Food and Nutrition

Health Professional Advisory

Enterobacter sakazakii Infection and Powdered Infant Formulas

Background:

On April 9, 2002, the United States Food and Drug Administration (USFDA) issued an alert to US Health Care Professionals regarding the risk associated with *Enterobacter sakazakii* infections among neonates fed milk-based, powdered infant formulas. Historically, there have been several small *E. sakazakii* outbreaks reported among infants fed milk-based, powdered formula products from various manufacturers. In addition to powdered milk-based formulas, powdered human milk fortifiers may also pose a hazard.

E. sakazakii is a motile peritrichous, gram-negative rod from the family *Enterobacteriaceae*. This organism used to be known as a "yellow pigmented *Enterobacter cloacae*" until 1980, when it was introduced as a new species based on differences in DNA-DNA hybridization, biochemical reactions, and antibiotic susceptibility. *E. sakazakii* is a rare, but life-threatening cause of neonatal meningitis, sepsis, and necrotizing enterocolitis. In general, the reported case-fatality rate varies from 40-80 % among newborns diagnosed with this type of severe infection. The type of meningitis caused by *E. sakazakii* may lead to cerebral abscess or infarction with cyst formation and severe neurologic impairment.

There is still a paucity of information on the ecology of this bacterium. However, studies have shown that this organism can be isolated from hospital and processing plant environments. Reports have also suggested a correlation between *E. sakazakii* infection and powdered infant formulas. Similarly, it has been reported that premature infants and those with underlying medical conditions may be at highest risk for developing an *E. sakazakii* infection.

Several outbreaks of *E. sakazakii*, in Neonatal Intensive Care Units (NICUs), have been reported worldwide including countries such as England, Netherlands, Greece, US and Canada. In Canada, two incidents of neonatal meningitis caused by *E. sakazakii* were reported in two Canadian hospitals (1990, 1991). It should be noted that healthy infants may not always be immune to *E. sakazakii* infections. It has been reported that in Iceland, a healthy, full-term, newborn infant became ill prior to hospital discharge and suffered permanent neurological sequelae as a result of an *E. sakazakii* infection.

Health Canada is drawing attention to the fact that powdered infant formulas are not commercially sterile products. Unlike liquid formulas, which are subjected to sufficient heat to render them commercially sterile, powdered infant formulas are not processed at high enough temperatures for sufficient time to achieve commercial sterility. Ready-to-use liquid infant formulas are available only in a commercially sterile form and indicated for premature or low-birth weight infants. However,"transition" infant formulas which are used for premature or low-birth weight infants after hospital discharge, may be either powdered or liquid. Human milk fortifiers which are added to pre-term breast milk are also available in powdered or liquid forms. A number of formulas, including formulas for infants with metabolic conditions are only available in powdered form. Powdered soy-based infant formulas may also become contaminated with *E. sakazakii* through improper cleaning of production lines and may, therefore, pose a safety hazard.

Recommendations:

Based on the above, Health Canada recommends that formula products be selected based on nutritional and medical needs. Whenever possible, an alternative to powdered formulas, such as ready-to-feed and concentrated liquid formulas, should be chosen in the NICU setting and for immunocompromised infants. If there is no alternative, the following steps will help control or minimize the risk:

Preparation of powdered infant formulas in a laminar flow hood by trained personnel and using sterilized water, which should minimize contamination from the environment. Refer to the following document for detailed procedures. Preparation of Formula for Infants: Guidelines for Health-Care Facilities, American Dietetic Association (updated April, 2002). (official document in English; a French translation is available on Health Canada's Website.

GMPs and proper sanitation should be adhered to at all times when manufacturing and preparing any type of infant formula, liquid or powder. Since *E. sakazakii* has been isolated from hospital and processing plant environments, there is a potential for contamination with this pathogen during processing, preparation and reconstitution of infant formulas.

For better assessment of the risk associated with *E. sakazakii* infections related to infant formulas, Health Canada urges Health Care professionals to promptly report adverse symptoms associated with the consumption of infant formulas to the nearest Canadian Food Inspection Agency (CFIA) office (For more information, please visit CFIA's or the blue pages).

At present, Health Canada is determining whether additional precautionary steps are required to ensure the safe manufacturing and handling of infant formulas. Health Canada is fully committed to communicating pertinent information to Health Care Professionals and consumers, if, and as soon as it becomes available.

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