Investigating hepatitis B immunity in patients presenting to a paediatric oncology unit: Are these patients at risk of infection?

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Reminder: What is hepatitis B?

- Hepadnaviridae family
- Variety of liver diseases
- Acute and chronic hepatitis
  - Acute infection
    - self-limiting, asymptomatic illness
    - occasionally fulminating
  - Chronic hepatitis
    - asymptomatic carrier (number of years)
    - life-threatening complications - cirrhosis and hepatocellular carcinoma

Hepatitis B in South Africa

- Endemic in sub-Saharan Africa
- Prevalence 8-20% among certain population groups
- Acute and chronic infection common in black South Africans
  - 5-16% in rural black males
  - 2.7-4% in urban black females
  - Estimated 3-4 million black South Africans with chronic HBV infection


Hepatitis B in children in SA

- Rural areas → HBV acquired early in life (<5y)
- Development of chronic infection inversely related to age:
  - Younger age = ↑ risk of becoming chronic carrier
  - Chronic carrier → complications
    - cirrhosis
    - hepatocellular carcinoma

Hepatitis B transmission in childhood

- Horizontal transmission predominant during early childhood (developing countries)
- Not related to sexual or perinatal exposure
- Transmission between family members in communities with poor socio-economic and hygienic conditions
- Mode unsure
  - Body fluids, mainly saliva
  - Ritual scarification and open weeping sores


HBV vaccination in SA

- HBV vaccine included in EPI-SA at 6, 10 and 14 weeks of age, from April 1995
- No ‘catch-up’ vaccination attempted
- Subsequent studies = expected decrease in HBV carriage rate
- Vaccinated children in SA = low HBsAg carriage 0% to 2.7%

Current vaccine strategy in SA

• Heberbiovac administered as monovalent vaccine
• Safe and compatible with other EPI antigens
• More immunogenic than other HBV vaccines
• BUT Advantages of polyvalent vaccines
  – cost reduction
  – simplified delivery logistics
  – increased levels of acceptance by families


Who else should be vaccinated?

• SA Guideline for the management of chronic hepatitis B: 2013
• Vaccination recommended in individuals at risk of HBV infection
  – haemodialysis or oncology patients
  – transplant candidates
  – receiving frequent blood or blood product transfusions
  – household contacts of HBsAg-positive individuals

Is hepatitis B vaccination effective?

- Highly immunogenic and effective
- Protective levels of anti-HBs (>10mIU) in 75-87% of children
- None or very few children positive for HBsAg or HBV DNA
- Duration of vaccine-induced immunity not known
- Antibody levels decline rapidly after vaccination BUT immune memory thought to extend into adulthood
- Currently no ‘booster’ doses recommended
- Waning of immunity → adolescents at risk of HBV infection


What about immune compromised patients?

- Lower levels of anti-HBs
- Slower primary and secondary humoral responses
- Clinically significant HBV infection in immune compromised patients after loss of anti-HBs
- Boosters to keep anti-HBs above 10mIU/mL
- Additional or double doses for non-responders
- Vaccine administered when immune response likely to be maximal

HBV in paediatric oncology

- Immune compromised children with chronic HBV → enhanced viral replication
- Few able to clear HBsAg during first year of infection
- Often have high levels of infective HBsAg and HBeAg in saliva → highly infectious
- Immunosuppressive agents
  - reactivation of dormant infection, re-appearance of HBsAg
  - previous antibodies to HBsAg disappear or unable to prevent recurrence of infection
  - high risk of becoming chronic carriers of HBV


HBV in paediatric oncology

- Risk factors increasing susceptibility to HBV:
  - frequent prolonged hospital admissions
  - severe immune compromised states
  - repeated venepunctures
  - frequent blood product administration
  - destruction of mucous membranes secondary to chemotherapy
- Adverse prognostic role in terms of disease-free survival:
  - acute hepatitis leads to delays in chemotherapy
  - risks of cirrhosis and hepatocellular carcinoma

Why do this research?

• Various studies have assessed duration of immunity to hepatitis B after primary immunisation in infancy
• Immune memory to vaccination shown to be protective in a large percentage of well children, not assessed in patients on immunosuppressive therapy
• Patients have acquired hepatitis B in SBAH paediatric oncology unit despite being vaccinated (EPI-SA)
• This study reports on immunity to hepatitis B at first presentation to a paediatric oncology unit

Methods: Patients and samples

• Hospital-based audit of patient records
• All children presenting to SBAH paediatric oncology unit
• 1 January 2012 to 31 August 2013
• Demographic data and diagnosis documented
• HBV serology reviewed on all patients
• Approved by Medical Research Ethics Committee
Methods: Serology

- Routine screening hepatitis A, B, C on all new patients
- Anti-HBs antibody levels classified:
  - >100mIU/ml = complete protection
  - 10-100mIU/ml = partial protection
  - <10mIU/ml = no protection


Debate: Anti-HBs antibody levels

- What level is protective?
- >10mIU/ml if normal immune response
- Immune memory persists in healthy children even if anti-HBs titers <10mIU/ml
- Immune memory not assessed in patients on immunosuppressive therapy
  - Defects in immunologic functioning
  - Immune memory may not be protective

Results: Patient characteristics

- 167 patients
  - 103 boys
  - 64 girls
- 12.6% HIV positive

Results: Diagnoses

- 42% Solid Tumours
- 18% Benign
- 17% Acute Leukaemia
- 23% Lymphoma
Results: Age distribution

![Age distribution chart]

Results: Hepatitis B immunity

![Hepatitis B immunity chart]
Results: Leukaemia group (n=30)

![Bar chart showing immune status for AML, ALL, and CML groups.]

- Not immune
- Low immune
- Immune

Results: HIV patients (n=21)

![Bar chart showing immune status for NHL, Hodgkins, Kaposi, Nasopharyngeal, and SAA cases.]

- Not immune
- Low immune
- Immune
Conclusion

• Only 24% of patients immune to HBV (anti-HBs >100mIU/ml)
• Most patients (76%) at risk for infection
• Infected patients high viral loads and highly infectious
• Protection needed!

Recommendations

• All patients should be screened at first visit
• Active immunisation if anti-HBs titers <100mIU/ml
• Response to immunisation documented
• Frequent re-testing (3-monthly)
• Treatment and close follow-up of infected patients to prevent horizontal transmission
What about the general population?

• HBV is still a problem in SA
• Current immunisation schedule may not be sufficient
  – Booster needed?
  – Higher index of suspicion needed?
• Further research needed!

References

Thank you!