DUR Capsules
News and Information for West Virginia Providers from the West Virginia Bureau for Medical Services (WVBMS)

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Topics Covered in This Issue

HEPATITIS C

Introduction

- Hepatitis C is an infection of the liver caused by the Hepatitis C Virus (HCV). It is currently the most common blood-borne virus in the Unites States and can be either acute or chronic. Chronic infections represent 70%–85% of all cases, with an estimated 2.7–3.9 million people in the United States being affected.
- There are six distinct genotypes with more than 50 subtypes of HCV. Treatment options and duration of therapy can differ depending on genotype and subtype. For this reason, testing is necessary to choose the most appropriate treatment regimen.

Recent Advancements in Care

- Despite the alarming number of affected persons in the country, advancements in treatment now offer the ability to cure more patients than ever before. These advances have made treatment regimens shorter in duration, better tolerated, and more effective.

- Until a few years ago, only two drugs were approved by the Food and Drug Administration (FDA) for hepatitis C treatment: pegylated interferon (peg-IFN) and ribavirin (RBV).
  - Peg-IFN is a weekly injection with significant side effects. Many patients with HCV were unable to tolerate it or stopped therapy due to these side effects.
  - RBV is a twice daily oral medication that must be used in combination with the peg-IFN to treat hepatitis C. Today, it is most often used in combination with one of the newly approved drugs.
- In December 2013, Sovaldi® (sofosbuvir) was the first drug that allowed patients with genotypes 2 and 3 to be treated with pills only, offering an interferon-free regimen with RBV.
- In October 2014, the FDA approved Harvoni® (ledipasvir/sofosbuvir), the first drug that allowed patients with genotype 1 to be treated with only one pill, eradicating the necessity for weekly injections of interferon or RBV. Cure rates for Harvoni are greater than 90% after a treatment duration of 8–12 weeks.
- In December 2014, Viekira Pak™ (ombitasvir/paritaprevir/ritonavir tablets; dasabuvir tablets) was approved. It is also an oral, peg-IFN-free regimen. Viekira Pak is approved for HCV/HIV co-infection and people who have had a liver transplant. Treatment lasts 12–24 weeks with a 95% cure rate.
- For a quick guide to all the current treatments, visit http://www.hepatitisc.uw.edu/page/treatment/drugs.
- Interferon therapy has largely been replaced by the newer and stronger oral medications in the United States, and its use is also expected to decrease in other countries as more all-oral treatment options become available.

Comparison of Newer Agents vs. Older Treatment Regimens

- New regimens are less complicated, more efficacious, carry fewer side effects, and have a shorter treatment duration than do the older regimens.
- **Treatment Duration**:
  - The shorter duration of therapy associated with the newer agents is linked to a greater rate of adherence. Peg-IFN-based treatment regimens last 12–18 months. Harvoni, for example, has a treatment duration of only 8–24 weeks.
- **Simplicity of Regimen**:
  - Peg-IFN is a weekly injectable agent and requires supplementation with twice daily ribavirin. Newer agents offer the ability to take all-oral medications, including once daily options.
- **Efficacy**:
  - Despite the lengthy treatment of interferon therapies, the virus is only cleared in about 50% of patients. Additionally, peg-IFN in not an option for patients with psychiatric conditions, liver failure, or autoimmune diseases. The newer agents have much greater cure rates and versatility.
- **Side Effects**:
  - New treatments such as Harvoni have a very mild side effect profile, with headache being the most common. This can easily be treated with acetaminophen or an aspirin. Older regimens with interferon cause flu-like symptoms such as fatigue, fever, chills, headache, and body aches. Cognitive changes, depression, and irritability are also common with interferon treatment. Due to the intolerability of the older regimens, many patients would

discontinue treatment, remaining infected. RBV can include side effects such as anemia that can worsen existing heart disease and lead to a heart attack.

- **Costs:**

  Due to the substantial costs of the new HCV therapies, healthcare resources have been shifted dramatically. The new therapies entered markets in 2014. As more agents have entered the market, costs have decreased; however, these therapies still warrant significant budgetary considerations. These new therapies cost around $80,000 per regimen and considering the slow progression of the disease in general, many states have opted to prioritize coverage to patients with liver complications or who fall into a high risk category for rapid progression of the disease. Recently, West Virginia BMS decreased the fibrosis threshold from F3 to F2 to expand benefits to more members. A full list of preferred regimens and the prior authorization request form may be found on the Agency's website: http://www.dhhr.wv.gov/bms/Programs/WaiverPrograms/IDDW/IDDProviderinfo/Documents/Hepatitis%20C%20Criteria%20v2017.1e.pdf.

