Imported food risk advice

Mycotoxins 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

Mycotoxins are secondary metabolites produced by a range of fungi from genera such as *Aspergillus*, *Penicillium*, *Fusarium*, and *Alternaria* that contaminate crops and foods around the world. Their occurrence in foods is affected by a number of factors including climate, agricultural practice and postharvest storage conditions (Warth et al. 2016).

A significant body of literature deals with contamination of foods with mycotoxins (Alshannaq and Yu 2017; Wild and Gong 2010). These include cereals, peanuts, tree nuts and dried fruits, with levels generally found to be higher in lower-income countries with less well developed agricultural practices and regulatory structures (Wild and Gong 2010).

Research on the presence of mycotoxins in human milk is more limited and relates mainly to aflatoxin M1 (AFM1) and ochratoxin A (OTA) (reviewed by (Cherkani-Hassani et al. 2016; Warth et al. 2016)). Aflatoxins are genotoxic and considered to be carcinogenic in humans (WHO 2017; Wild and Gong 2010). OTA causes adverse effects on the kidney in experimental animals, although a causal relationship between OTA exposure and human illness has not yet been established (Bui-Klimke and Wu 2014; Bui-Klimke and Wu 2015; WHO 2008).

A small number of studies have reported the presence of other mycotoxins (including zearalenone, fumonisin B1, nivalenol and HT-2 toxin) in human milk samples, but the available information is too limited to draw any conclusions regarding the likely levels that may be present and their significance for human health (Magoha et al. 2014; Massart et al. 2015; Rubert et al. 2014; Valitutti et al. 2018; Warth et al. 2016). Therefore this risk advice is focused on AFM1 and OTA.

Presence in human milk

AFM1 is a metabolite of aflatoxin B1 (AFB1), and is found in milk or milk products obtained from humans or livestock that have ingested food contaminated with AFB1. Recent reviews of the available literature on mycotoxins in human milk reported that levels of AFM1 are generally very low in European and South American countries but are higher in sub-Saharan Africa as well as Egypt and Turkey (Cherkani-Hassani et al. 2016; Warth et al. 2016).

OTA is excreted into human milk and has been found at a range of concentrations in different regions (WHO 2008). Levels of OTA in human milk are low in most European and South American countries, with higher levels found in human milk from Egypt, Turkey and Sierra Leone (Cherkani-Hassani et al. 2016; Warth et al. 2016).

Warth et al. (2106) noted that there are significant limitations in most of the available studies of mycotoxins in human milk. Not all studies report adequate details on the methodology used, in particular information on the

accuracy of the analytical methods used. Some studies are based on small sample sizes, and the proportion of samples that tested positive for AFM1 or OTA is very variable, ranging from 100% to as low as 0.5%.

Adverse health effects

The World Health Organization (WHO) reports that few, if any, adverse effects have been associated solely with consumption of human milk containing background levels of environmental chemicals. This is in contrast to the established evidence that human milk and the practice of breast-feeding confer significant health benefits to infants (WHO Undated).

Information on the adverse health effects of AFM1 and OTA is summarised below.

Aflatoxins are potent genotoxic carcinogens and induce tumours in the liver of animals and humans. In humans, their potency is higher in individuals infected with hepatitis B virus (WHO 2017; Wild and Gong 2010). AFB1 is considered the most potent carcinogen. The carcinogenic potency of AFM1 has been calculated to be an order of magnitude lower than that of AFB1 (WHO 2002, 2017).

The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives (JECFA) recently evaluated the risks to human health from aflatoxins in food (WHO 2017). JECFA did not conduct a risk assessment specific to AFM1 in human milk, but noted that it occurs as a consequence of maternal exposure to AFB1. The Committee considered that this exposure was minimal in developed countries but can be problematic in rural subsistence farming areas of developing countries. Estimates of dietary exposure to AFM1 were much lower than estimated dietary exposures to AFB1. Overall, the Committee concluded that, given the relative cancer potencies and international dietary exposure estimates for AFB1 and AFM1, AFM1 will generally make a negligible contribution to aflatoxin-induced cancer risk for the general population (WHO 2017).

OTA is produced by several *Penicillium* and *Aspergillus* fungal species. The major target organ for OTA is the kidney. Studies have shown that OTA induces progressive nephropathy in mice, rats, dogs and pigs, and kidney tumours in rats and mice (EFSA 2006; WHO 2008). The available epidemiological evidence does not show a clear causal link to human disease (Bui-Klimke and Wu 2014; Bui-Klimke and Wu 2015; WHO 2008).

JECFA established a provisional tolerable weekly intake (PTWI) of 100 ng/kg bw for OTA. The most recent dietary risk assessment by JECFA concluded that dietary exposure to OTA from cereals, mainly based on European data, was about 8-17 ng/kg bw/week, well below the PTWI (WHO 2008). Similarly, the European Food Safety Authority (EFSA) found that exposures of adult Europeans to OTA from a range of foods were below the tolerable weekly intake (TWI) of 120 ng/kg bw established by EFSA (EFSA 2006). Given that maternal exposures are estimated to be below the PTWI, exposures of breast fed infants are also unlikely to be of significant health concern.

