Heroin anticraving medications: A systematic review

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To link to this article: http://dx.doi.org/10.3109/00952990.2010.505991

Published online: 19 Oct 2010.
Heroin Anticraving Medications: A Systematic Review

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**Background:** Heroin craving is a trigger for relapse and dropping out of treatment. Methadone has been the standard medication for the management of heroin craving. **Objectives:** We explored the medication options other than methadone which may have heroin anticraving properties. **Methods:** To be selected for the review, articles had to include outcome measures of the effect of the studied medication on subjective and/or objective opiate craving and be of the following two types: (1) randomized, controlled, and/or double-blind clinical trials (RCTs) examining the relationship between the studied medication and heroin craving; (2) nonrandomized and observational studies (NRSs) examining the relationship between the studied medication and heroin craving. Thirty-three articles were initially included in the review. Twenty-one were excluded because they did not meet the inclusion criteria. We present the results of 12 articles that met all the inclusion criteria. **Results:** Some new medications have been under investigation and seem promising for the treatment of opiate craving. Buprenorphine is the second most studied medication after methadone for its effect on opiate craving. At doses above 8 mg daily, it seems very promising and practical for managing opiate craving in patients receiving long-term opioid maintenance treatment. **Conclusions and Scientific Significance:** In doses higher than 8 mg daily, buprenorphine is an appropriate treatment for opiate craving. More research with rigorous methodology is needed to study the effect of buprenorphine on heroin craving. Also more studies are needed to directly compare buprenorphine and methadone with regard to their effects on heroin craving.

**Keywords:** heroin, anticraving, medications

**INTRODUCTION**

Craving is a subjective phenomenon that may be defined as an increased desire to use drugs or alcohol while being drug abstinent. It is associated with the use of substances that have reward-reinforcing (euphoric) properties such as alcohol, cocaine, and heroin. Although craving is a subjective phenomenon, it can be triggered by environmental factors such as being exposed to drug-related cues. In the case of heroin, craving may occur because of the need to alleviate withdrawal symptoms (negative craving) or an increased desire to use heroin because of its euphoric effect (positive craving). A number of imaging studies have examined the physiologic correlates of craving. Zijlstra et al. (1) reported in their imaging study using single photon emission computed tomography (SPECT) that opiate-dependent subjects had lower baseline dopamine (DA) type 2 receptors (D2R) in the left caudate nucleus compared with normal subjects. They also found that opiate-dependent subjects demonstrated higher DA release after cue-exposure in the right putamen than controls. They added that chronic craving and anhedonia were positively correlated with DA release. They suggested that the treatment strategies that increase D2Rs may, therefore, be an interesting approach to prevent relapse in opiate addiction. Sell et al. (2) used positron emission tomography (PET) to study brain activity in opiate addicts being exposed to heroin-related and neutral cues. They found that the self-reports of “urge to use” correlated strongly with increased regional blood flow in the inferior frontal and orbitofrontal cortex target regions of the mesolimbic dopaminergic system implicated in conditioning and reward. Xiao et al. (3) studied brain activity in a group of thirsty heroin addicts being exposed to water and drug-related cues using functional magnetic resonance imaging (fMRI). They found that drug-related cues activated bilateral inferior frontal cortex confirming the critical role of prefrontal cortex in opiate craving. Their results suggest that heroin craving may involve different neural circuits other than the desire to basic physiological derives, such as thirst. Shi et al. (4,5) reported in two studies that methadone maintenance treatment (MMT) reduces cue-induced heroin craving. They assessed craving by a 10-point visual analog scale (VAS) (6–7), where participants were asked “how much do you feel the urge to use heroin.” In their most recent study (5), brain-imaging PET was used to study the integrity of the striatum DA neurons in patients receiving MMT and in patients with prolonged abstinence compared with normal people. They found that there is a long-lasting impairment...
in the striatal DA neurons (DA transporter uptake in bilateral putamen but not in bilateral caudate), which is more prominent in methadone-maintained patients compared with patients with prolonged abstinence. However, heroin craving was significantly less in patients receiving MMT. Therefore, despite the efficacy of MMT in reducing subjective heroin craving, it may prolong the recovery process of the striatum DA neurons in the brain of recovering addicts. Langleben et al. (8) also studied heroin craving using fMRI in methadone-maintained patients. They postulated that the medial prefrontal cortex and the extended limbic system in methadone-maintained patients with a history of heroin dependence remains responsive to salient drug cues, which suggests a continued vulnerability to relapse.

