Standard Operating Procedure

Management of chronic HCV infection in adults

Special Region (1)

Union of Myanmar

Version 1.0

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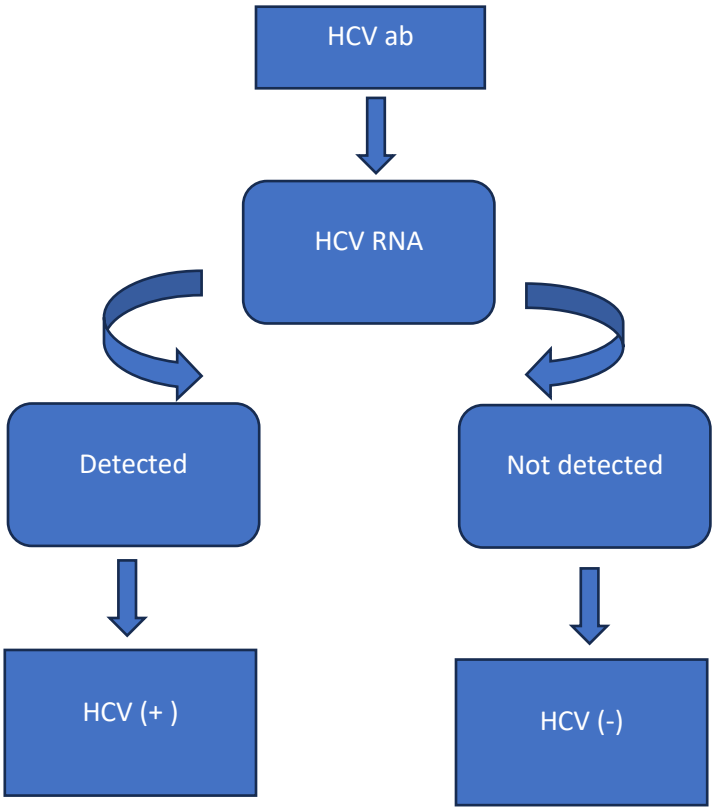
Approved by: Internal Medicine Unit

1. Overview

Clinical objective of HCV treatment is to reduce all-cause mortality and liver related health adverse consequences, including end stage liver disease and hepatocellular carcinoma by achieving virological cure (evidenced by a sustained viral response).

SVR, an effective cure of HCV infection, has also been associated with patient-important outcomes such as decreased mortality, decreased liver-related complications, and improved quality of life.

2. Diagnosis of HCV



3. Initial Investigation for HCV treatment

ALT, AST, SB, ALP, PT, serum albumin, USG abdomen, alpha-fetoprotein (if cirrhosis), serum creatinine, CP (auto), random blood sugar.

4. Treatment for HCV infection

<table>
<tr><th colspan="2">Treatment naïve</th><th colspan="3">Treatment experienced</th></tr>
<tr><td rowspan="2">Without cirrhosis or CHILD-A cirrhosis</td><td rowspan="2">CHILD-B & C cirrhosis</td><td colspan="2">Chronic infection or CHILD-A cirrhosis</td><td rowspan="2">CHILD B & C cirrhosis</td></tr>
<tr><td>Previous Sofosbuvir based</td><td>Previous Gleclaprevir/pibrentasvir based</td></tr>
<tr><td>Gleclaprevir/pibrentasvir for 8 weeks
Or
Sofosbuvir/velpatasvir for 12 weeks</td><td>Sofosbuvir/velpatasvir for 12 weeks</td><td>Glecaprevir/pibrentasvir 16 weeks</td><td>Gleclaprevir/pibrentasvir + sofosbuvir + ribavirin 16 weeks</td><td>Get opinion from hepatologist</td></tr>
</table>

Note

- Both Gleclaprevir/pibrentasvir and Sofosbuvir/velpatasvir regimens result in SVR rates in excess of 95 %.
- Sofosbuvir/velpatasvir regimen can be used in patients with any degree of renal or liver impairment.
- Gleclaprevir/pibrentasvir regimen can be used in any degree of renal impairment and can cause risk of worsening liver function or failure.
- Anaemia is common among patients receiving ribavirin.