Risk mitigation

Australian and overseas milk bank guidelines do not include recommendations to specifically screen donors for levels of mycotoxins (Hartmann et al. 2007; HMBANA 2015; NICE 2010).

The American Academy of Pediatrics notes that the pooling process with donor milk makes it very unlikely that non-infectious contaminants will represent a significant exposure risk (Committee on Nutrition, Section on Breastfeeding, Committee on Fetus and Newborn 2017). Pooling of human milk from multiple donors is common practice amongst many human milk banks, 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).

Evaluation of uncertainty

There is uncertainty as to whether mycotoxins may be present in human milk and milk products and if so, which mycotoxins are present and at what concentrations. Researchers have noted that there is a need for further work to better understand lactational transfer rates, the pattern of mycotoxins and their metabolites in human milk in different populations and mycotoxin exposures in infants who are not breastfed.

Risk characterisation

Risk assessments conducted by JECFA and EFSA have concluded that dietary exposures to AFM1 and OTA are unlikely to be of public health concern. Levels of AFM1 in human milk in Europe were considered to be minimal and exposure to OTA in the diet was well below the PTWI in Europe indicating that exposure via human milk is also unlikely to be of significant health concern.

Overall, on the basis of the available evidence FSANZ considers that mycotoxins in imported human milk and human milk products are unlikely to present a potential medium or high risk to public health and safety.

This is consistent with WHO advice which notes that few if any adverse effects have been associated with consumption of human milk containing background levels of environmental chemicals, in contrast to the established evidence that human milk confers significant health benefits to infants.

This risk advice was compiled in: March 2019, updated October 2019

References

Alshannaq A, Yu J-H (2017) Occurrence, Toxicity, and Analysis of Major Mycotoxins in Food. International journal of environmental research and public health 14

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

Bui-Klimke T, Wu F (2014) Evaluating weight of evidence in the mystery of Balkan endemic nephropathy. Risk Analysis 34:1688–1705

Bui-Klimke TR, Wu F (2015) Ochratoxin A and human health risk: A review of the evidence. Critical Reviews in Food Science and Nutrition 55:1860–1869

Cherkani-Hassani A, Mojemmi B, Mouane N (2016) Occurrence and levels of mycotoxins and their metabolites in human breast milk associated to dietary habits and other factors: A systematic literature review, 1984–2015. Trends in Food Science & Technology 50:56–69

Committee on Nutrition, Section on Breastfeeding, Committee on Fetus and Newborn (2017) Donor Human Milk for the High-Risk Infant: Preparation, Safety, and Usage Options in the United States. Pediatrics 139

EFSA (2006) Opinion of the Scientific Panel on contaminants in the food chain [CONTAM] related to ochratoxin A in food. EFSA Journal 4:365

Haiden N, Ziegler EE (2016) Human Milk Banking. Annals of nutrition & metabolism 69 Suppl 2:8–15

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.

Magoha H, Meulenaer B de, Kimanya M, Hipolite D, Lachat C, Kolsteren P (2014) Fumonisin B1 contamination in breast milk and its exposure in infants under 6 months of age in Rombo, Northern Tanzania. Food and Chemical Toxicology 74:112–116

Massart F, Micillo F, Rivezzi G, Perrone L, Baggiani A, Miccoli M, Meucci V (2015) Zearalenone screening of human breast milk from the Naples area. Toxicological & Environmental Chemistry 98:128–136

NICE (2010) Donor milk banks: service operation. Clinical guideline. www.nice.org.uk/guidance/cg93. Accessed 3 July 2018

Rubert J, León N, Sáez C, Martins CPB, Godula M, Yusà V, Mañes J, Soriano JM, Soler C (2014) Evaluation of mycotoxins and their metabolites in human breast milk using liquid chromatography coupled to high resolution mass spectrometry. Analytica Chimica Acta 820:39–46

Valitutti F, Santis B de, Trovato CM, Montuori M, Gatti S, Oliva S, Brera C, Catassi C (2018) Assessment of Mycotoxin Exposure in Breastfeeding Mothers with Celiac Disease. Nutrients 10:336

Warth B, Braun D, Ezekiel CN, Turner PC, Degen GH, Marko D (2016) Biomonitoring of Mycotoxins in Human Breast Milk: Current State and Future Perspectives. Chemical Research in Toxicology 29:1087–1097

WHO (Undated) Biomonitoring of human milk. Technical note, Geneva Switzerland

WHO (2002) Evaluation of certain mycotoxins in food.: Fifty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical report series, vol 906, Geneva Switzerland

WHO (2008) Safety evaluation of certain food additives and contaminants.: Prepared by the sixty-eighth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food additives series, vol 59. World Health Organization, Geneva Switzerland

WHO (2017) Evaluation of certain contaminants in food: Eighty-third report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical report series, vol 1002. World Health Organization, Geneva Switzerland

Wild CP, Gong YY (2010) Mycotoxins and human disease: A largely ignored global health issue. Carcinogenesis 31:71–82