Melamine Tainted Milk Products - Situation in Hong Kong

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Events So Far

On 11 September 2008, the media began to report an outbreak of kidney stones in infants and young children in China Mainland. In some cases, the bilateral kidney stones caused complete obstruction of the urinary tract leading to acute kidney failure. There were 3 deaths. Many brands of infant formula were heavily contaminated with melamine. As of October 15, over 54000 cases have sought treatment in the Mainland, with 5824 cases still under treatment in hospitals, while 43603 cases have been discharged home.

As Hong Kong is so closely inter-connected with the Mainland, the Hong Kong SAR Government, medical professionals and parents were concerned that infants and young children in Hong Kong, including those residing in the Mainland, may be affected by melamine tainted milk products (MTMP). As of October 16, 40042 infants / children have attended the Designated Clinics (DCs) set up by Hospital Authority (HA) for initial assessment and 11485 cases were subsequently referred to the 9 Special Assessment Centres (SACs). So far, 3 cases of kidney stones were detected at the SACs. With 5 other cases detected by other centres, a total of 8 cases of stones with a history of consumption of MTMP have been reported to HKSAR’s Centre for Health Protection (CHP).

It is now clear that the widespread and severe outbreak of melamine related kidney stones observed in the Mainland has not occurred in Hong Kong. The heavily contaminated milk and milk products were not distributed in Hong Kong.

Melamine Contamination, Toxicology, Health Effects

Any amounts of melamine should not be added into food. However, as it is widely used in plastics, dishware, adhesives, molding compounds, coatings and flame retardants, a tiny amount of melamine may be found in food as a contaminant. The problem in the Mainland was fraudulent adulteration to boost the apparent protein content of milk. Melamine levels of up to 2563 mg/kg were detected in some milk products. According to Sanlu Group, contaminated milk was used in the manufacture of powdered infant formula processed before August 6 and tainted milk powder has also been used in the manufacture of a number of other products. Hence the detection of melamine in other milk related products was reported across many parts of the world.

Melamine is not metabolised and is rapidly eliminated in the urine. No human data are available. In animal feeding studies, high doses of melamine have an effect on the urinary bladder, causing inflammation, formation of stones and crystals in urine. Animal studies have generally not shown any renal toxicity or the formation of kidney stones. However, a combination of melamine and cyanuric acid does cause renal toxicity as observed in the earlier outbreak of acute renal failure in cats and dogs. It appears that melamine and its structural analogues, such as cyanuric acid, may act together to form crystals. The crystal formation is concentration dependent and likely to occur only at high-dose levels. So far, the presence of cyanuric acid has not been confirmed in the current event in the Mainland.

Infants and young children are highly susceptible as milk is their major food and the amount of melamine intake per body weight is much higher than that of adults. With exposure to a very high melamine level (e.g. 2563 mg/kg) for a sustained period of time, it is not surprising there is stone formation.

Health-based Guidance Values and Risk Assessment

Following the pet food incident in 2007, the US FDA has published an interim safety/risk assessment and has established for melamine a tolerable daily intake (TDI) of 0.63 mg/kg bw/day. The European Food Safety Authority has adopted a TDI of 0.5 mg/kg bw/day.

Considering a TDI of 0.5 mg/kg bw/day, this would allow a 50kg person to a tolerable amount of 25 mg melamine per day. Assuming the person would drink one litre of milk per day, this would indicate that the TDI would be reached at a level of 25 mg melamine per litre of milk. Considering a 5kg infant, the TDI would be 2.5 mg per day. This amount would be reached when consuming 750 ml liquid (or reconstituted) formula if contaminated at a level around 3.3 mg/l (ppm).

HKSAR has taken a lead to define the legal limit for melamine in food. Under the amended Harmful Substances in Food Regulation (Cap. 132 AF), milk and food intended to be consumed principally by children under the age of 36 months and any food intended to be consumed principally by pregnant or lactating women shall not contain melamine exceeding 1 mg/kg. For other food, melamine level shall not exceed 2.5 mg/kg. Subsequently Canada and New Zealand have adopted the same standard.
HKSAR’s Centre for Food Safety (CFS) has adopted a TDI of 0.63 mg/kg bw/day for adult and 0.32 mg/kg bw/day for a child under age of 3, as children are more sensitive to melamine.