NEONATAL ABSTINENCE SYNDROME

Introduction

Opiate use has increased dramatically in the United States in recent years. People in the United States consume opioid pain relievers (OPR) at a greater rate than any other nation in the world and consume twice as much per capita as the second ranking nation, Canada. In 2012, healthcare professionals dispensed an average of 82.5 opioid prescriptions per 100 persons nationally. West Virginia ranked third, dispensing an average of 137.6 opioid prescriptions per 100 persons in this report.[6] Because of the increase in OPR utilization, there has also been an increase in opioid-associated adverse effects including overdose, death, and infants born physically dependent on opiates. Neonatal Abstinence Syndrome (NAS) is a withdrawal syndrome that occurs in infants after in-utero exposure to opioids. The increase in NAS parallels the increase in OPR use in the United States, which suggests that preventing or decreasing opioid overutilization may help prevent or decrease the incidences of NAS.[7] The incidences of NAS within the United States has increased from 3.4 (95% CI: 3.2–3.6) per 1,000 hospital births in 2009 to 5.8 (95% CI: 5.5–6.1) per 1,000 hospital births in 2012, totaling 21,732 infants with the diagnosis in 2012. Aggregate hospital charges for NAS increased from $732 million to $1.5 billion from 2009 to 2012. Approximately 81% of NAS cases nationally were attributed to state Medicaid programs in 2012.[7] During 2016, 291 infants enrolled in West Virginia Medicaid were born and received a diagnosis of NAS. Historically, NAS was considered as a condition primarily affecting infants born to mothers who used illicit drugs during pregnancy, such as heroin. In more recent years, however, many of the infants affected by NAS were born to mothers who had used OPRs, which is due, in part, to the national opioid epidemic this nation is facing.[8] A few factors have been found to increase the risk and severity of NAS in opioid-exposed infants, including maternal use of chronic opioid pain relievers, concurrent tobacco use, and concurrent benzodiazepine and SSRI use during pregnancy.[9,10] Complications associated with NAS can include low birth weight, feeding difficulties, jaundice, irritability, transient tachypnea, meconium aspiration, respiratory distress syndrome, hypertonia, hyperthermia, autonomic instability, and seizures.[7,8,10] The complications associated with NAS contribute to longer length of stay (LOS) for infants affected by this syndrome. Patrick et al found that infants diagnosed with NAS had an overall mean LOS of 16 days, and those requiring pharmacologic treatment had a mean LOS of 23 days.[7] Longer LOS results in a greater economic burden and may have a negative effect on

maternal attachment. If NAS is suspected in an infant, the Finnegan scoring system is used to measure the severity of the symptoms and to determine if the infant needs pharmacologic interventions. Ultimately, the Finnegan scoring system assists healthcare providers in determining the following:

- Which infants require pharmacologic therapy
- How dosing should be escalated
- When weaning should occur

The Finnegan scoring system is a 31-item scale used to identify the presence and severity of different NAS symptoms and is performed every 3–4 hours. A score of ≥ 8 is highly suggestive of NAS. Typically, when an infant scores an 8 or higher on the Finnegan scale and does not respond to nonpharmacologic treatment, pharmacologic treatment of symptoms is warranted.

Treatment of NAS

Nonpharmacologic[6,7,10,11,12]

All infants at risk for developing NAS should be managed with a nonpharmacologic approach, which has been shown to decrease the severity of NAS and improve outcomes. Typical nonpharmacologic treatments include creating a quiet environment with decreased environmental stimulation, frequent hypercaloric feeds to minimize hunger and promote growth, rooming in, and the encouragement of breastfeeding when appropriate. Encouraging mothers of infants born with NAS to breastfeed has been shown to reduce symptoms and complications associated with NAS, reduce the need for pharmacologic treatment, increase mother and infant bonding and attachment, and may protect the mother against addiction relapse.[8,12]

Pharmacologic[6,7,10]

If the infant is not responsive to nonpharmacologic treatment options and has a Finnegan score of ≥ 8, most institutions will implement a pharmacologic approach. Pharmacologic treatment and care of infants with NAS varies from institution to institution. This is due in part to the absence of large, randomized trials comparing pharmacologic regimens. Lack of national treatment guidelines leaves protocol development and pharmacologic treatment options up to individual hospitals.[6,7] None of the current medications used to treat NAS are FDA approved for this indication but commonly used medications include morphine, methadone, phenobarbital, clonidine, and buprenorphine. The American Academy of Pediatrics, multiple Cochrane reviews, and other expert reviews have identified opioid replacement as first-line treatment for NAS, but there still remains no universal standard of care.[10] In some cases, hospitals will use a non-opioid first-line medication, while others may use a dual-agent approach. Typically, the same approach to treatment is used with any of the medications listed above: rapid up titration in dose to control symptoms followed by a gradual weaning of approximately 10% per day if symptoms of withdrawal allow. Once the infant has been successfully weaned, discharge can occur.

As the number of infants born with NAS continues to increase, changes in the way healthcare is managed need to be made to help address this public health issue. The sheer number of OPRs prescribed needs to decrease in order to reduce opioid exposure in general, especially in women of childbearing age. There is a need for more randomized, controlled clinical trials to help determine the most effective pharmacologic treatment approach to treating NAS. Institutional protocols should be developed and closely adhered to in order to increase the effectiveness of managing NAS while decreasing LOS and cost. Lastly, access to maternal treatment programs are essential. Guidance on how to manage pregnant women with OPR dependency is needed, similar to the literature

supporting medication-assisted treatment (MAT) in pregnancy that was developed in the context of heroin use.[8]

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