One may speculate from these studies that heroin-dependent patients may have structural and functional brain abnormalities, which could increase their risk for heroin craving and relapse. This may also be the case of the patients receiving MMT. We reported in a recent review study (9) that methadone may help with heroin craving but patients receiving MMT may still be at risk of cue-induced heroin craving and relapse. Methadone has been the standard treatment of heroin dependence since the 1960s (10,11). Despite the effectiveness of methadone in reducing heroin use (12–16), there have been reports about patients using heroin while receiving MMT (17–19). Opiate craving may play a factor for the continued use of heroin despite receiving MMT. Craving could be a trigger for relapse and dropping out during any phase of treatment. Therefore, we wanted to conduct a literature review to explore the medication options other than methadone, which may play a role in reducing heroin craving.

METHODS

Literature Search

Studies eligible for inclusion in the review were retrieved from the PubMed® database from 1965 to September 2009 using the major medical subject headings “Methadone” (all fields) and “craving.” Only articles written in English language were included. Additional reports were identified from the reference lists of retrieved articles, as well as by manual review of the tables of contents of journals on drug of abuse included in the psychiatry and substance abuse subject category listing 2009 of the Journal Citation Reports®. Abstracts of medical meetings were excluded.

Selection, Extraction, and Collection of Data

To be selected for the review, articles had to include outcome measures of the effect of the studied medication on subjective and/or objective opiate craving and be of the following two types:

1. Randomized, controlled, and/or double-blind clinical trials (RCTs), examining the relationship between the studied medication and heroin craving.

2. Nonrandomized and observational studies (NRSs), examining the relationship between the studied medication and heroin craving.

Case reports were excluded from the review.

OUTCOME MEASURES

1. Effect of opiate agonist medications on subjective and/or objective opiate craving.

2. Effect of opiate antagonist medications on subjective and/or objective opiate craving.

3. Effect of DA antagonist medications on subjective and/or objective opiate craving.

4. Effect of other (experimental) medications on subjective and/or objective opiate craving.

RESULTS

Thirty-three articles were initially included in the review. Twenty-one were excluded because they did not meet the inclusion criteria. We present the results of 12 articles that met all the inclusion criteria (Table 1).

Effect of Opiate Agonist Medications on Subjective and/or Objective Opiate Craving

Six studies (22,27–31) explored the effect of the opiate agonist medication (buprenorphine) on subjective and/or objective opiate craving. Four studies reported that buprenorphine may decrease heroin craving and two studies reported that lower doses of buprenorphine may not be effective for the reduction of heroin craving.

Effect of Opiate Antagonist Medications on Subjective and/or Objective Opiate Craving

Two studies (23,24) explored the effect of opiate antagonist medication (naltrexone) on subjective and/or objective opiate craving. They reported that naltrexone did not reduce heroin craving.

Effect of DA Antagonist Medications on Subjective and/or Objective Opiate Craving

One study (26) explored the effect of DA antagonist medications on subjective and/or objective opiate craving. This study reported that the DA antagonist (Haldol) did not reduce heroin craving.

Effect of Other (Experimental) Medications on Subjective and/or Objective Opiate Craving

Three studies (20,21,25) explored the effect of other (experimental) medications on subjective and/or objective opiate craving.
TABLE 1.
Articles that studied heroin anticraving medications.

<table>
<thead>
<tr>
<th>References</th>
<th>Sample/techniques used to study craving</th>
<th>Medication (anticraving) studied</th>
<th>Conclusions</th>
</tr>
</thead>
</table>
| Shi et al. (20) | – Number: 60  
– Imaging: none  
– Craving scales: VAS  
– Lab.: none  
– Others: HAMA, BDI, BP, HR | Rapamycin | • A single high dose of rapamycin (5 vs. 2.5 mg) significantly reduces the craving but not anxiety induced by drug-related cues  
• These findings suggest that rapamycin merits outpatient clinical trials as a possible pharmacotherapy for relapse prevention from drug-related cue-induced craving |
| Shi et al. (21) | – Number: 45  
– Imaging: none  
– Craving scales: VAS  
– Lab.: none  
– Others: HAMA, BDI, BP, HR | Tetrodotoxin (TTX) | • Low-dose TTX (10 µ gram) is acutely effective in reducing cue-induced increases in heroin craving and associated anxiety |
| White et al. (22) | – Number: 12  
– Imaging: none  
– Craving scales: VAS  
– Lab.: UDS  
– Others: SOWS, OOWS | Probuphine | • Probuphine implants provided continuous steady-state delivery of buprenorphine until their removal at 6 months. Withdrawal and craving remained low throughout the 6 months. These results suggest that probuphine implants offer significant promise for enhancing delivery of effective opioid substitution treatment while minimizing risk for abuse of medication |
| Hyman et al. (23) | – Number: 14  
– Imaging: none  
– Craving scales: VAS  
– Lab.: none  
– Others: differential emotion scale, BPP | Naltrexone | • Naltrexone-treated opioid abusers demonstrated vulnerability to stress and drug cue-induced craving and arousal responses that may contribute to the high rates of noncompliance and relapse among opioid dependent individuals undergoing naltrexone treatment |

