Imported food risk advice

Hepatitis C 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 C virus (HCV) belongs to the *Flaviviridae* family of viruses. It is a roughly spherical, enveloped virus with a RNA genome (Lindenbach et al. 2013; Ray and Thomas 2010). HCV is sensitive to heat, ultraviolet light irradiation, aldehydes, alcohols and detergents (Pfaender et al. 2015; Song et al. 2010). Like all viruses, HCV can multiply in living host cells but cannot replicate in food (Codex 2012). HCV can cause potentially life threatening illness with chronic sequelae.

Transmission

HCV is a bloodborne virus and can be transmitted parenterally[1] or via mother-to-infant transmission (predominantly *in utero* or during delivery). The rate of mother-to-infant transmission of HCV is 5-12%. HCV can also be transmitted sexually, although this is infrequent (Le Campion et al. 2012; Pfaender et al. 2013; Ruiz-Extremera et al. 2000). It is unclear if HCV can be transmitted through human milk (Lawrence and Lawrence 2001; Ruiz-Extremera et al. 2000). A systematic review found no association between breastfeeding by HCV seropositive mothers and the risk of HCV transmission to infants (Cottrell et al. 2013). However, transmission of HCV from symptomatic mothers with a high HCV viremia to HCV-RNA negative infants has been documented, potentially occurring via breastfeeding (Kumar and Shahul 1998). Also, mothers with cracked or bleeding nipples could increase the risk of transmission to infants (Peters et al. 2016).

Limited studies have shown a range in prevalence of HCV in human milk (0-100%) (Mast 2004), demonstrating a high degree of uncertainty around the overall prevalence of HCV in human milk. HCV RNA has been detected in 100% of colostrum samples from asymptomatic HCV seropositive mothers (n=60) (Kumar and Shahul 1998). Conversely, however, no HCV RNA has been detected from colostrum samples from HCV seropositive viremic mothers (n=28) (Spencer et al. 1997). HCV seroprevalence in pregnant women and potential human milk donors ranges from <1% in non-endemic countries to >15% in endemic countries (Cohen et al. 2010; Roberts and Yeung 2002; Shebl et al. 2009).

Disease severity

HCV is a severe hazard as it causes potentially life threatening illness with chronic sequelae. Approximately 80% of individuals infected with HCV as a child develop a chronic HCV infection. Most children are asymptomatic, although some cases develop hepatomegaly[2] (EPHN 2005; Squires and Balistreri 2017). The sequelae of chronic HCV infection includes liver damage, liver failure and liver cancer and can be fatal. Individuals with HCV infection have 10-20% probability of developing cirrhosis[3] over 20-30 years. Once cirrhosis develops, HCV seropositive individuals have a

[1] Route does not involve the gastrointestinal tract, e.g. intravenous
[2] Enlargement of the liver
[3] Scarring of the liver

3-6% probability of developing liver failure and a 1-5% probability of developing hepatocellular carcinoma[4] each year (CDC 2015; Reddy et al. 2012).

Infectivity

The infective dose of HCV in human milk is not known as the role of human milk in transmission is unclear. Perinatal transmission is associated with higher viral loads. Very large doses (>10^6 RNA copies/ml in the blood of the mother) were associated with transfer of HCV to infants (Okamoto et al. 2000; Yeung et al. 2014). Also, the viral load in human milk is significantly lower than in blood (Kumar and Shahul 1998; Lin et al. 1995).

Risk mitigation

Controls are needed to minimise contamination of human milk with HCV. Pasteurisation of the milk is a primary control, however donor screening to exclude HCV seropositive individuals can reduce the viral load in the donor milk to be pasteurised. A study by Song et al. (2010) demonstrated that heating cell cultured-derived HCV (2.5×10^4 focus-forming units/ml) in culture medium at 60^{o}C for 8 min inactivated the virus. Holder pasteurisation (62.5^{o}C for 30 min) is the method of choice to eliminate contamination of banked human milk. International human milk banks, including those in Australia, routinely perform Holder pasteurisation on human milk and serologically screen donors for HCV to ensure the microbiological safety of donor human milk (Bharadva et al. 2014; Hartmann et al. 2007; HMBANA 2015; UKAMB 2003).

Evaluation of uncertainty

There is uncertainty around the prevalence of HCV in human milk, the transmissibility of HCV through human milk and the viral load required for this potential method 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 HCV can be present in human milk. Large doses are required for infection to occur, with higher viral loads associated with perinatal transmission. There is a medium likelihood of exposure as although there is a moderate incidence of HCV amongst potential donors and HCV can be shed by donors, the role of human milk in HCV transmission is unclear. Also, cracked or bleeding nipples could permit bloodborne virus transfer. HCV causes severe disease and can be fatal. HCV in imported human milk and human milk products presents a potential medium or high risk to public health and safety.

