Antiphospholipid syndrome (APS) is a disease that destroys phospholipids, a type of fat. Without phospholipids in the blood, blood clots are more likely to form. Clots usually form in the legs, lungs, or brain. In women, clots from APS can lead to complications in pregnancy.

Approximately 40–50 people out of 100,000 have APS. It is usually diagnosed in young to middle-aged adults, and women are more likely to develop APS than men.

**What are the risk factors for APS?**
- Autoimmune diseases such as lupus or rheumatoid arthritis where the immune system mistakenly destroys healthy cells
- Infections such as syphilis, hepatitis C infection, or HIV infection
- Medications that treat heart problems (e.g., propranolol, quinidine, or hydralazine), medications that treat seizures (e.g., phenytoin), or medications that treat infections (e.g., amoxicillin)
- Relatives with APS

**What are the symptoms of APS?**
- Clots in the legs cause leg pain or swelling, sores, or lacy-like rash called livedo reticularis
- Clots in the lungs cause chest pain or difficulty breathing
- Clots in the brain cause arm or leg numbness, confusion, or headache
- Pregnancy complications like recurrent miscarriages or premature births

**How is APS diagnosed?**
APS is diagnosed based on symptoms and the detection of the antibodies that damage normal cells in your blood tests. Two blood tests separated by 12 weeks are required to confirm the diagnosis.

**What are the treatments for APS?**
Currently, there is no treatment to prevent the loss of phospholipids. The present treatment is the use of anticoagulants (blood thinners) to decrease the risk of forming clots.

Heparin or enoxaparin (Lovenox®) are two blood thinners commonly used to treat APS. These are injections that work quickly and are often started in combination with an oral blood thinner. It can take several days for oral blood thinners to work, so the injections are used to prevent clots during that time period. Once the oral blood thinner starts working, the heparin or enoxaparin injections are stopped while the oral blood thinner is continued.

Warfarin (Coumadin®) is the most common oral blood thinner. It is effective in preventing clot formation, but may increase the risk of bleeding. Patients on warfarin or other blood thinners should report any bruising or bleeding events to their healthcare provider.

Aspirin may be used in addition to warfarin to further prevent clot formation.

**International Normalized Ratio (INR) test:**
Patients on warfarin are required to go to a clinic regularly for INR tests to make sure the warfarin dosage is appropriate. The INR test measures the time it takes for blood to clot, and the optimal result of this test is between 2 and 3. If the INR is below 2, blood clots are more likely to form. If the INR is above 3, bleeding is more likely.

**Treatment of APS during pregnancy**
The typical treatment for APS in pregnant women is the combination of aspirin with heparin or enoxaparin injections. Warfarin is generally not recommended to treat APS during pregnancy because of the risk of birth defects.

*By Yawen Deng, PharmD Candidate*
Harvoni® (ledipasvir/sofosbuvir) for Hepatitis C

Ledipasvir/sofosbuvir is the first treatment for HCV genotype 1 that does not require peginterferon. Treatment with ledipasvir/sofosbuvir is much more convenient than prior treatment options because it only requires taking one tablet per day. Response rates in clinical trials were greater than 90% in patients with or without cirrhosis. Treatment was also effective in patients who had failed other HCV regimens. Patients can be treated in as few as 8 weeks or for as long as 24 weeks depending on prior treatment status and the presence of cirrhosis.

Ledipasvir inhibits HCV NS5A protein. NS5A interacts with viral RNA and is required for replication, although the mechanism by which NS5A acts is still under investigation.

Sofosbuvir inhibits HCV NS5B RNA-dependent RNA polymerase. Sofosbuvir is a nucleotide prodrug that is metabolized to the active uridine analog (GS-461203), which is incorporated into HCV RNA and acts as a chain terminator. The active metabolite is not a substrate of human DNA, RNA, or mitochondrial RNA polymerase.