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### TABLE 1. (Continued)

<table>
<thead>
<tr>
<th>References</th>
<th>Sample/techniques used to study craving</th>
<th>Medication (anticraving) studied</th>
<th>Conclusions</th>
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</thead>
<tbody>
<tr>
<td>Dijkstra et al. (24)</td>
<td>– Number: 272</td>
<td>– Naltrexone</td>
<td>• Use of opiates is associated with increased craving and abstinence is associated with less craving, independent of the use of naltrexone</td>
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<tr>
<td></td>
<td>– Imaging: none</td>
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<td></td>
<td>– Craving scales: VAS</td>
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<td></td>
<td>– Lab.: UDS</td>
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<td></td>
<td>– Others: ASI, OCUUS, DDQ</td>
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<tr>
<td>Comer and Sullivan (25)</td>
<td>– Number: 12</td>
<td>– Memantine</td>
<td>• Memantine was well tolerated and modestly effective in reducing the subjective craving but not the reinforcing effect of heroin</td>
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<tr>
<td></td>
<td>– Imaging: none</td>
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<tr>
<td></td>
<td>– Craving scales: VAS, HCQ</td>
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<tr>
<td></td>
<td>– Lab.: UDS</td>
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<tr>
<td></td>
<td>– Others: DEQ, BP, pupil photo</td>
<td></td>
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<tr>
<td>Franken et al. (26)</td>
<td>– Number: 17</td>
<td>– Haloperidol 2 mg vs. placebo</td>
<td>• The improvement on the general selective attention with haloperidol in heroin users can be interpreted as evidence that the dopamine levels are increased during the Stroop Task test with placebo</td>
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<td></td>
<td>– Imaging: None</td>
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<tr>
<td></td>
<td>– Craving scales: Desire for DDQ</td>
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<td></td>
<td>– Lab.: None</td>
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<td></td>
<td>– Others: Emotional Strop Task</td>
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<td>to assess cognitive processing of drug cues.</td>
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<tr>
<td>Fudala et al. (27)</td>
<td>– Number: 326</td>
<td>– Buprenorphine with or without Naloxone</td>
<td>• Buprenorphine and naloxone in combination and buprenorphine alone are safe and reduce the use of opiates and the craving for opiates among opiate-addicted persons who receive these medications in an office-based setting</td>
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<tr>
<td></td>
<td>– Imaging: none</td>
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<td></td>
<td>– Craving scales: VAS</td>
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<td></td>
<td>– Lab.: UDS</td>
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<td></td>
<td>– Others: None</td>
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<tr>
<td>Greenwald et al. (28)</td>
<td>– Number: 14</td>
<td>– Buprenorphine</td>
<td>• High-dose buprenorphine (16 mg vs. 2 and 4 mg) attenuated opioid drug-seeking behavior,</td>
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<tr>
<td></td>
<td>– Imaging: none</td>
<td></td>
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<tr>
<td></td>
<td>– Craving scales: HCQ</td>
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<td></td>
<td>– Lab.: UDS</td>
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<tr>
<td>Comer et al. (29)</td>
<td>– Number: 18</td>
<td>– Buprenorphine</td>
<td>* The results of this study demonstrated that the reinforcing effects of heroin were not fully antagonized by these doses (8 vs. 16 mg) of the tablet formulation of buprenorphine and that 16 mg reduced heroin self-administration relative to 8 mg.</td>
</tr>
<tr>
<td></td>
<td>– Imaging: none</td>
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<td>– Craving scales: VAS</td>
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<td>– Lab.: UDS</td>
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<td>– Others: SOWS, DEQ, VS, pupil photo</td>
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<tr>
<td>Greenwald et al. (30)</td>
<td>– Number: 14</td>
<td>– Buprenorphine</td>
<td>* Heroin craving among nonabstainers (those who remained heroin-positive during study) was significantly higher compared with abstainers (those who remained drug-free during the study) and was reduced in dose-related manner by hydromorphone (HYD) injections.</td>
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<tr>
<td></td>
<td>– Imaging: none</td>
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<tr>
<td></td>
<td>– Craving scales: HCQ, VAS</td>
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<tr>
<td></td>
<td>– Lab.: UDS</td>
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<tr>
<td></td>
<td>– Others: pupil photo, VS, w/d questionnaire, ARCI</td>
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*(Continued)*
craving. Those studies reported that those three experimental medications (rapamycin, tetrodotoxin, and memantine) may reduce heroin craving at various degrees.

