Logistic problems to face Delta Hepatitis in the Amazonian Countries

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Disclosures

• Clinical research
  – BMS

• Speaker
  – Bayer, Biolab, Janssen

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HDV is a challenge to science

Defective virus
Hybrid particle – chimera
Unique life cycle among human pathogens
HDV

• The less common, less known but more severe and rapidly progressive form of viral hepatitis
  – Particularly severe acute and chronic presentations
  – Faster and more frequent progression to cirrhosis –15ys earlier
  – Mortality from HDV-related cirrhosis is 2 times higher than that related to HBV
  – Risk of HCC in HDV-related cirrhosis is up to 3 times higher than the related to HBV
  – Mortality of HDV-related HCC is up to 2 times higher than that related to HBV

(Rizzetto et al, 1983; Fattovich et al, 2000; Su, 2006; Serrano, 2009; )
- 15 - 20 million people infected worldwide
- Nonuniform and focal distribution

- Mediterranean: 23%
- Central Africa: 42%
- South Pacific Islands: 70%
- Focal areas in the Middle East and Central Asia – 17%

Northern South America: 67%
Unsolved problems to face Delta Hepatitis in the Amazonian Countries
Scientifics problems to be faced

why delta hepatitis occurs so irregularly, even within highly endemic areas?

(Braga et al., 2012)
Genotypes

• Distribution
  – Type 1: most widespread worldwide
  – Type 2: Asia (Taiwan, Japan, Russia)
  – Type 3: Northern South America
  – Type 4: Japan
  – Types 5-8: Africa

• Features
  – Pathogenicity: Gen-3 > Gen-1 > Gen-2
  – Gen-3: severe forms (associated with HBV gen F)

Differences in response to treatment?

Therapeutic challenge

- Specific inhibitors against HDV are not available
- HBV inhibitors have little / no effect on HDV
  - Production of HBsAg is little affected by current drugs
- Interferons
  - Still considered the only available treatment
  - Low response rate

Standard and pegylated interferon therapy of HDV infection: A systematic review and meta-analysis

Few studies / small samples / methodological differences

(Alavian et al., 2012)
New therapeutic approaches

- Prenylation inhibitor
  - Lonafarnib - NIH trial currently ongoing

- Drugs that potentially suppress the expression of HBsAg
  - Clevudine – suppressed HDV viremia in woodchucks w/ marked reduction in HBsAg levels
  - REP 9AC – inhibits release of HBsAg from infected hepatocytes – proof-of-concept trial ongoing

(Heidrich et al., 2013; Casey et al, 2005; Glenn, 2006; Bordier et al, 2003; Mahtab et al., 2010; http://www.clinicaltrials.gov/ct2/show/NCT01495585?term=lonafarnib&rank=11)
Partial responders at one year of treatment should continue treatment

Relapsers after treatment shall be readmitted early – risk of decompensation

Prolonged analogues use needs to be tested and deserves serious consideration
- Review the indication for the exclusive use of lamivudine as analogue in co-infection HBV / HDV
- Review the indication for use of analogues for just one year
- Conduct systematic observations of prolonged use of analogues
How to monitor? Scientific problems

- Anti-HDV IgM
  - Related to disease activity
- HBsAg quantification
  - Potentially useful tool
- HDV-RNA
  - Lack of standardization and validation of molecular techniques
  - Comparability? Performance between genotypes?
- Predictors of response (?)
  - RVR, slow responders? stopping, extending?

(Fonseca, 2008; Farci, 2006; Erhardt et al, 2006; Castelnau et al, 2006; Manesis et al, 2007)
How to monitor?

Logistic problems

- Urgently provide HDV-RNA test in the healthcare network

- Standardize and validate the HDV-RNA for genotype 3
How to avoid the spread of disease?

• Migration to the Amazon
  – Systematic vaccination of working fronts
    • Hydroelectric, mining, etc

• Migrations from Amazon
  – Hyperendemicity not controlled despite systematic vaccination for HBV
    • Vaccine escape?
How to treat patients with chronic viral hepatitis scattered in the Amazon?
Just a refrigerator!

It’s impossible!
You have a lot to learn in the Amazon