Dosage of DAAs in HCV treatment

Gleclaprevir/pibrentasvir

- 300 mg gleclaprevir/120 mg pibrentasvir orally once daily

Sofosbuvir/velpatasvir

- 400mg sofosbuvir/100mg velpatasvir orally once daily

Ribavirin

- Target dose of ribavirin is 1000 mg daily for individuals <75 kg and 1200 mg daily for individuals ≥75 kg. However, because ribavirin may not be optimally tolerated in patients with decompensated cirrhosis, we start ribavirin at a lower dose (e.g., 600 mg daily) and increase as tolerated to target dose. If ribavirin cannot be used at all, a 24-week duration of the ribavirin-free regimen is recommended to maximize the likelihood of SVR. However, for genotypes 1 and 2 infection, 12 weeks without ribavirin may be reasonably effective.

Adverse effects of HCV antiviral drugs

Class adverse effects are HBV reactivation and hepatic decompensation. 524 cases of liver failure are reported to the US Food and Drug Administration (FDA) over the course of one year, with an estimated 250,000 individuals treated over a similar time frame. Cases of hepatic decompensation or failure, including events with fatal outcomes, have been reported in patients who received HCV protease inhibitor-containing regimens. Many of the cases were in patients with decompensated (Child class B or C) cirrhosis, among whom these agents are not recommended.

Sofosbuvir/velpatasvir

most common adverse events are fatigue, headache, nausea, nasopharyngitis, and insomnia.

Gleclaprevir/pibrentasvir

most adverse effects were mild, with headache and fatigue.

Ribavirin

Hemolytic anemia has been reported with ribavirin therapy; anemia associated with ribavirin may worsen underlying cardiac disease and lead to fatal and nonfatal myocardial infarctions. Avoid use in patients with significant/unstable cardiac disease.

Drug interaction

Sofosbuvir/velpatasvir - coadministration of sofosbuvir-velpatasvir is not recommended with rifampin, rifabutin, rifapentine, amiodarone, St. John's wort, carbamazepine, phenytoin, phenobarbital, oxcarbazine, tipranavir/ritonavir, or efavirenz.

Increased gastric pH levels decrease absorption of velpatasvir; thus, coadministration with proton pump inhibitors is ideally avoided. If a proton pump inhibitor is necessary, they can be coadministered, sofosbuvir-velpatasvir should be administered with food and taken four hours prior to omeprazole 20 mg (other proton pump inhibitors have not been studied).

Gleclaprevir/pibrentasvir - Coadministration is not recommended with carbamazepine, ethinyl estradiol-containing medications (such as oral contraceptive agents), St. John's wort, efavirenz, darunavir, lopinavir, ritonavir, and certain statins (atorvastatin, lovastatin, and simvastatin).

Special populations

HIV/HCV coinfection

The regimen options for patients with HIV/HCV coinfection are the same as those for patients with HCV monoinfection. Where available, pangenotypic regimens (eg, sofosbuvir-velpatasvir and glecaprevir-pibrentasvir for initial antiviral therapy) are generally preferred options.

HCV/HBV coinfection

If patient has already met the criteria to start antiviral medication for HBV, treat as HBV monoinfection.

In those patients who do not meet treatment criteria for HBV monoinfection, monitoring of HBV DNA levels every 4 to 8 weeks during treatment and for 3 months posttreatment is indicated because HBsAg-positive patients are at risk of HBV DNA and ALT flares with HCV treatment. HBV Treatment should start during HCV

Liver function and, if available, HCV RNA should be monitored at four-week intervals during HCV therapy. In the event of unexplained increases in liver enzymes and during and/or after completion of HCV therapy, repeat HBsAg testing and HBV DNA should be performed. HBV reactivation is suggested by conversion from an undetectable to a detectable HBV DNA or a rise in HBV DNA level by >2 log international units and may warrant antiviral therapy for HBV infection.

Pregnancy with HCV infection

Antiviral therapy during pregnancy is not an option since the safety and efficacy of direct-acting antiviral agents in pregnancy have not been evaluated (and they should thus not be used in pregnant patients). Further studies are needed to assess these issues and inform the potential role of these antiviral agents to treat maternal HCV infection and prevent transmission to the infant.

HCV monoinfection does not impact delivery route. Postpartum, women with HCV infection (without HIV infection) can breastfeed, but should abstain from breastfeeding when their nipples are cracked or bleeding.

The safety and efficacy of all HCV antiviral agents during pregnancy are unknown; thus, antiviral therapy of such patients should be delayed until after delivery.

5. Recommended SVR check

SVR12 (check viral load 12 weeks after post treatment) is the main endpoint investigation for clearance of HCV.

6. Reference

- Uptodate.com
- bestpractice.bmj.com
- QuaterWatch: Monitoring FDA MedWatch Reports. Institute For Safe Medication Practices. January 25, 2017. http://www.ismp.org/quarterwatch/pdfs/2016Q2.pdf.