**DISCUSSION**

**Effect of Opiate Agonist Medications on Subjective and/or Objective Opiate Craving**

In this review we tried to explore opiate agonist medication options other than methadone that may have heroin anticraving properties. Our results demonstrated that buprenorphine is the second most studied medication after methadone for heroin anticraving properties. A total of six studies (22,27–31) tested the effect of buprenorphine on subjective heroin craving. None of those studies used imaging to correlate the self-reported subjective craving with brain imaging as an objective measure for craving. Also none of those studies used cue-elicited paradigms to measure craving for patients on buprenorphine maintenance treatment. Despite these limitations the studies provided valuable information about the potential efficacy of buprenorphine in reducing opiate craving. Four studies reported that buprenorphine is an effective medication for reducing heroin subjective craving. White et al. (22) used a long-acting buprenorphine implants (probuphine) for a period of 6 months and tested its safety, efficacy in reducing heroin self-administration, and craving. Craving for heroin was assessed using a 100-mm VAS that asks respondents to quantify their desire for heroin by marking a linear visual scale from 0 to 100. They found that probuphine implants provided continuous steady-state delivery of buprenorphine until their removal at 6 months. Withdrawal symptoms and craving remained low throughout the 6 months. These results suggest that probuphine implants offer significant promise for enhancing delivery of effective opioid substitution treatment while minimizing risk for the abuse of medication.

Fudala et al. (27) used buprenorphine alone and in combination with naloxone in a multicenter placebo-controlled trial to measure illicit heroin use and craving. They also used the VAS to measure heroin craving. Participants were asked to rate “the most intense craving I ever had” during the preceding 24 hours on a 100-mm VAS. They found that buprenorphine and naloxone in combination and buprenorphine alone are safe, reduce the use of opiates and the craving for opiates among opiate-addicted persons who receive these medications in an office-based setting. Greenwald et al. (28) compared low-dose buprenorphine (2 and 4 mg) to high-dose (16 mg) for drug-seeking behavior and subjective craving. They used the heroin-craving questionnaire (HCQ) to measure craving. They found that high-dose buprenorphine attenuated opioid drug-seeking behavior, heroin-craving self-reports, and increased sensitivity to alternative reinforcement. Ling et al. (31) in another multicenter study also found that higher doses of buprenorphine (8 mg) were associated with significantly better retention, illicit drug use, and craving compared with lower doses (1 mg). They

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**TABLE 1.**

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<th>Conclusions</th>
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</thead>
<tbody>
<tr>
<td>Ling et al. (31)</td>
<td>– Number: 735</td>
<td>– Buprenorphine</td>
<td>• Outcomes in the 8-mg group were significantly better than in the 1-mg group in all four efficacy domains (retention, illicit drug use, craving, and global rating by patient and staff)</td>
</tr>
<tr>
<td></td>
<td>– Imaging: none</td>
<td></td>
<td>• The findings support the safety and efficacy of buprenorphine and suggest that an adequate dose of buprenorphine will be a useful addition to pharmacotherapy</td>
</tr>
</tbody>
</table>

VAS, visual analog scale; HAMA, Hamilton anxiety scale; BDI, Beck depression inventory; BP, blood pressure; HR, heart rate; UDS, urine drug screen; SOWS, subjective opiate withdrawal scale; OOWS, objective opiate withdrawal scale; P, pulse; ASL, addiction severity index; OCDUS, obsessive compulsive drug use scale; HCQ, heroin-craving questionnaire; DDQ, drug desire questionnaire; DEQ, drug effects questionnaire; w/d, withdrawal; ARCI, addiction research center inventory.
measured subjective craving by asking participants about opioid craving at any time during the past 7 days and marking it on 100-mmVAS.