In clinical trials, more than 90% of patients treated with ledipasvir/sofosbuvir achieved a sustained virologic response (SVR) 12 weeks after treatment completion. Three phase III randomized, open-label trials (ION-1 to 3) evaluated ledipasvir/sofosbuvir as monotherapy and in combination with ribavirin. Addition of ribavirin to ledipasvir/sofosbuvir treatment was not associated with improvement in outcome. Relapse (2 consecutive measurements with detectable HCV RNA or a detectable HCV RNA level at the last available measurement during the post-treatment period after achieving an undetectable level) rates were very low in the trials.

Ledipasvir/sofosbuvir was not compared to other treatments for hepatitis C in the 3 studies, so how it compares to other treatments is unknown. The studies only included patients with HCV genotype 1, so the results may not be generalizable to patients with other genotypes.

Adverse reactions to ledipasvir/sofosbuvir were generally mild and included fatigue (13-18%), headache (11-17%), nausea (6-9%), diarrhea (3-7%), and insomnia (3-6%). No absolute contraindications to ledipasvir/sofosbuvir were identified in the clinical trials. However, ledipasvir/sofosbuvir may interact with P-gp inducers and acid-reducing agents, leading to reduced efficacy. P-gp inducers (such as rifampin and St. John’s wort) decrease ledipasvir/sofosbuvir levels by increasing its elimination. Acid-reducing agents may decrease absorption of ledipasvir because solubility of ledipasvir decreases with increased gastric pH. Ledipasvir/sofosbuvir does not undergo CYP450 metabolism.

By Robert Mayer, PharmD Candidate

REFERENCES:

Dosage:
One tablet (90 mg ledipasvir and 400 mg sofosbuvir) taken by mouth once daily with or without food.

Treatment Duration:
- Treatment-naive with or without cirrhosis: 12 weeks*
- Treatment-experienced without cirrhosis: 12 weeks
- Treatment-experienced with cirrhosis: 24 weeks

* 8 weeks of therapy may be considered in treatment-naïve patients without cirrhosis who have pre-treatment HCV RNA levels less than 6 million IU/mL. Relapse was greater for 8 week treatment than 12 week treatment in phase III trial.

Pregnancy
Category B. No data in humans.

Renal Impairment
Safety has not been established in patients with renal failure.

Hepatic Impairment
Safety and efficacy has not been established in patients with decompensated cirrhosis.
Cleviprex™ (clevidipine) Injection for Acute Hypertension

Cleviprex™ (clevidipine) is an intravenous (IV), short-acting, third-generation, dihydropyridine calcium channel blocker. It was approved for the treatment of acute hypertension when oral therapy is not feasible or warranted.1 Clevidipine effectively decreases blood pressure in patients undergoing cardiac surgery.2-4 Fewer treatment failures occurred with clevidipine than with placebo in patients undergoing cardiac surgery in 2 double-blind trials (ESCAPE-1 and ESCAPE-2).2,3 Treatment failure was classified as lack of efficacy (no reduction in blood pressure), insufficient efficacy (did not achieve 15% reduction), or safety failures (adverse events). Clevidipine (0.5 mg/mL in 20% lipid solution) or placebo (20% lipid emulsion) were administered via peripheral or central venous infusion for at least 30 minutes in each trial. The initial rate of infusion was 0.4 mcg/kg/min for both treatments. Infusion rates were titrated to response or to a maximum of 8 mcg/kg/min. 2,3

The ESCAPE-1 trial evaluated clevidipine for the management of preoperative hypertensive episodes in patients undergoing cardiac surgery.2 Preoperative systolic blood pressure had to be ≥160 mmHg for enrollment in the study. Fifty-three patients received clevidipine and 52 patients received placebo. Clevidipine reduced blood pressure to target levels within a median of 6 minutes. Fewer patients had treatment failure with clevidipine (7.5%) than with placebo (82.7%; p<0.0001).2

ESCAPE-2 compared clevidipine to placebo for the management of postoperative hypertensive episodes in patients following cardiac surgery.3 Patients were included in the study if their systolic blood pressure was ≥140 mmHg within 4 hours of cardiac surgery. Sixty-one patients received clevidipine and 49 received placebo. Treatment success was achieved in significantly more patients in the clevidipine group than placebo (91.8% vs. 20.4%, p<0.0001). Median time to target systolic blood pressure was 5.3 minutes with clevidipine treatment. Five patients in the clevidipine group failed treatment—1 due to atrial fibrillation, 2 due to hypotension, and 2 due to insufficient efficacy.3

