

Assessment on Dietary Melamine Exposure from Tainted Infant Formula

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Objective To estimate the dietary melamine exposure in Chinese infants and young children from the consumption of melamine adulterated Sanlu infant formula. **Methods** Four age groups of infants and young children (3, 6, 12, and 24 months) were chosen as the assessed subjects and the maximum amount of infant formula consumption was estimated based on the recommended usage level in the package insert of Sanlu infant formula and other brands. Melamine was analyzed in 111 Sanlu infant formula samples collected from the markets in Beijing and Gansu province using the LC-MS-MS with a limit of quantification of 0.05 mg/kg. Four levels of melamine concentration were chosen to estimate the dietary intakes, including the mean, median, 90th percentile, and maximum. **Results** The infants of 3 months had the highest intake of melamine, and with the increase of the age (month), the intake decreased. Based on the median melamine concentration (1 000 mg/kg) as an example, the melamine intakes for the infants of 3, 6, 12, and 24 months were 23.4, 21.4, 15.0, and 8.6 mg/kg bw/d, respectively. **Conclusion** Dietary melamine intakes from tainted Sanlu infant formula significantly exceeded the TDI level (0.2 mg/kg bw/d) recommended by the WHO Expert Meeting in 2008. However, the present assessment has some limitations including the poor representative samples, the varied melamine concentrations in the adulterated Sanlu infant formula, and other brand infant formula possibly consumed by these infants.

Key words: Dietary exposure assessment; Melamine; Infant formula

INTRODUCTION

Several thousand infants and young children in China suffered acute kidney failure caused by kidney stone since September of 2008. After an immediate and careful investigation, the Ministry of Health of China confirmed that these cases were related to the ingestion of infant formula contaminated with melamine which had been deliberately added into raw milk to falsely boost its apparent protein content because of its high nitrogen content^[1]. Animal studies have shown that melamine has a low toxicity but a long-term consumption of high dose could cause the formation of kidney stone^[2-3].

According to the General Administration of Quality Supervision, Inspection and Quarantine of China (AQSIQ), up to 22 infant formula manufacturers across the country were found to have melamine in some of their products (levels ranged between 0.09 mg/kg and 2 560 mg/kg)^[4]. Among those,

Sanlu brand had the highest detection rate of melamine and also the highest level of melamine in infant formula samples. Epidemiological investigations and clinical examinations confirmed that melamine tainted Sanlu infant formula was the cause of this urinary tract stone epidemic in China.

In order to provide information on the occurrence of melamine and its analogs in infant formula and other dairy products, a Melamine Analysis Group was set up in the Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention (China CDC). Therefore, the melamine content in Sanlu infant formula was measured and the relevant data became available. The present report was to estimate the dietary exposure of melamine in infants and young children during the melamine crisis on the basis of the melamine content in the formula and the hypothetical infant formula consumption data.

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MATERIALS AND METHODS

Subjects

Four groups of infants and young children aged 3, 6, 12, and 24 months were chosen as the assessed subjects. The mean body weight (kg) of each age group was estimated according to the growth and development of Chinese infants^[5].

Infant Formula

The most contaminated Sanlu infant formula samples were collected from the markets in Beijing and Gansu province (one of the heavily affected areas).

Infant Formula Consumption

The maximum amount of infant formula consumption in the four age groups was estimated based on the recommended usage level in the package insert of Sanlu infant formula and other brands.

Melamine Concentrations in Sanlu Infant Formula

Melamine concentration (mg/kg) in a total of 111 Sanlu infant formula samples was determined using the LC-MS-MS method^[6], and the limit of quantification (LOQ) was found to be 0.05 mg/kg.

Intake Estimates of Melamine

The melamine intake in the four age groups, expressed as mg melamine per kg body weight per day (mg/kg bw/d), was calculated by multiplying the actual measured melamine concentration (mg/kg) by the daily maximum amount of infant formula consumption (kg/d), and then divided by the mean

body weight (kg).

RESULTS

Infant Formula Consumption

Based on the recommended usage level in the package insert of Sanlu infant formula and other brands, the maximum amount of infant formula consumption for the four age groups of infants and young children was estimated (Table 1). For the infants aged 6 months with a mean body weight of around 7 kg, the maximum formula consumption was about 0.15 kg/d.

