Imported food risk advice

Hepatitis B virus in human milk and human milk products

Context of this risk advice

- Human milk means expressed milk collected from lactating women to be fed to infants that are not the biological infants of the women supplying the milk.
- Human milk products means products derived from human milk that have been specially formulated to meet the specific nutritional needs of infants such as fortifiers and formula.
- The level of risk for this hazard in human milk and human milk products was determined assuming that the most vulnerable category of infants (preterm infants in hospital neonatal intensive care units) would be receiving the products.

Nature of the hazard

Hepatitis B virus (HBV) belongs to the *Hepadnaviridae* family of viruses. It is an enveloped virus with a DNA genome and icosahedral capsid (Seeger et al. 2013; te Winkel and Schaefer 2015). HBV is sensitive to aldehypes and alcohol (Sattar et al. 2001), however the level of inactivation of HBV in human milk subjected to Holder pasteurisation is uncertain (Oliveira et al. 2009). Like all viruses, HBV can multiply in living host cells but cannot replicate in food (Codex 2012). HBV can cause potentially life threatening illness with chronic sequelae.

Transmission

HBV can be transmitted sexually, parenterally[1], via mother-to-infant transmission (predominately occurs during delivery) or through mucosal contact with infected blood or other bodily fluids (CDC 2015; Pol et al. 2011; Shih and Liu 2017). The rate of mother-to-infant transmission of HBV is 5-10% regardless of feeding method (human milk versus formulae) (Shih and Liu 2017; Zhang et al. 2014). Whilst HBV has been detected in human milk, the role of breastfeeding in HBV transmission is unclear (Petrova and Kamburov 2010; Zhang et al. 2014). Two systematic reviews found that breastfeeding by HBV seropositive mothers did not increase the risk of HBV infection in vaccinated infants (Shi et al. 2011; Zheng et al. 2011). Under the Australian National Immunisation Program the HBV vaccine should be given to all infants as soon as practicable after birth. The recommendation is that it be given within 24 hours (DOH 2018a). However, in preterm infants the HBV vaccine is less immunogenic than in full term infants. As such, the HBV vaccine may be inadequate to protect preterm infants, increasing their vulnerability to HBV infection (Freitas da Motta et al. 2002; Oliveira et al. 2009). In Australia it is recommended to give preterm infants an additional HBV booster in addition to the four-dose schedule recommended for all infants (DOH 2018b). Also, mothers with cracked or bleeding nipples could expose the infant to infectious doses of HBV through blood (Kupek and Savi 2017; Pronczuk et al. 2002).

Studies have shown that HBV surface antigen was detected in 58-100% of colostrum samples from HBV seropositive mothers (Lin et al. 1993; Oliveira et al. 2009). HBV seroprevalence in pregnant women and potential human milk donors ranges from <1% in non-endemic regions to >20% in endemic regions (Cohen et al. 2010; Euler et al. 2003; Liu et al. 2007; Petrova and Kamburov 2010).

Disease severity

HBV is a severe hazard as it causes potentially life threatening illness with chronic sequelae. Individuals infected as a neonate have >90% chance of developing a chronic HBV infection. Most infants are asymptomatic, however some develop fever, jaundice and liver tenderness (Karnsakul and Schwarz 2011). The sequelae of chronic HBV infection include liver damage, liver failure and liver cancer. About 25% of individuals who become chronically infected during

[1] Route does not involve the gastrointestinal tract, e.g. intravenous

childhood will eventually die from serious liver conditions such as cirrhosis[2] or hepatocellular carcinoma[3] (CDC 2015; Koziel and Thio 2010).

Infectivity

The infective dose of HBV in human milk is not known as the role of human milk in transmission is unclear. Perinatal transmission in vaccinated infants is associated with higher viral loads. Very large doses (>10^8 DNA copies/ml in the mother's blood) has been associated with transfer of HBV to infants who had received hepatitis B immunoglobulin and HBV vaccination (Wiseman et al. 2009). Preterm infants, who do not respond as well to HBV vaccine, or unvaccinated infants may be more susceptible to HBV infection.

Risk mitigation

Controls are needed to minimise contamination of human milk with HBV. Potential human milk donors should be screened to exclude HBV seropositive individuals from donating. International human milk banks, including those in Australia, routinely perform serological screening of donors for HBV to ensure the microbiological safety of donor human milk (Bharadva et al. 2014; Hartmann et al. 2007; HMBANA 2015; UKAMB 2003).

HBV DNA has been detected by polymerase chain reaction in naturally contaminated human milk following Holder pasteurisation (62.5^{o}C for 30min). However as HBV cannot be cultured *in vitro*, it is not known if the virus is still viable after the pasteurisation process (Hilfenhaus et al. 1997; Oliveira et al. 2009).

Evaluation of uncertainty

There is uncertainty around the transmissibility of HBV through human milk and the viral load required for this potential mode of transmission. If assumed to be the same as perinatal transmission via blood, then infectivity would be considered to be very low.

Pooling of human milk from multiple donors is common practice amongst many human milk banks and would dilute the viral load from a single donor, however some milk banks only pool milk from individual donors (Haiden and Ziegler 2016). The Australian Red Cross milk bank pasteurises human milk in single donor batches (Australian Red Cross 2018).

Risk characterisation

There is evidence that HBV can be present in colostrum. Large doses are required for infection to occur, with higher viral loads associated with perinatal transmission in vaccinated infants. There is a medium likelihood of exposure as although there is a moderate incidence of HBV amongst potential donors, a high proportion of HBV seropositive mothers shed the virus, and the HBV vaccine is less effective in preterm infants; the role of human milk in HBV transmission is unclear. Also, cracked or bleeding nipples could permit bloodborne virus transfer. HBV causes severe disease and can be fatal. HBV in imported human milk and human milk products presents a potential medium or high risk to public health and safety.

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[2] Scarring of the liver

[3] Cancer of the liver

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