This risk advice was compiled in: August 2018, updated October 2019

References

Australian Red Cross (2018) Milk bank media release. Australian Red Cross Blood Service, Melbourne. https://www.donateblood.com.au/milk-bank-media. Accessed 2 July 2019

Bharadva K, Tiwari S, Mishra S, Mukhopadhyan K, Yadav B, Agarwal RK, Kumar V, Infant and Young Child Feeding Chapter, Indian Academy of Pediatrics (2014) Human milk banking guidelines. Indian Pediatrics 51:469–474

CDC (2015) Hepatitis C information. Centers for Disease Control and Prevention, Atlanta. https://www.cdc.gov/hepatitis/hcv/index.htm. Accessed 16 July 2018

Codex (2012) Guidelines on the application of general principles of food hygiene to the control of viruses in food (CAC/GL 79-2012). Codex Alimentarius, Rome. http://www.fao.org/fao-who-codexalimentarius/codex-texts/guidelines/en/. Accessed 22 May 2018

Cottrell EB, Chou R, Wasson N, Rahman B, Guise JM (2013) Reducing risk for mother-to-infant transmission of hepatitis C virus: A systematic review for the U.S. Preventative Services Task Force. Annal of Internal Medicine 158:109–113

[4] Cancer of the liver

EPHN (2005) Three broad modalities in the natural history of vertically acquired hepatitis C virus infection. Clinical Infectious Diseases 41:45–51

Haiden N, Ziegler EE (2016) Human Milk Banking. Annals of Nutrition & Metabolism 69:8–15

Hartmann BT, Pang WW, Keil AD, Hartmann PE, Simmer K (2007) Best practice guidelines for the operation of a donor human milk bank in an Australian NICU. Early Human Development 83:667–673

HMBANA (2015) Guidelines for the establishment and operation of a donor human milk bank. Human Milk Banking Association of North America, Fort Worth

Kumar RM, Shahul S (1998) Role of breast-feeding in transmission of hepatitis C virus to infants of HCV-infected mothers. Journal of Hepatology 29:191–197

Lawrence RM, Lawrence RA (2001) Given the benefits of breastfeeding, what contraindications exist? Pediatric Clinics of North America 48:235–251

Le Campion A, Larouche A, Fauteux-Daniel S, Soudeyns H (2012) Pathogeneisis of hepatitis C during pregnancy and childhood. Viruses 4:3531–3550

Lin HH, Kao JH, Hsu HY, Ni YH, Chang MH, Huang SC, Hwang LH, Chen PJ, Chen DS (1995) Absence of infection in breast-fed infants born to hepatitis C virus-infected mothers. The Journal of Pediatrics 126:589–591

Lindenbach BD, Murray CL, Thiel HJ, Rice CM (2013) Flaviviridae. In: Knipe DM, Howley PM (eds) Fields virology, 6th edition, Ch 25. Lippincott Williams & Wilkins, Philadelphia, pp 712–746

Okamoto M, Nagata I, Murakami J, Kaji S, Iitsuka T, Hoshika T, Matsuda R, Tazawa Y, Shiraki K, Hino S (2000) Prospective reevaluation of risk factors in mother-to-child transmission of hepatitis C virus: High virus load, vaginal delivery, and negative anti-NS4 antibody. The Journal of Infectious Diseases 182:1511–1514

Peters MD, McArthur A, Munn Z (2016) Safe management of expressed breast milk: A systematic review. Women and Birth 29:473–481

Pfaender S, Heyden J, Friesland M, Ciesek S, Ejaz A, Steinmann J, Steinmann J, Malarski A, Stoiber H, Tsiavaliaris G, Bader W, Jahreis G, Pietschmann T, Steinmann E (2013) Inactivation of hepatitis C virus infectivity by human breast milk. Journal of Infectious Diseases 208:1943–1952

Pfaender S, Brinkmann J, Todt D, Riebesehl N, Steinmann J, Steinmann J, Pietschmann T, Steinmann E (2015) Mechanisms of methods for hepatitis C virus inactivation. Applied and Environmental Microbiology 81:1616–1621

Ray SC, Thomas DL (2010) Hepatitis C. In: Mandell GL, Bennett JE, Dolin R (eds) Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 7th edition, Ch 154. Churchill Livingstone, Philadelphia, pp 2157–2185

Reddy KR, Belle SH, Fired MW, Afdhal N, Navarro VJ, Hawke RL, Wahed AS, Doo E, Meyers CM, SyNCH Study Group (2012) Rationale, challenges, and participants in a Phase II trial of a botanical product for chronic hepatitis C. Clinical Trials 9:102–112

Ruiz-Extremera A, Salmeron J, Torres C, Munoz de Rueda P, Gimenez F, Robles C, Miranda MT (2000) Follow-up of transmission of hepatitis C to babies of human immunodeficiency virus-negative women: The role of breast-feeding in transmission. The Pediatric Infectious Disease Journal 19:511–516

Song H, Li J, Shi S, Yan L, Zhuang H, Li K (2010) Thermal stability and inactivation of hepatitis C virus grown in cell culture. Virology Journal 7:40

Spencer JD, Latt N, Beeby PJ, Collins E, Saunders JB, McCaughan GW, Cossart YE (1997) Transmission of hepatitis C virus to infants of human immunodeficiency virus-negative intravenous drug-using mothers: Rate of infection and assessment of risk factors for transmission. Journal of Viral Hepatitis 4:395–409

Squires JE, Balistreri WF (2017) Hepatitis C virus infection in children and adolescents. Hepatology Communications 1:87–98

UKAMB (2003) Guidelines for the establishment and operation of human milk banks in the UK. United Kingdom Association for Milk Banking, London. https://www.rcpch.ac.uk/sites/default/files/asset_library/Research/Clinical%20Effectiveness/Endorsed%20guidelines/Milk%20Banks/donor%20guidelines%203rd%20ed%20FINAL.pdf. Accessed 8 February 2018

Yeung CY, Lee HC, Chan WT, Jiang CB, Chang SW, Chuang CK (2014) Vertical transmission of hepatitis C virus: Current knowledge and perspectives. World Journal of Hepatology 6:643–651