TABLE 1

Maximum Consumption of Infant Formula in Various Ages of Infants and Young Children

Age (mon)	Mean Body Weight* (kg)	Maximum Consumption** (kg/d)
3	5.5	0.129
6	7	0.15
12	10	0.15
24	14	0.12

Note. *Estimates based on the growth and development of Chinese infants. **Estimates based on the recommended usage level in the package insert of Sanlu infant formula and other brands.

Melamine Concentration in Sanlu Infant Formula^[7]

The melamine concentrations in 111 Sanlu infant formula samples and 52 other samples collected from the affected areas in Gansu province were found to vary from <0.05 to 4 700 mg/kg (Table 2). The median levels for all samples and those samples collected from the affected areas in Gansu province were 1 000 and 1 700 mg/kg, respectively.

TABLE 2

Melamine Concentrations in Sanlu Infant Formula Samples

Sample	No. of Samples	Mean (mg/kg)	Median (mg/kg)	90th Percentile (mg/kg)	Maximum (mg/kg)	Range (mg/kg)
A	111	1 212	1 000	2 600	4,700	<0.05-4 700
B	52	1 674	1 700	2 880	4,700	<0.05-4 700

Note. Sample A: all samples. Sample B: samples collected from affected area in Gansu province. LOQ, 0.05 mg/kg.

Melamine Exposure in Different Scenarios

Data shown in Table 3 demonstrated that infants of 3 months had the highest intake of melamine, and with the increase of the age (month), the intake decreased. Based on the median melamine concentration (1 000

mg/kg) as an example, the melamine intake by infants aged 3, 6, 12, and 24 months were 23.4, 21.4, 15.0, and 8.6 mg/kg bw/d, respectively. In the scenario of the 90th percentile melamine concentration (2 600 mg/kg), the intakes in the four age groups could reach 22.3 - 61.0 mg/kg bw/d.

TABLE 3
Intake Estimates of Melamine from Sanlu Infant Formula (111 Samples)

Age (mon)	Melamine Intake Estimates (mg/kg bw/d)			
	Mean Conc. (1 212 mg/kg)	Median Conc. (1 000 mg/kg)	90th Percentile Conc. (2 600 mg/kg)	Maximum Conc. (4 700 mg/kg)
3	28.4	23.4	61.0	110.2
6	26.0	21.4	55.7	100.7
12	18.2	15.0	39.0	70.5
24	10.4	8.6	22.3	40.3

Note. Four points of melamine concentration were chosen to estimate the dietary intakes, including the mean, the median, the 90th percentile, and the maximum.

DISCUSSION

Melamine, used primarily in the synthesis of melamine formaldehyde resins^[8], was the culprit of this tainted milk crisis happened last September in China and has caused a very serious health outcome^[1,9-10].

A timely and efficient dietary exposure assessment on melamine from the tainted infant formula is essential for its risk characterization, management, and communication. The dietary exposure based on the maximum consumption of melamine-tainted infant formula at the median levels of melamine detected in the most contaminated Sanlu brand was estimated to range from 8.6 to 23.4 mg/kg body weight per day (Table 3), which is about 40-120 times as much as the TDI of 0.2 mg/kg body weight proposed by the WHO Expert Meeting^[11]. The present assessment provide a rational explanation for the dramatic health outcome in the affected infants.

Ideally, individual data on infant formula consumption and individual melamine concentration in infant formula from a large number of diagnosed urinary tract stone cases and healthy infants should be used in the exposure assessment, in order to assess the dose-response relationship. However, these data are not available and to a large extent, not possible. This is a main limitation of this dietary exposure assessment. Additionally, we are fully aware that there are some other major uncertainties in the above exposure assessment practice. For example, the melamine concentrations in the adulterated Sanlu infant formula are not stable and it is impossible for all children to consume Sanlu product only. In addition, the infant formula samples analyzed are not necessarily representative. Therefore, the intake estimates are very conservative and the use of these exposure estimates should be very cautious.

The present dietary exposure assessment on melamine from Sanlu infant formula is, however, helpful for the melamine risk assessment, even though it has some limitations discussed the above.

We fully agree with the WHO expert meeting report which stated that, "Once additional occurrence data become available, the above dietary exposure assessment should be refined, and governments should be encouraged to publish and disseminate dietary exposure estimates in a timely manner, where possible"^[12].

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