Two studies (30,31) reported that lower doses of buprenorphine (8 mg or less) may not be effective in reducing heroin craving. Comer et al. (29) compared buprenorphine 8–16 mg to study the effect of those doses on heroin self-administration and craving. They used the VAS to measure subjective craving. Participants were asked along a 100-mm line, how much they “wanted” heroin, cocaine, alcohol, and tobacco. They found that the reinforcing effects of heroin were not fully antagonized by these doses (8 vs. 16 mg) of the tablet formulation of buprenorphine and that the 16 mg reduced heroin self-administration relative to 8 mg. They also found that ratings of “wanting heroin” as a measure of craving were consistently elevated when measured by the VAS. Greenwald et al. (30) tested in an earlier study (1999) the heroin craving in two groups of volunteers receiving buprenorphine maintenance (2, 4, and 8 mg). The first group (abstinent) was drug-free during the period of study and the other group tested positive for heroin (nonabstinent). They used the HCQ to measure craving. They found that heroin craving among nonabstainers was significantly higher compared with abstainers and was reduced in dose-related manner by hydromorphone injections. One may speculate from these studies that lower doses of buprenorphine may not be as effective as higher doses in reducing opiate craving.

Overall buprenorphine seems to be a promising medication for alleviating heroin craving. It is a partial mu-opioid receptor agonist that may not trigger euphoria and priming for opiate use (32). It was approved in the United States in October 2002 for an office-based treatment of opiate dependence (33–35). The availability of buprenorphine has opened a new avenue for the treatment of opiate dependence in addition to methadone. Methadone was the only option for the maintenance treatment since the 1960s. Several studies compared buprenorphine to methadone to test their efficacy in reducing heroin self-administration and retention in treatment (36–48). There are only few studies that directly compared buprenorphine to methadone to explore their effect on heroin craving (49,50). Some studies have used cue-elicited paradigms (51–58) and brain imaging (4,5) to test craving in patients receiving MMT. There are no data about using these techniques for patients receiving buprenorphine maintenance. In general, more research has been done on methadone compared with buprenorphine regarding their effect on heroin craving. Most probably, this is due to the availability of methadone in the market for more than four decades. Buprenorphine may provide an alternative to methadone for the management of opiate craving. Some patients may not qualify for MMT, for example, patients with cardiac arrhythmias (59) or other chronic medical conditions (60). In other circumstances, availability may play a role in the selection of the opioid agonist medication. For example, physicians who practice in rural areas may not have access to methadone clinics and rely only on buprenorphine for office-based opiate agonist treatment. Patient preference or side effects could be other factors for the selection.

Effect of Opiate Antagonist Medications on Subjective and/or Objective Opiate Craving

Two studies (23,24) tested the effect of naltrexone on heroin craving. They both used the VAS to measure opiate craving in patients receiving naltrexone maintenance. After an imagery condition, participants were asked to rate “how clearly and vividly they were able to imagine the scenario on VAS of 0–10 or to rate their craving for drugs on a 100-mm horizontal line from no craving to extreme craving” (23). Both studies reported that naltrexone did not reduce heroin craving. Hyman et al. (23) reported that naltrexone-treated opioid-dependent individuals were vulnerable to stress, drug cue-induced craving, and arousal responses. They added that these responses may contribute to the high rates of noncompliance and relapse among opioid abusers or opioid-dependent individuals undergoing naltrexone treatment. Dijkstra et al. (24) reported that the use of opiates is associated with increased craving and abstinence is associated with less craving, independent of use of naltrexone. These data demonstrate that naltrexone may not be an optimal medication for targeting opiate craving.

Effect of DA Antagonist Medications on Subjective and/or Objective Opiate Craving

Franken et al. (26) used a single dose of Haldol (2 mg) to test its effect on heroin craving. They used the drug desire questionnaire (DDQ) to test heroin craving. They also used the emotional Stroop test to assess cognitive processing of drug cues. They assumed that the improvement on the general selective attention with Haldol (DA antagonist) in heroin users may reduce heroin craving and can be interpreted as evidence that the DA levels are increased during the Stroop Task test with placebo. However, the study was unable to confirm that DA antagonist could reduce cue-elicited cravings.