Hospital Response Plan - Screening and Treatment Centres

To assess the situation in Hong Kong and to reassure the public (parents), the Food and Health Bureau and HA set up a response plan to screen infants and children under the age of 12. On September 20, a designated clinic was set up at the Princess Margaret Hospital. However, as many MTMPs were detected in the Mainland and Hong Kong, the demand for screening escalated very sharply and acutely. HA set up a Task force to handle the “crisis” including an Executive panel, Experts group, Task group and Communication panel.

Eighteen DCs were quickly set up at HA’s GOPCs, commenced operation on September 23 to meet the demand and expectation. At the DCs, history of consumption of MTMP and renal symptoms were assessed. Urine analysis was performed. If an infant / child has continuous (one month) consumption of MTMPs from the Mainland or those listed by HKSAR CFS and / or symptoms of renal stone / disease / failure, he /she is referred to the SACs for further investigation, including blood tests* and ultrasound of the kidneys (* from October 10, blood test for creatinine is only indicated for cases with positive history or findings). Suspected or confirmed MTMP-stone cases were referred to the Paediatric Renal Centre at Princess Margaret Hospital for investigation and treatment so as to gain experience in managing and study such a new disease entity.

Clinical Picture

For surveillance purposes, the reporting criteria of a suspected case to CHP is a child presenting with renal disease including urinary calculi and with history of exposure to melamine containing dairy products. On October 17, CHP refined the case definitions for suspected case, probable case (a suspected case melamine intake exceeding the defined TDI for a significant duration) and confirmed case (with laboratory confirmation).

As of October 16, out of the 11485 cases who have undergone detailed assessments at the SACs, 3 cases of stone were detected by ultrasound scan (stone size > 4mm). Five other cases were detected by other centres. The clinical picture of these 8 cases was very mild. Renal function was normal. Apart from one case which required lithotripsy, the other cases were treated conservatively (with extra fluid). In one of the cases, the stone had disappeared. (see table 1).

A Hong Kong delegation has visited Hebei and Beijing to gain first hand experience in the investigation and treatment of MTMP related stones. Two third of the cases were associated with consumption of Sanlu Milk products. There is a dose-dependent phenomenon. These MTMP related stones are relatively soft and can pass out spontaneously with measures to increase urine flow + alkalinisation of urine. Only a few patients required surgical intervention. Cystoscopy retrograde intubation into the ureter may dislodge the stone / sands. Percutaneous kidney drainage and removal of stones were required in some cases. Extracorporeal shock wave lithotriptor is not used as application is difficult and hazardous in infants / children. Once the urinary obstruction is relieved, the general condition and renal function are back to normal.

Issues

(1) One discussion point is case definition, as it is not easy to accurately quantify the amount of MTMP taken. There is a background noise of a very small number of kidney stones being detected in children every year. Another issue requiring further deliberation and follow up is possible long term renal effects. Some form of long term follow-ups is necessary for a selected group of high risk patients (yet to be defined). HKSAR FHB has set up an Expert Panel on Melamine Incident to formulate effective procedures and methods for medical assessment and treatment, and to propose follow-up measures on medical and health services.

(2) Mass health screening inevitably detected false positive cases. A significant proportion of the initial urine analysis was positive for proteinuria and/or haematuria detected by albustix and haemastix, but was negative on further testing by repeat test, urinary protein determination and urine microscopy. Nevertheless, false positive finding generates additional work load and some degree of anxiety for the parents.

(3) This massive screening programme mounted by the Hospital Authority is a heavy burden on the already stretched resources of the Hospital Authority. Many staff have to take on extra duty outside office hours and during weekends to clear up the waiting list. Over 10,000 ultrasound scans have been performed, yet another 10,000 cases are awaiting ultrasound scan. Although the attendance at the DCs has subsided considerably, it will take considerable resource and time to clear the backlog of investigations.

(4) It is now clear that fortunately the children in Hong Kong have not been exposed to the batch of very toxic MTMPs. However as it is important to ensure the health of our children, there was no option but to mount such a drastic and big scale response to a health scare for Hong Kong.

[Information and data are as available on 16 October 2008 and is subject to change and update]