Management of Patients with Chronic Hepatitis B: The Alaska Experience

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Disclosures

- I have no conflicts of interest regarding this presentation
Outline of Presentation

- Background:
  - Goals and components needed for programs to manage persons with chronic HBV infection
  - Natural history of hepatitis B virus (HBV)
- The Alaska Native Tribal Health Consortium (ANTHC) program for the management of persons with chronic HBV
  - Monitoring for immune active HBV
  - Surveillance for hepatocellular carcinoma (HCC)
- Lessons learned from this program that might be applied in other settings in the US
Goals of a Management Program for Persons with Chronic HBV

- To reduce the incidence of end stage Liver Disease (ESLD): Liver Failure
- To reduce the incidence of HCC
- To detect HCC at a potentially curable stage
- To reduce risk of transmission to others: contact screening and vaccination plus barrier protection for unvaccinated contacts
- To provide interventions and educational material to both providers and patients to protect their liver from other deleterious conditions
  - Vaccination for HAV
  - Healthy eating and exercise to avoid non alcoholic fatty liver disease (NAFLD)
  - Prudent intake of alcohol
Critical Components needed to develop a program to manage patients with chronic HBV infection

- Identification of HBV infected persons
- Linkage of persons with chronic HBV to care:
  - Providers with knowledge needed to manage chronic HBV
  - In Alaska by using a computerized registry to assist in management
- Laboratory and radiology facilities needed for program
- Identify patients with chronic HBV needing treatment
- Facilities for treating HCC: surgical resection, ablative therapy, embolization and transplant
- Issues of patient compliance
- Cost effective approaches are important
HBV Cascade of Care

Identification by screening
Linkage to Routing F/O
Identification or persons needing treatment
Initiating therapy when appropriate
Natural Progression of HBV Infection

Perinatal Transmission → Immune Tolerant Phase

- HBeAg+ Immune Active Phase
  - 90%-100%
  - 90%
  - 20%-40%

Anti-HBe Seroconversion

- 80%-90%
  - Inactive HBV
    - 20%-40%
    - 0.5%-1.0%/yr
  - Anti-HBe+ Immune Active Phase

- 10%-20%
  - Horizontal Transmission

Clearance of HBsAg
Mathematical Model: Age-specific hepatitis B-related cirrhosis and HCC mortality

Goldstein Int J Epidemiol 2005;34;1329-39
Alaska Native Health System

- Owned and operated by Alaska Native Tribal Organizations
- 45% of Alaska Native persons live in remote villages not connected to the road system
  - Clinics there are staffed by Community Health Aide Practitioners who receive 16 weeks of medical instruction: limited lab, no radiographic facilities
  - Air transportation usually needed to regional health facility for more intensive care
- Regional Hospitals and Clinics staffed with physicians and/or midlevel providers
  - Regional hospitals have lab and radiology facilities
- Tertiary Care hospital in Anchorage with primary care providers, specialists and advanced laboratory and radiology capabilities
Challenges in Delivering Services for Managing Chronic HBV in Alaska

- About half of patients live in a community where ultrasound capabilities are not available.
- Air transportation is required to reach the nearest community with ultrasound:
  - Cost of air transportation is between $200 and $500.
  - Trip to Anchorage for specialized care can cost up to $1,000.
Village, Regional Hub Hospital/Clinics and Tertiary Hospital in Alaska

Distance is >4,000 km from east to west and >2,000 km from north to south
Background: HBV

- High rates of acute and chronic HBV and HCC were found in the Alaska Native Population in the 1970’s

- From 1983-1987, 52,000 Alaska Native Persons were tested for hepatitis B seromarkers and 40,000 with negative markers were vaccinated and universal newborn immunization was introduced
  - 80% of population including 90% in endemic areas were screened
  - 1560 persons with chronic hepatitis B virus (HBV) infection were identified
  - All identified persons have been followed prospective since then (median f/u 28 years)
Five Alaska HBV Genotypes Found in Alaska Native People

Significantly higher rates of HCC in patients with genotypes C and F vs. B and D.

Median age of HBeAg Seroconversion for genotype C is 47 years vs. < 20 years for A, B, D and F.
HBV Vaccination

- Vaccination of at risk groups, household contacts and susceptible persons is a very important
- Universal infant vaccination and catch-up programs can potentially:
  - Eliminate acute HBV infection
  - Reduce the prevalence of chronic HBV especially in children
  - Reduce incidence of HCC as has been documented in Taiwan, Thailand and Alaska
Incidence Symptomatic Hepatitis B in Alaska Native Peoples 1981-2008

- CDC/HIS Vaccine Demonstration Program begins in 16 villages of Yukon Kuskokwim Delta and Norton Sound
- Statewide Program begins—all susceptibles immunized—pregnant women screened/infants HBvax + HBIG—begin universal newborns immunization

Year
Rate per 100,000

Yukon Kuskokwim Delta
Statewide
As of 2013, there are no Alaska Native children known to be HBsAg-positive.
HCC in Alaska Natives <20 years of age

P value for trend = 0.002  
Hepatology 2011;54:801-7
The ANTHC HBV Registry

- Computerized registry containing pertinent clinical and laboratory data on all patients with chronic HBV
- Microsoft Excel and Access is used as platform for the registry
- The registry automatically sends out letters to all patients on regular intervals, including reminder letters when patients have missed a scheduled visit time
- Laboratory data is downloaded into registry including unscheduled tests
- All laboratory data is reviewed by a hepatologist and the hepatitis B registry RN
ANTHC Program to Provide Care for Persons with Chronic Hepatitis B

