

# **Counseling Patients With Chronic Hepatitis C Virus Infection**



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# Disclosure Information



Dr Bhattacharya has reported the following financial relationships with commercial firms:

- Research support from: Vertex Pharmaceuticals, Inc

# Outline



- Over-the-counter and prescription medications
- Alcohol and cannabis
- Diet and modifying obesity
- Complementary and alternative medicines

# Over-the-Counter and Prescription Medications



# Over-the-Counter and Prescription Medications



- Acetaminophen
- Nonsteroidal antiinflammatory drugs (NSAIDs)
- Vitamin D
- Iron supplementation

# Acetaminophen

- **Stable liver disease without cirrhosis**
  - Double-blind 2-period crossover study of 20 patients with chronic, stable liver disease (8 with cirrhosis) who tolerated acetaminophen (4g/day) for 13 days without adverse events
  - Based on limited data and possible adverse effects, most experts would limit to 2 g per day
- **Cirrhosis**
  - No prospective long-term studies of acetaminophen
  - Half-life of acetaminophen in patients with cirrhosis is double that in healthy controls
  - Based on limited data and possible adverse effects, most experts would limit to 1 g per day

# NSAIDs



- **Stable liver disease without cirrhosis**
  - May be tolerated in mild chronic liver disease
- **Cirrhosis**
  - Greatest concerns are of associated renal impairment and hepatorenal syndrome
  - Also can cause mucosal bleeding secondary to thrombocytopenia and coagulopathy of advanced liver disease; greater risk in portal hypertension
  - Should be avoided in patients with cirrhosis

# Vitamin Supplements: Vitamin D

- Vitamin D
  - May improve interferon alfa signaling and may have antiviral effects, deficiency may contribute to liver fibrosis
- Vitamin D in vivo effects
  - Vitamin D deficiency increases risk of bone disease, and advanced liver disease also increases risk of bone fracture
  - Cohort analyses demonstrate that low vitamin D levels are associated with nonresponse to interferon alfa–based therapy
  - Randomized trials of vitamin D supplementation in HCV genotype 1 patients treated with peginterferon alfa and ribavirin showed improved virologic responses
  - Results require further confirmation
- Recommendations
  - Vitamin D supplements to maintain 25-hydroxyvitamin D levels at or above 20 ng/mL, may require 2000 to 4000 IU per day of nutritional vitamin D



# Vitamin Supplements: Iron (Fe)

- Excess Fe accumulation in the liver may occur in chronic liver disease
  - Up to 30% of those with hepatitis C virus (HCV) or alcoholic cirrhosis demonstrate serum accumulation of Fe; 10% with liver tissue deposition
- High hepatic Fe concentrations can be detrimental
  - Predictor of nonresponse to interferon alfa therapy
  - Animal (rat) studies: enhanced hepatotoxicity to alcohol when Fe coadministered
- Avoid excessive Fe in chronic liver disease
  - Choose multivitamin without Fe, unless Fe deficiency anemia is present
  - Dietary Fe not harmful

Riggio O, Montagnese F, Fiore P, et al. *Am J Gastroenterol*.1997;8:1298-1301. Bisceglie AM, Axiotis CA, Hoofnagle JH, et al.*Gastroenterology*.1992;102:2108-13. Olynk JK, Reddy R, Di Bisceglie AM, et al. *Gastroenterology*.1995;108:1104-9. Van Thiel DH, Friedlander L, Fagiuoli S, et al.*J Hepatol*.1994;4:10-5. Stal P, Hultcrantz R.*J Hepatol*.1993;17:108-15.

# Alcohol and Cannabis



# Alcohol

- Alcohol use
  - Associated with increased risk of cirrhosis, hepatocellular carcinoma, and mortality when greater than 48 g daily
- Alcohol use and HCV
  - Synergistic effect
  - Heavy alcohol use (> 50 g/day or > 5 drinks/day) associated with increased fibrosis
  - Light and moderate use also have an effect
    - ✦ Degree of fibrosis correlates with degree of use
    - ✦ Less than 31 g per day also exerted some effect on probability of increased fibrosis, with 31 g to 50 g per day exerting greater effect

Thun MJ, Peto R, Lopez AD, et al. *N Engl J Med*.1997;337:1705-14. Poynard T, Bedossa P, Opolon P.*Lancet*.1997;349:825-32. Monto A, Patel K, Bostrom A, et al.*Hepatology*. 2004;39:826-834. Hezode C, Lonjon I,Roudot-Thoraval F, et al.*Aliment Pharmacol Ther*.

