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Opioid Maintenance Treatment: Methadone, Buprenorphine, and Naltrexone
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Abstract
Opioid dependence plagues the United States with millions of people suffering from the effects. Throughout recent years, there has been a surge in research in treatment options for patients suffering from opioid dependence. Three medications have stood out: methadone, buprenorphine, and naltrexone. The purpose of this study was to investigate the three and decipher which provides the best outcomes for patients. Research was conducted by reviewing literature via PubMed, PsychINFO and Cochrane. A review of the literature found that methadone has been used the longest and has been shown to be efficacious, but can be severely limiting for patients due to lack of clinics and the need for daily dosings. As a result, buprenorphine was developed as an alternative medication with similar efficacy and retention rates to combat the daily dosages and provide a more readily available medication. Unfortunately buprenorphine also has geographical limitations. Naltrexone is the newest medication added to the mix. Orally, it has poor retention, but an extended release form has been developed that is showing promise. There are no geographical limitations associated with naltrexone and the extended release form allows for only monthly injections. Going forward with opioid treatment, medications like naltrexone and those that are more readily available will become more widely used for treatment as patient preference is pointing towards medications that are not limited by geography or frequent dosing.

Introduction
• Opioid addiction plagues our country. Short term opioid use has been shown to be beneficial for patients, but many of those patients continue to receive opioids for years (Lembke, Humphreys, & Newmark, 2016). The addiction ranges from patients receiving chronic opioid prescriptions to those buying them on the street and abusing. This epidemic has become a significant public health problem. There is increased morbidity and mortality associated with opioid use, as well as an increase in the spread of HIV and hepatitis (Nisen et al., 2016).• Opioid maintenance therapy has been shown to reduce the use of abused opioids. Patients are able to return to normal social functioning and decrease their criminal activity. This also decreases the transmission of infectious diseases such as HIV and hepatitis (Nunes et al., 2015).• The Substance Abuse and Mental Health Services Administration endorses three medications to use for opioid maintenance treatment: buprenorphine, methadone, and naltrexone. While all three have their benefits and their challenges, this researcher has reviewed the current literature to make an informed decision as to which is the best treatment option of the three (buprenorphine, methadone, and naltrexone) for patients in need of opioid maintenance treatment.

Statement of the Problem
• With the increasing opioid addiction epidemic in our country, effective treatment options are necessary to reverse the trend. Many different pharmacological options are available for opioid maintenance therapy, but research is needed to show which medication has the best efficacy taking into factor such aspects as relapse rates and patient compliance.

Research Question
• Of the three pharmacological opioid maintenance therapy options endorsed by the Substance Abuse and Mental Health Services administration: methadone, buprenorphine, and naltrexone, which has the best outcomes for patients taking into account efficacy, retention rate, availability, and patient preference?

Literature Review
A review of the literature provided the following main points:
- Methadone
  - Schukit (2016) states that methadone is superior to placebo for both managing withdrawal and retention in treatment plans.
  - Per Uebelaker et al. (2015), patients do not feel that methadone is the best treatment option, noting barriers such as location and time. They do not feel they are drug free.
- Buprenorphine
  - Nielsen et al. (2016) found that buprenorphine and methadone have similar retention and efficacy, but that buprenorphine may be safer as it has less sedation and respiratory depression.
  - Lobmaier et al. (2013) discussed the abuse potential of buprenorphine and as such recommend the combination of buprenorphine and naltrexone.
- Naltrexone
  - Rosenthal (2013) researched an implantable form of buprenorphine that was found to be three times as effective as placebo and similar to sublingual buprenorphine.
  - Lobmaier et al. (2010) found that oral naltrexone is similar only to placebo except in highly motivated individuals for treatment.
  - Nunes et al. (2015) researched an extended release form that has significantly better outcomes than placebo and oral. At 24 weeks, 80% of patients had drug free urines as compared to 15% on placebo.

Discussion
Methadone has been used the longest for opioid maintenance treatment. It is tried and true, but patient preference is poor. Patients are limited by location of methadone clinics and the daily dosages.

Buprenorphine is a newer medication, but has shown similar retention and efficacy to methadone. Providers are still limited by certification, but not location so are more abundant. Dosage is not daily.

Naltrexone is the newest treatment of the three. It is little better than placebo as an oral medication, but has shown promise in extended release and implantable forms. These forms allow for at least a month of treatment per dose and have also been used to discontinue the use of buprenorphine. There is no limitations to prescribers.

Naltrexone allows for more patient autonomy and reduces the time and travel barriers seen with buprenorphine and methadone. It can bring opioid treatment to rural areas that otherwise were without.

Medications for Rehabilitation from an Opioid-Use Disorder, According to the Patient’s Treatment Goal.

<table>
<thead>
<tr>
<th>Stage of Function</th>
<th>Full Abstinence from Opioids</th>
<th>Opioid Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Naltrexone</td>
<td>Buprenorphine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Action</th>
<th>Naltrexone</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blocks opioid</td>
<td>high</td>
<td>Long-term maintenance with the use of an oral, long-acting opioid</td>
<td>Long-term maintenance with the use of an oral, long-acting opioid</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Restriction</th>
<th>Patient must be opioid-free</th>
<th>No misuse of depressant drugs or medical contraindications; can be used only in specialized programs, not in office-based practices</th>
<th>No misuse of depressant drugs or medical contraindications; can be used in office of physicians with special training</th>
</tr>
</thead>
</table>

Applicability to Clinical Practice
First and foremost, there must be a change in how opioids are prescribed by providers. CDC came out with revised guidelines in March of 2016 for primary care providers addressing when to prescribe, how to select, and how to assess and address risk with patients.

Treatment options must also change. Patient preference affects treatment and preference has been towards long acting medications that require little travel and little time constraints. Drugs like methadone need to be more readily available and have more effective delivery methods. This shift must be in attitudes towards opioid misuse. It is a chronic disease similar to hypertension and diabetes. Patients and providers alike must realize that like any other chronic disease, treatment may be on going.

References

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