- Reminder letters are sent every 6 months to all patients
  - List of Patients in community/region sent to provider along with lab slips for each patient with bar code
- Blood drawn in village clinic or hospital then centrifuged and separated
- Sera mailed ANMC lab for liver panel, AFP and HBV DNA
  - Results downloaded and reviewed by Hepatologist and HBV Registry RN who make evaluation and treatment decisions
  - All patients had baseline testing for HBV DNA in 2001
- Patients with normal LFT & AFP results sent a letter, others with abnormal results are contacted by phone
Evaluation of Abnormal Results

- 40,385 Laboratory visits have been performed on persons with chronic HBV since 1982
- AFP cutoff: 10 ng/ml, patients with levels above referred to nearest facility for liver US
- Follow-up HBV DNA testing is performed at ANMC in all high risk patients:
  - Any Patient with elevated ALT or AST
  - Those with personal or family history of HCC
  - Those with known cirrhosis
  - Those with previous HBV DNA elevations above 2,000 IU/ml
Delinquent letters

- If patient has not had testing by 3 months after the date the letter was sent, a reminder letter is again sent out: This is repeated every 3 months until testing is performed

- Other important components to maintain patient contact
  - Registry RN calls patient to remind them to have testing
  - Registry RN call village clinic or regional hospital to ask for help in reaching out to patient for testing
  - Use of telemedicine Vidyo clinics for direct provider/patient interaction
Identification of persons in the Immune Active Phase of HBV for Antiviral Therapy

- Persons with elevated ALT and HBV DNA >2,000 IU/ml levels are recommended for liver biopsy and FibroScan done at ANMC.
- Persons with moderate to severe inflammation or fibrosis ≥ Metavir/Ishak 2 and those without liver biopsy with ALT > twice upper limit of normal and HBV DNA >20,000 treated as per AASLD Practice Guidelines.
- Only Tenofovir or Entecavir are used for initiation of treatment per AASLD Guidelines.

*Lok & McMahon. Hepatology 2009*
HCC Surveillance in Alaska Native Persons with Chronic HBV

- All persons get a letter to have AFP/LFT drawn every 6 months
- A second letter every 6 months to have a liver US done is sent to:
  - Men > 40, women > 50 years living in a community with US
  - Persons with a family history of HCC or cirrhosis regardless of community
- US with suspicious lesions are reviewed by tele-radiography and referred for triphasic CT or MRI
Areas of Uncertainty

- 50% of Alaska Natives with chronic HBV infection had one or more abnormal ALT or AST over an 8-year period
  - 40% met criteria for immune active HBV (elevated ALT, HBV DNA >2,000 IU/ml)
  - 25% had used alcohol heavily prior to testing
  - 30% had the metabolic syndrome and were presumed to have NAFLD
  - 5% had other reasons for abnormal ALT

Spradling et al. J Hepatology 2014;61:785-91
Other Liver Disease Registries used at ANTHC

- Chronic hepatitis C registry: 2,500 patients are followed in a similar manner as those with HBV
- Autoimmune liver disease registries for Alaska Native persons with autoimmune hepatitis and primary biliary cholangitis
ANTHC Liver Disease Website

- HHS funded
- Used throughout the IHS and elsewhere
- Updated constantly
- Reviewed quarterly by our advisory group of indigenous patients living with HCV

- Contents of Website
- Patient Information portal
- Provider Information portal
- Hepatitis B and C management and Treatment
- Liver Connect – Past presentations
- The website is constantly updated as new treatments are approved
Liver Disease/Hepatitis Program

Website

http://www.anthctoday.org/community/hep/providers/index.html
Other Tools Used to Deliver Care to Patients with Viral Hepatitis

- Participation in IHS Project Echo as consultants and in Pacific Northwest Echo
- Liver Connect: a monthly statewide and IHS wide telemed education program that can also used for case presentations
- Use of telemed Vidyo clinics to interact directly with patient and provider living in rural and remote communities
Public Health Usefulness of Registries

- Reminder letters also can include educational information, such as:
  - Recommendations for screening for other virus (Hepatitis A screening and vaccination)
  - Useful educational information about hepatitis infection: for example new treatments, healthy diet, coffee is good for your liver etc.
  - Information for family members and close contacts
  - Information for referral options for management
Conclusions: The Alaska Native Viral Hepatitis Program has Demonstrated:

- Universal newborn and childhood vaccination can eliminate acute and chronic HBV in children as well as HCC in children.

- The ANTHC Program for the management of Hepatitis B has been shown to be an effective way to provide services for persons living in remote communities who need antiviral therapy and diagnose HCC at a potentially curable stage.
Challenges in Programs for Chronic HBV

- One size for interval of follow-up testing and clinic visits doesn’t fit all: Interval for follow-up could vary by
  - Different phases of HBV
  - Different HBV genotypes
  - Age
  - Sex
  - Presence of other liver conditions such as NAFLD, HIV, HCV, HDV, Alcohol use
Limitations of any Management Program

- Patient compliance in going to clinic for laboratory testing after receiving notification: About 50% have testing on time in any given year
- Compliance of patients on antiviral therapy
- Lifestyles that can accelerate liver disease: Obesity and alcohol
Lessons Learned

- Registries and reminder letters can help practitioners and managed care programs and other group programs to care for persons with chronic HBV infection
  - These programs can be also helpful in managing persons living in rural communities in the US
- Patients need regular follow-up, a minimum of every 6 months is recommended, but follow-up can be done without provider visits each time by using registries and ancillary personnel
- For the best success, patients need to be participating in their care
The Alaska Native Medical Center Campus