# Cannabis

- **Biologic effects**
  - Cannabinoid receptor types 1 and 2 regulate progression of experimental liver fibrosis
- **Use is associated with liver disease**
  - Daily cannabis use is associated with a higher risk of moderate to severe liver fibrosis
  - Combination of moderate to heavy alcohol use is associated with an even greater risk of fibrosis
  - Predictor of steatosis
- **Should be discouraged in those with chronic HCV**

Ishida JH, Peters MG, Jin C, et al. *Clin Gastroenterol Hepatol*. 2008;6(1):69-75.

Hézode C, Zafrani ES, Roudot-Thoraval F, et al. *Gastroenterology*. 2008;134(2):432-9.

# Diet and Modifying Obesity



# Diet and Modifying Obesity

- Obesity
  - Higher risk of advanced fibrosis with increasing obesity
- Elevated body mass index
  - Predictor of response to peginterferon alfa and ribavirin–based therapy
- Insulin resistance, without diabetes or obesity, is associated with treatment response, similar to HCV genotype
  - Insulin-sensitizing agents, including metformin or pioglitazone, have not improved HCV treatment outcomes

Monto A, Alonzo J, Watson JJ, et al. *Hepatology*. 2002;36:729-736. Eslam M, Aparcero R, Kawaguchi T, et al. *Aliment Pharmacol Ther*. 2011;34(3):297-305. Pattullo V, Heathcote J. *Liver Int*. 2010;30(3):356-64. Romero-Gómez M, Diago M, Andrade RJ, et al. *Hepatology*. 2009; 50: 1702-08. Harrison SA, Hamzeh FM, Han J, et al. *Hepatology*. 2012.56(2):464-73. Serfaty L, Forns X, Goeser T, et al. *Gut*. 2012;61(10):1473-80.

# Diet and Modifying Obesity

- Weight loss (ideally 10%) and exercise may help
- Protease inhibitor use may mitigate the effects of insulin resistance on response
  - Baseline insulin resistance did not impact virologic response, in 1 telaprevir study

Monto A, Alonzo J, Watson JJ, et al. *Hepatology*. 2002;36:729-736. Eslam M, Aparcero R, Kawaguchi T, et al. *Aliment Pharmacol Ther*. 2011;34(3):297-305. Pattullo V, Heathcote J. *Liver Int*. 2010;30(3):356-64. Romero-Gómez M, Diago M, Andrade RJ, et al. *Hepatology*. 2009; 50: 1702-08. Harrison SA, Hamzeh FM, Han J, et al. *Hepatology*. 2012.56(2):464-73. Serfaty L, Forns X, Goeser T, et al. *Gut*. 2012;61(10):1473-80.

# Complementary and Alternative Medicines





# Complementary and Alternative Medicines

- 42% of patients with chronic HCV use at least 1 herbal product
  - Milk thistle extract in 72%
  - Others commonly include S-adenosyl methionine (SAMe)
- Some herbal extracts associated with fulminant hepatitis

# Complementary and Alternative Medicines

- Silymarin (milk thistle)
  - Animal model data suggest hepatoprotection during various liver insults
  - SyNCH trial (2012): double-blind, placebo-controlled
    - ✦ No change in serum ALT or HCV RNA during 24 weeks of silymarin
  - HALT-C study (2008)
    - ✦ No difference in anti-HCV efficacy or ALT but somewhat better quality of life

Fried MW, Navarro VJ, Afdhal N, et al. *JAMA*.2012;308:274-282.

Seeff LB, Curto TM, Szabo G, et al. *Hepatology*.2008.

Feld JJ, Modi AA, El-Diwany R, et al. *Gastroenterology*.2011;140(3):830-9.

# Complementary and Alternative Medicines

- **SAMe**
  - Has been shown to improve interferon alfa signaling
  - Supplementation improved early second-phase HCV viral kinetics, with modest improvement in SVR
  - Role in interferon alfa–sparing regimens unclear

Fried MW, Navarro VJ, Afdhal N, et al. *JAMA*.2012;308:274-282.

Seeff LB, Curto TM, Szabo G, et al. *Hepatology*.2008.

Feld JJ, Modi AA, El-Diwany R, et al. *Gastroenterology*.2011;140(3):830-9.

# Summary



- **Over-the-counter and prescription medications**
  - Limit acetaminophen to 2 g daily, 1 g daily in cases of cirrhosis
  - Avoid NSAIDs in cases of cirrhosis
  - Avoid Fe supplementation unless Fe-deficiency anemia present
- **Alcohol and cannabis**
  - Advise patients to avoid alcohol and marijuana
- **Diet and modifying obesity**
  - Obesity associated with increased risk of fibrosis
  - Weight loss and exercise recommended as adjunct to therapy
- **Complementary and alternative medicines**
  - Insufficient evidence to support their use

# End



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