Limitations of the ESCAPE studies included potential influence on arterial blood pressure by other medications given prior to initiation of the study drugs. In addition, the data may not be generalizable since the trials were only conducted in patients undergoing cardiac surgery.2,3 Clevidipine was more effective at maintaining systolic blood pressure than nitroglycerin, sodium nitroprusside, and nicardipine in the ECLIPSE trials.4 The ECLIPSE studies were 3 randomized, open-label studies comparing clevidipine to the active controls either perioperatively (nitroglycerine and sodium nitroprusside) or postoperatively (nicardipine). The incidences of death, myocardial infarction, stroke, and renal dysfunction were similar between clevidipine and the other medications. One limitation of the study was the open-label design, although the committees analyzing safety were blinded. While clevidipine administration was standardized among the study centers, the comparator drugs were administered according to institution-specific protocols, which may have affected the results and limits generalizability.4

Adverse events reported were similar between clevidipine and comparator treatments in the ESCAPE and ECLIPSE trials.2,4 The most common events reported in the clevidipine group in each trial include atrial fibrillation, fever, nausea, acute renal insufficiency, and insomnia.2,4 Clevidipine use is contraindicated in patients with soy or egg allergies, patients with defective lipid metabolism, and patients with severe aortic stenosis.3

Clevidipine should be administered via a central or peripheral line.5 Clevidipine dosing should be initiated at 1-2 mg/hour. The dose should be doubled at 90 second intervals initially, then increased by less than double every 5-10 minutes as the blood pressure reaches goal. A dose increase of 1-2 mg/hour should reduce the systolic blood pressure by approximately 2-4 mmHg. The typical maintenance dose is 4-6 mg/hour to achieve the desired therapeutic response. The maximum dose is 16 mg/hour. Because clevidipine is formulated as a lipid emulsion, no more than 1000 mL or an average of 21 mg/hour clevidipine should be given within 24 hours due to lipid load restrictions.5

In clinical trials, clevidipine effectively lowered blood pressure in acute hypertensive episodes when compared to placebo and standard treatment. Clevidipine appears to be a safe alternative to commonly used agents, such as sodium nitroprusside and nicardipine, with the added benefit of providing superior blood pressure control. Further trials need to be completed to determine efficacy and long-term safety of clevidipine for blood pressure reduction.

By Teale Steffes, PharmD Candidate

References on Page 4
Antiphospholipid Syndrome References (from page 1)


Clevidipine References (from page 3)


Guillain-Barré Syndrome References (from page 6)


Seasonal affective disorder (SAD) affects approximately 5% of US adults. The definite cause remains unknown.\(^1\,^2\) Several mechanisms are thought to contribute to seasonal depression including a shift in circadian rhythm, melatonin irregularities, and depleted serotonin stores.\(^1\,^2\) Many options are available for the treatment of SAD.\(^3\,^5\) Light boxes are as effective as certain pharmacological treatments, and their minimal side effects make them a desirable option for SAD treatment.\(^3\,^5\)

**Signs/Symptoms of SAD**
- Hypersomnia
- Changes in diet or unusual weight gain
- Difficulty concentrating
- Easily fatigued
- Depression
- Feeling of lethargy

**Light box therapy**

Light box therapy is comparable to medications in the treatment of SAD.\(^3\,^5\) The majority of available light boxes consist of a bank of florescent lights with a UV filter which blocks the majority of harmful effects. Currently there is no standardized dose or duration of light therapy for treatment of SAD. However, the general consensus is that about 5,000-10,000 light intensity (lux) for a duration of about 30 minutes is effective for treatment of SAD. Morning light seems to be better tolerated than evening light. Depending on the light box, patients should position the light roughly 24 inches away from themselves.\(^3\,^5\)

