment for OUD available to every veteran who might benefit. OAT is effective at increasing opioid abstinence, improving social functioning, and re-ducing criminal justice involvement (Krupitsky et al., 2011; Syed and Keating, 2013). However, not all patients with OUD have a positive response to OAT because of both provider reluctance to use addictive substances as treatment as well as patient fears of stigma, adverse re-actions, and fears of physical withdrawal symptoms. Access is also limited in many locations (International Harm Reduction Association, 2010; Krupitsky et al., 2010). Given these concerns, alternative phar-macologic treatments for OUD are clearly needed.

One uncommonly used option for the treatment of OUD is nal-trexone, a well-established and efficacious treatment (Tetrault and Fiellin, 2012). As an opioid receptor antagonist, naltrexone effectively blocks the euphoria associated with use of opioids (Farabee et al., 2016), but compliance with oral administration is notoriously poor (Tetrault and Fiellin, 2012). In order to improve treatment adherence, a once monthly, intramuscular (IM), extended-release formulation of naltrexone (XR-NTX; Vivitrol ®) has been approved by the FDA and brought to market. IM naltrexone is associated with a significantly higher rate of opioid abstinence than placebo, reduces opioid craving, and increases treatment retention (Crits-Christoph et al., 2016; Syed and Keating, 2013). Patients given IM naltrexone have fewer opioid-related and non-opioid-related hospitalizations compared to patients given oral naltrexone, buprenorphine, or methadone (Baser et al., 2011). However, it is rarely used, even as compared to other forms of OUD treatment which are also infrequently used for poorly understood reasons (Alanis-Hirsch et al., 2016).

It is unknown whether veterans who use IM naltrexone differ in clinically important ways from those who receive either OAT or no pharmacologic treatment at all for OUD. A developing literature on multi-morbidity in health care (Boyd and Fortin, 2010; North et al., 2016; Tinetti et al., 2012) suggests that, while most treatments are evaluated for FDA review in studies that exclude patients with co-morbidities, as was the case for IM naltrexone (Krupitsky et al., 2011; Krupitsky et al., 2013), in real-world practice, such co-morbidities are common and often shape treatment in important ways. We hypothe-sized that multi-morbidity would be common in the use of IM nal-trexone, and that effective treatments, which are rarely used, may be most likely to be selected for difficult-to-treat patients in whom multi-morbidity plays a prominent role.

The present study uses Fiscal Year (FY) 2012 VHA administrative data to examine utilization rates and correlates of IM naltrexone use as compared to both OAT and to use of no pharmacological treatment among veterans with OUD. Veterans in these three treatment groups were compared by demographic factors, psychiatric and medical co-morbidities, health service utilization, and numbers of psychotropic prescription fills. This analysis sought to identify distinct characteristics of veterans prescribed IM naltrexone in the hope of better under-standing its use and finding more effective approaches to promoting its consideration for veterans who may benefit from this little-used treat-ment.

2. Methods

The present study included a cross-sectional analysis of data ob-tained from national VHA administrative databases for Fiscal Year (FY)

2012 (October 1, 2011 to September 30, 2012). Data were derived from the encounter file of all outpatient service use, the patient treatment file of inpatient discharge abstracts, and the pharmacy benefits manage file of filled prescriptions.

2.1. Sample characteristics

Veterans were identified via VHA administrative data as having an OUD diagnosis in Fiscal Year 2012 (FY2012; October 1, 2011 to September 30, 2012). OUD was defined by the ICD-9 codes for either opioid abuse or opioid dependence (304.0x, 305.5x, and 304.7x) at any point during FY2012. For this analysis, we only included veterans with OUD from facilities that treated at least 5 OUD patients with IM nal-trexone in FY2012 in order to exclude facilities that made little or no use of this treatment. Only 16 of 155 VA medical centers met this cri-terion, and at these medical centers only 179 veterans of 16,402 di-agnosed with OUD (1.09%) filled a prescription for IM naltrexone. Nationally, across all VA medical centers, only 256 of 99,394 (0.26%) veterans diagnosed with OUD received IM naltrexone.

Veterans diagnosed with OUD at these medical centers were clas-sified into three groups: those who filled at least one prescription for IM naltrexone (179, 1.1%), veterans who received opioid agonist therapy, i.e., methadone maintenance, identified by use of clinic stop 523 and/or buprenorphine, identified through filling of at least one prescription for Suboxone ® (n = 3143, 19.1%), and veterans who received no phar-macotherapy for OUD from VHA (n = 13,080, 79.7%). Patients who received the buprenorphine transdermal patch were excluded since this is designated for pain management rather than OAT. Veterans who used both OAT and IM naltrexone were classified in the naltrexone group.

2.2. Measures

2.2.1. Demographic characteristics

Demographic characteristics included age, gender, geographic loca-tion of residence, race/ethnicity, receipt of a VA pension, disability, and homelessness. Geographic location (i.e., urban vs. rural status) was based on zip code data and the Rural-Urban Commuting Area (RUCA) (WWAMI Rural Health Research Center, 2014). OEF/OIF era status was determined using data provided to the VA from the Department of Defense. Disability was determined by service connection status of < 50% or ≥50%. Homelessness was defined as the use of specialized VA homeless program services in FY2012 and/or receipt of a V60.0 ICD-9 diagnostic code (re-flective of lacking housing) (Edens et al., 2011).

2.2.2. Medical diagnoses

Medical diagnoses were obtained from documented clinical diag-noses in the VA Computerized Personal Record System (CPRS). Medical problems were chosen according to their inclusion in the Charlson index of medical severity (18, 19) and identified from standard International Classification of Diseases, Ninth Revision (ICD-9) diag-nostic codes. Major medical problems, based on the Charlson index, included congestive heart failure, chronic obstructive pulmonary dis-ease, hepatic disease, and diabetes mellitus. Prevalent pain-related di-agnoses were also included in the analyses, including musculoskeletal pain, insomnia, diabetes-related pain, fibromyalgia, and headache. A summary variable indicating any pain diagnosis was also created.

2.2.3. Psychiatric diagnoses

Psychiatric diagnoses were clustered into eight categories: bipolar disorder, schizophrenia, major depression, anxiety disorder, post-trau-matic stress disorder (PTSD), adjustment disorder, personality dis-orders, and alcohol use disorder. Additional variables were created representing dual diagnoses (i.e., veterans with both a mental health diagnosis and a substance use diagnosis) and veterans with serious mental illness (schizophrenia, bipolar disorder or major depressive disorder). Diagnoses are based on outpatient encounters in FY2012.