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Review article

Use of Buprenorphine in treatment of refractory depression—A review of current literature

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ABSTRACT

Objective: Current treatment strategies for depressive disorders have limited efficacy, leaving many patients unimproved or with significant residual symptoms. The development of additional treatments represent a significant unmet need for providers. Several lines of evidence suggest that the opioid system may be involved in regulation of mood and incentives salience. Intervention based on modifying central opioid receptors may represent a novel approach to treatment of depressive disorders among those unresponsive to accepted treatments.
Data sources: We searched the English language literature using keywords: Buprenorphine AND Major Depression; Buprenorphine AND Bipolar Depression; Buprenorphine AND Affective Disorders.
Results: Use of low dose buprenorphine as augmentation of pharmacotherapy for depression has shown promise in several reported studies. Effect size of available randomized controlled studies is comparable if not greater than most accepted augmentation strategies.
Conclusion: Review of available literature on the use of buprenorphine in individuals with treatment resistant depression demonstrated efficacy in the treatment of depressive disorders. Further prospective randomized controlled trials should be undertaken to evaluate the efficacy of buprenorphine as an adjunct for depression refractory to current pharmacotherapies.

Contents

1. Background

Depressive disorders are highly prevalent worldwide with a lifetime prevalence of 21% within the population of the United States (Kessler et al., 2005) and at least 15% globally. Depression increases the risk for death by suicide, is a factor affecting the course of many chronic medical illnesses resulting in increased disability, burden of disease and contribution significantly to morbidity, and mortality (Bromet et al., 2011; Ferrari et al., 2013).

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Analysis of large naturalistic clinical trials has shown the limits of current treatments for depression (Gaynes et al., 2009; APA, 2010). The development of new approaches for treatment refractory depression (TRD) has been identified as a significant unmet need among psychiatric providers (Zarate et al., 2013) with an estimated prevalence of 30% of subjects failing to respond to current recommended treatments (Hirschfeld et al., 2002). Electroconvulsive Therapy (ECT) has response rates of 50–75% in this patient population leaving a percentage of 10–20% who are unresponsive (TRD) (Prudic et al., 1996).

The antidepressant and mood elevating effects of opiate medications have been recognized for decades (Berrocoso et al., 2009; Tenore, 2008). In the 19th century, the "opium cure" for melancholia was the first systematic psychiatric pharmacotherapy with defined indications and dosages (Webber et al., 1988). Until replaced by the MAOIs and tricyclic antidepressants in the 1950s, opiates were considered first line for treatment of major depression (Berrocoso et al., 2009). Since introduction of the antidepressants, investigations of the use of opiates for treatment of depression have been limited (Emrich et al., 1982; Mongan and Callaway, 1990; Bodkin et al., 1995; Callaway, 1996; Resnick and Falk., 1987; Kosten et al., 1990; Gerra et al., 2006; Nyhuis et al., 2008; Karp et al., 2014; Fava et al., 2016; Yovell et al., 2016; Ehrich et al., 2015). Basic scientists however, have produced accumulating evidence for the involvement of the endogenous opioid system in affective disorders (Webber et al., 1988). A bidirectional relationship has been described between sensory generation and central perception of painful experiences. This connection can be explained by established shared neural networks. Public concerns over opioid abuse potential, dependence and dangers in overdose had led to the avoidance of such medications until the 1980s. Since the 1950s, agents with agonist-antagonist or partial agonist activity have emerged (SAMHSA, no date) as alternatives to conventional opioids. The effect of these agents has effects on mood and influences the organization of incentives to activation of behaviors with consequences for reward and pleasure.

Activation of reward centers by these agents might have implications for treatment of depressive disorders where diminished hedonic response is involved.

2. Methodology

This review of literature complies with the criteria provided in the Preferred-Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). A Medline literature search (1980–2016) was conducted using the keywords: Buprenorphine AND Major Depression; Buprenorphine AND Bipolar Depression; Buprenorphine AND Affective Disorders. Results were supplemented by references gleaned from citations of search returns and credible online sources. Based on pre-established criteria, only English literature pertaining to humans was considered. Due to paucity of quality available studies, all available studies reporting the use of low dose Buprenorphine in augmentive treatment of mood disorders, with outcome measure analysis, were reviewed. Studies involving both opioid dependent and naïve individuals were included (Fig. 1).

The aim of this broad review is to provide an overview of all currently available outcome studies involving the use of Buprenorphine in augmentative treatment of mood disorders (Table 1).

3. Endogenous opioid system in affective disorders

Depressive disorders have been associated with dysregulation of the endogenous opioid system, particularly the mu and kappa opioid receptor tone (Kennedy et al., 2006; Carlezon et al., 2009). Agonists at the mu receptors are known to release both serotonin and dopamine in CNS. There has been increasing interest in the role of the kappa receptor as a regulator of mood and motivation

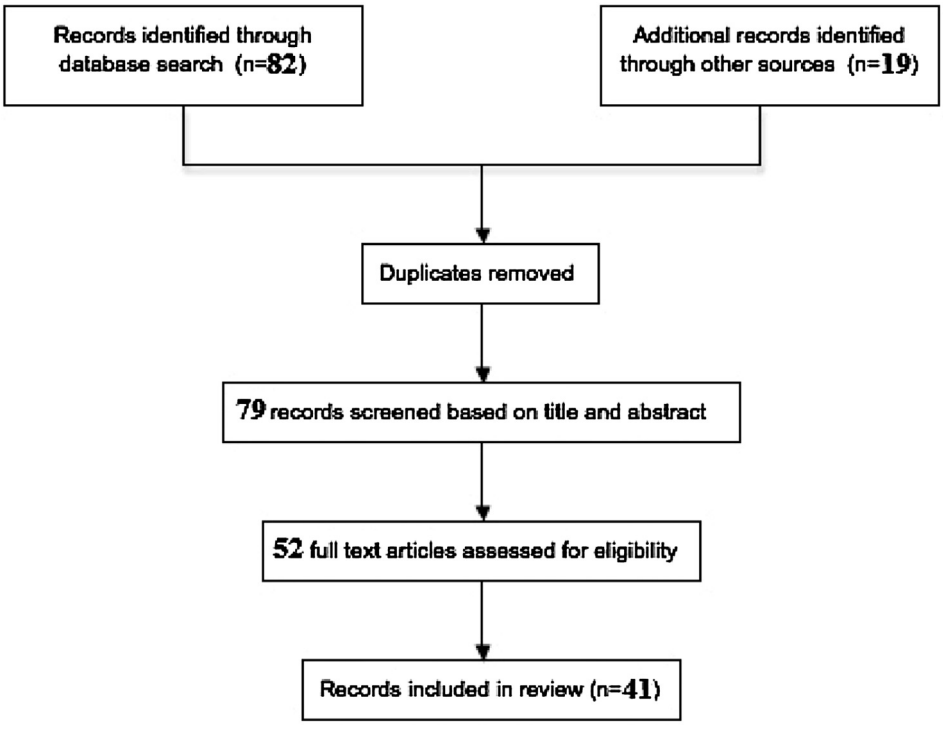

Fig. 1. Flow diagram outlining selection of studies.