Full effect from light box therapy is usually seen within 2 weeks, with some patients experiencing a response within 4 days of therapy.\(^3\,^5\) As light therapy is non-invasive with few adverse effects, it should be considered as a treatment option for most individuals with SAD. Light box therapy combined with medication does not offer any advantages, as adjunctive therapy is not more effective than either agent used alone.\(^7\)

**Dawn Light**

Studies suggest light therapy that gets progressively brighter in the morning during hours of sleep is as effective as light box therapy.\(^3\) The dawn stimulation study supported this hypothesis. Study subjects were placed in one of three groups. In the dawn group, light intensity increased from 0430 to 0600 to a maximal intensity of 250 lux. The light therapy group was given bright light at an intensity of 10,000 lux for 30 minutes each morning. The placebo group was given a faux dawn light each morning with an intensity of 0.5 lux. Those in the dawn group had a 73% greater response in clinical depression scores compared to those in the placebo group.\(^7\) More studies are needed to determine the proper administration, duration, and dose of dawn light.

**Medications**

Medications, such as SSRIs, appear to be a safe and effective option for the treatment of seasonal depression.\(^4\,^8\) Some guidelines recommend that seasonal depression should be treated the same way as other types of depression with pharmacological agents. Many antidepressants take about a month to reach their full effect and a month to taper off. Treating a disease that only lasts a few months each year with medications that have such large lag periods is not ideal. Especially when treatments with less severe side effects are readily available.\(^4\)

**Bottom line:**
Seasonal affective disorder is a common type of depression that can easily be treated with light therapy rather than medication.

**By William Rotter, PharmD Candidate**

**REFERENCES:**

<table>
<thead>
<tr>
<th>Amount of evidence supporting light therapy for SAD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Therapy</strong></td>
</tr>
<tr>
<td>Light box therapy (5,000 -10,000 lux)</td>
</tr>
<tr>
<td>Dawn Light</td>
</tr>
<tr>
<td>Low Light</td>
</tr>
<tr>
<td>Combination with medication</td>
</tr>
</tbody>
</table>
PATIENT INFORMATION:
Guillain-Barré Syndrome—An Overview

Guillain-Barré syndrome (GBS) is caused when a person’s immune system attacks his or her own nerve cells. This leads to numbness, weakness, and tingling in the arms and legs. The exact cause of GBS is unknown. GBS is often preceded by an infection or, in rare cases, vaccinations. Infections or vaccinations might change the appearance of nerve cells, so the immune system attacks the cells.

GBS is rare and can occur even if a person has not been vaccinated. There are approximately 1.8 cases of GBS per 100,000 people each year in the United States.

Symptoms of GBS:
- Symptoms occur on both sides of the body
- Tingling in fingers, toes, ankles, or wrists
- Weakness in legs that spreads to upper body
- Unsteady step
- Difficulty with swallowing, eye/facial movements, and speaking
- Severe pain, aches, or cramps that worsen at night
- Hard time breathing
- Fast heart rate

Risk Factors for GBS:
- Over 50 years old
- Male gender
- Recent infection (1/2 to 2/3 of people with GBS had previous infection)

Diagnosis of GBS:
Diagnosis is based on a person’s symptoms. GBS can be hard to identify in the early stages because symptoms are similar to other diseases. Diagnosis can be confirmed by testing nerve and muscle function or a spinal fluid sample.

Treatment of GBS:
- No known cure
- Available treatments decrease symptom severity
- Two options for treatment
- Plasma exchange
- Immunoglobulin injections, which help the immune system, attack invading organisms
- Physical therapy

Recovery from GBS:
Recovery can take months to years. Muscle aches, pain, and fatigue can occur with normal activity after recovery.

Things To Remember:
- Earliest symptoms are back and leg pain, numbness, and weakness
- An infection followed by weakness suggests GBS
- Lack of knee-jerk reflex is a red flag for severe GBS
- Healthcare providers are your best resource
- If symptoms of GBS occur, contact your provider for an appointment or report to an emergency department

By Teale Steffes, PharmD Candidate

References on Page 4

From: http://www.medcomic.com/031313.html