Effect of Other (Experimental) Medications on Subjective and/or Objective Opiate Craving

Three studies (20,21,25) tested the effect of new medications on opiate craving. Those studies showed promising results. Shi et al. tested the effect of rapamycin and tetrodotoxin (TTX) on cue-induced heroin craving in two identical studies in China. Craving was assessed by a 10-point VAS where participants were asked “how much do you feel the urge to use heroin.” It was reported that rapamycin (20) has been tested in animals and theoretically it inhibits the mTOR (serine-threonine kinase enzyme that controls cell growth) pathway and, thereby, prevents various types of synaptic plasticity and the associated conditioning and memory formation (61,62). Also, in a conditioned place preference animal model, it was found that the
inhibition of the mTOR signaling pathway completely eliminated conditioned place preference for the drug. Therefore, Shi et al. proposed that rapamycin may reduce craving related to heroin cues in abstinent heroin addicts. They found that a single high dose of rapamycin (5 vs. 2.5 mg) significantly reduces the craving but not anxiety induced by drug-related cues. This finding suggests that rapamycin merits outpatient clinical trials as a possible pharmacotherapy for the relapse prevention from drug-related cue-induced craving.

TTX is a neurotoxin found in puffer fish and other marine animals. It was reported that when it was injected into the basolateral amygdala in rats, it abolished the ability of heroin-paired stimuli and heroin priming to reinstate responding for heroin (63). Also systemic administration of TTX significantly inhibited morphine withdrawal symptoms in rats and mice (64). Shi et al. (21) assessed the effect of a single intramuscular dose of TTX on cue-induced heroin craving and anxiety in abstinent heroin addicts. They found that low-dose TTX (10 μg) is acutely effective in reducing cue-induced increases in heroin craving and associated anxiety. At higher doses TTX could have suppressive effects on the respiratory and cardiovascular systems and, therefore, its therapeutic use has been limited. However, in this study it was found to be safe and has no adverse effects on respiration or cardiovascular system.

Comer and Sullivan (25) studied memantine effect on heroin craving. They used HCQ to measure heroin craving in patients maintained on memantine. Memantine is a noncompetitive NMDA receptor antagonist. It has been used in the treatment of Alzheimer’s disease and other neurological diseases. Memantine has been reported to inhibit morphine-conditioned place preference in rodents (65). Also it blocked morphine-induced reinstatement of conditioned place preference (66). They found that it was well tolerated and modestly effective in reducing the subjective craving but not the reinforcing effect of heroin. They postulated that although it is unlikely that memantine will be useful as a stand-alone maintenance medication for opioid dependence, it may have some utility as an adjunct treatment medication.

These new medications seem promising for the management of heroin craving. However, they are still in the experimental phase and more research is needed before they should be considered as an option for the treatment of opiate craving.

In conclusion, some new medications have been under investigation and seem promising for the treatment of opiate craving. Buprenorphine is the second most studied medication after methadone for its effect on opiate craving. Buprenorphine has many qualities that make it an effective treatment for opiate craving. It is a partial mu-receptor agonist that may hinder priming for opiates and is safe in overdose (32). It has kappa-receptor antagonistic properties that may improve dysphoric mood in this population (67). Sometimes dysphoria could be a trigger for craving and illicit drug use. At doses above 8 mg daily, it seems very promising and practical for managing opiate craving in patients receiving long-term opioid maintenance treatment, particularly for those who may not qualify for or desire MMT. Buprenorphine induction is easy, even for physicians with limited experience with opioid maintenance treatment (68). In 2005, the substance abuse and mental health service administration (SAMHSA) started funding a project to provide a support system for physicians who are willing to prescribe buprenorphine for office-based opioid agonist treatment. The American Society of Addiction Medicine (ASAM) implemented the project and called it the Physician Clinical Support System (PCSS). PCSS is established to offer peer mentorship for physicians who obtained the waiver to prescribe buprenorphine in the United States (69). Now, buprenorphine has been available in the United States for about 7 years. Many patients and physicians became familiar with buprenorphine. Many of the state Medicaid programs approved it for the office-based treatment of opioid dependence, and it became available on the formulary of the veteran administration health system (70). Overall buprenorphine maintenance treatment became available for a wider population of patients.

More research with rigorous methodology is needed to study the effect of buprenorphine on heroin craving. Also more studies are needed to directly compare buprenorphine and methadone with regard to their effects on heroin craving.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES


