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Medication-assisted therapy for opioid addiction

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Abstract

The “Medication-Assisted Therapy for Opioid Addiction” session was chaired by Dr. Betty Tai and had three presenters. The presenters (and their topics) were: Dr. Andrew J. Saxon (Methadone and Buprenorphine for Treatment of Opioid Addiction and HIV Risk Reduction), Dr. Walter Ling (Opioid Antagonist Treatment for Opioid Addiction), and Dr. Betty Tai (Chronic Care Model for Substance Use Disorder).

Keywords

opioid addiction; methadone; buprenorphine; chronic care model

1. Introduction

Currently, three medications are approved by the U.S. Food and Drug Administration (FDA) for treating opioid addiction. Classified by their underlying mechanisms, these medications include agonist (methadone), partial agonist (buprenorphine), and antagonist (naltrexone) agents. The three presentations in this session respectively provided an overview of agonists, antagonists, and a broader view of medication-assisted therapy to support a chronic care model for opioid addiction.

2. Presentations

Dr. Saxon is a professor in the Department of Psychiatry and Behavioral Sciences, University of Washington, and the director of the Center of Excellence in Substance Abuse Treatment and Education at the Veterans Affairs Puget Sound Health Care System. Dr. Saxon’s talk focused on methadone (a full opioid agonist at the mu-receptor) and buprenorphine (a partial opioid agonist). Methadone typically requires once-daily dosing for treatment of opioid addiction, though in rare circumstances (such as with a pregnancy) bid

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dosing is necessary. There is somewhat more flexibility in dosing of buprenorphine. Once-daily dosing works extremely well, but divided doses throughout a single day or three-times-per-week dosing are also possible. Buprenorphine has a superior safety profile compared to methadone. Methadone is formulated for oral administration and buprenorphine for sublingual administration. (A subdermal buprenorphine implant with a 6-month duration of action is being considered for approval by the U.S. FDA.) Both medications reduce mortality rates and improve other outcomes (e.g., illicit opioid use, HIV risk behaviors). A recently completed study that compared liver function of patients randomized to methadone or buprenorphine for 6 months of treatment did not find any major liver toxicity concerns among either treatment arm. Details of this presentation can be found in the article by Saxon et al. included in this special issue.

Dr. Ling is a professor of psychiatry at UCLA and director of the UCLA Integrated Substance Abuse Programs. Dr. Ling stated that the rationale for the antagonist approach to treating opioid addiction was originally based on the extinction model of animal experimentation. It was postulated that by blocking the euphorogenic effects of opioids at the opioid receptors, opioid use would become non-rewarding and, in time, animals—and humans—would cease opioid self-administration. Results of human laboratory extinction studies have been strikingly unsuccessful in generalizing into the real world, and the underlying assumption of the antagonist approach to treating opioid addiction has not been translated into clinical success. The decision to use or not use opioids appears to be related to cognition instead of extinction. Still, medication non-compliance has been singled out as the reason for the clinical failure of the opioid antagonist approach, and considerable resources have been expended to develop a sustained-release form of the antagonist naltrexone to ensure compliance. An injectable form of naltrexone, which lasts for approximately 4 weeks, and which once administered, is irretrievable, was approved for treatment of alcohol addiction in 2006 and for opioid addiction in 2010. So far, most experience with sustained-release naltrexone has been in populations of patients with limited therapeutic options. It remains to be seen whether the formulation will be a clinical success in open medical settings affording other treatment choices.

Dr. Tai is the director of the Center for Clinical Trials Network (CTN) at the National Institute on Drug Abuse (NIDA). Dr. Tai's talk focused on the need for adopting a chronic care model (CCM) to treat substance use disorder (SUD), as SUD is a chronic brain disease with frequent relapses and consequences that remain problematic for a long time, even after discontinuation of use [1]. Six core elements of a CCM are: (1) healthcare delivery system redesign to plan and manage preventive care, (2) healthcare organization support to allow organization-level leadership and resources to sustain CCM, (3) expert-informed decision support to generalist clinicians to manage cases so that separate specialty treatment is not needed, (4) improved clinical information systems to track and coordinate care, (5) fostering patient self-management, and (6) linking patients to access community resources (e.g., peer support groups, exercise programs, housing, home care programs) [2].

