Melamine Tainted Milk Product-related Renal Disorder - What Do We Know So Far?

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As the melamine milk tainted products (MTMP) crisis in Hong Kong has started to cool down, it is high time to review the experience gained on MTMP in the recent 1 1/2 months. Around 3 weeks after the Hospital Authority set up the screening and treatment programme for children with history of consuming MTMP, a melamine tainted milk product symposium was held on 18 October 2008 in the Princess Margaret Hospital (PMH). It was jointly organised by the Department of Paediatrics & Adolescent Medicine of PMH, the Hong Kong Paediatric Society and the Hong Kong Paediatric Nephrology Society.

The opening remarks were given by Professor Gabriel Leung (Under Secretary for Food & Health ) and Dr. Lily Chiu (Cluster Chief Executive, Kowloon West Cluster, Hospital Authority ).

While there are no previous human data on the toxicity of melamine, extrapolation from animal studies may be used to project the adverse effects on humans. Dr. SN Wong (Consultant Paediatrician, TMH) discussed on the outbreak of renal failure associated with ingestion of pet food containing melamine and cyanuric acid in cats and dogs in 2004 and 2007. Melamine alone is of low toxicity but studies have shown that combination of it with cyanuric acid leads to crystal formation and subsequent kidney toxicity. Renal histology in animals showed melamine-cyanuric acid crystals in distal tubules with tubulitis, necrosis and tubulointerstitial nephritis.

Human cases of toxicity of melamine were first reported on September 11, 2008 that infants and young children with kidneys stones and renal failure were admitted to hospitals in the China Mainland after consumption of infant formula contaminated with melamine. Dr. MC Chiu (Chief of Service, Dept of Paediatrics & Adolescent Medicine, PMH) presented on the outbreak in humans. By October 15, more than 54,000 cases had sought treatment for kidney stones and renal failure were reported. The visits to Hebei and Beijing by Hong Kong delegates were also presented. The vast majority of cases involved children below 3 years of age and were linked to the consumption of Sanlu powdered infant formula. From the experience of the Mainland, the stones were loose and sand-like which could be passed out spontaneously with hydration and alkalisation of urine. Surgical intervention including cystoscopic retrograde catheterisation into ureters, percutaneous kidney drainage, and lithotripsy (second line treatment) were required in some children.

As of 17 October, 40,772 had attended the DCs and 12,022 had been assessed in the SACs. The incidence of kidney stones is very low with only 5 cases detected (0.04%). The PMH SAC screening clinic, haematuria, proteinuria and abnormal USG were detected at 0.73%, 0.45%, and 2.9% respectively.

Investigation with USG only detects kidney stones and cannot exclude other kidney adverse effects of melamine such as tubular crystals and tubulointerstitial nephritis which have been reported in animal studies. Dr. WL Mak (Consultant Chemical
Pathologist, Toxicology Reference Laboratory, PMH) successfully developed an urine test for melamine and he discussed the possible clinical application for MTMP-related kidney disorders. Further studies would be required.

Dr. YY Ho (Consultant, Centre for Food Safety (CFS)) discussed on the surveillance, sampling and testing of milk and dairy products for melamine by the CFS. He also discussed on the amended Harmful Substances in Food Regulation standards for melamine which define a tolerable daily intake of 1mg/kg (1 ppm) for milk, any food intended to be consumed principally by children under the age of 36 months and those by pregnant or lactating women; and 2.5 mg/kg (2.5 ppm) for other food.

At the end of the symposium, there were fruitful discussion and conclusions by the expert discussants (Prof. Chan Yan Keung, Dr. Chow Chun Bong, Dr. Paul SF Lee, Dr. Leung Ting-Hung, Prof. Paul KH Tam, and Dr. Peggy SK Chiu) together with the speakers. The problem of MTMP-related renal disorder is much less severe than cases in the Mainland. All the suspected cases in Hong Kong suffered from small kidney stones ranging from 4 mm to 7 mm. This is probably related to the much lower level of melamine in our milk products (e.g. Yili melamine level of 9.9mg/kg in HK compared with Sanlu powdered infant formula melamine level of up to 2500 mg/kg in the Mainland). There are difficulties in confirming that the kidney stones are related to MTMP as there is no confirmatory test so far. Other causes of kidney stones have to be ruled out. The role of alkalinisation of urine still requires further evaluation and the constituents of the stones need to be well studied. In the Mainland, alkali therapy has been tried because uric acid has been found but if the stones contain melamine cyanuric complex then they will dissolve better in acid pH instead. It is not yet known what long-term complications such as tubulointerstitial nephritis melamine may cause. It definitely requires long term follow-up for those high risk cases.