Using results from the NIDA CTN trials as examples, it has been shown that medication-assisted therapy is effective in reducing opioid use, but the relapse rate is generally high once the medication is stopped at the end of the trial [3,4]. Furthermore, the chronic care

model, used in managing many other chronic illnesses (e.g., diabetes), does more than just provide reactive care to patients who are seeking treatment. It also provides proactive care for patients at wellness visits, emphasizing preventive services such as implementation of screening and brief intervention (SBI) for identified risky behavior [5]. It also provides opportunities for lifestyle monitoring and management. Therefore, a CCM is needed to properly and effectively address addiction [6]. Key factors to ensure CCM success are (1) improving providers' knowledge of treatment guidelines and skills in following treatment guidelines, (2) educating, engaging, and supporting patients' self-management, (3) enhancing the monitoring/reviewing/following-up of patients with multidisciplinary team service, and (4) leveraging health information technology systems (e.g., electronic health records (EHRs)) to support the first three elements [7,8]. Current NIDA efforts have been devoted to developing and adopting digitized SBI tools in primary care to define parameters for CCM research. A longitudinal disease registry for the SUD field is the critical first step in developing a CCM for SUD treatment. Although extensive research-based evidence is lacking, the conceptual and clinical indications suggest that such a CCM is highly desirable and has the potential to be effective in early prevention of high-risk substance abuse, reducing substance use among patients in treatment for SUD, and improving the quality of care of patients who have other co-morbid chronic illnesses and are negatively affected by unaddressed SUD [9].

3. Discussion

In the discussion session, the following questions were addressed.

(1) Why does NIDA CTN not include genetics in their studies?

While medication trials conducted by NIDA CTN produce reliable scientific results, it is clear that the same medication does not work equally for all patients. Genomic data can shed light on how genetic factors impact patients' unique responses toward a specific medication; thus, the genetic research component is needed to provide additional information that can advise effective patient-centered care. All CTN trials now collect blood samples to enable future genetic investigation. Due to resource limitations, decisions on whether to analyze the blood genetic elements will be reviewed and analyzed case by case. Recently, some CTN trials have produced interesting genetic findings [10].

(2) The best medical record system is the one used by U.S. Veterans Affairs (VA); is there a plan to use it?

Yes, Dr. Saxon, who works with the VA system and patient populations, has used the VA records for his research. CTN is exploring the VA system and the potential opportunity of moving intervention trials to real-world VA clinics, and, notably, the possibility of using VA medical records as the data source for trials.

4. Conclusions

Opioid addiction, a chronic, relapsing brain disease can be managed safely and effectively with three U.S. FDA-approved medications: (1) methadone (a mu-receptor agonist), (2)

buprenorphine (a mu-receptor partial agonist), and (3) injectable sustained-released naltrexone (a mu-receptor antagonist). These medications reduce mortality rates and improve other outcomes (e.g., illicit opioid use, HIV risk behaviors) in opioid-addicted patients. In order to enhance their treatment outcome, we propose that primary care providers adopt the chronic care model (CCM), which has been widely applied by primary care physicians who manage diabetes and hypertension with success [11]. The CCM targets the chronic nature of opioid addiction with a proactive care approach that encompasses preventive services in primary care settings and is attuned to the frequent monitoring of the chronic and relapsing characteristics of opioid addiction. Ideally, the care should be led by the primary care provider with a single, integrated treatment plan that addresses and integrates the whole patient's medical needs, including the treatment of other co-morbid conditions. The adoption of modern health information technology (HIT) can greatly facilitate patient monitoring and CCM care coordination.

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