Melamine toxicity in broiler chickens: A review

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ABSTRACT

Fewer than four years ago, melamine was a term known only to chemists although its use as a diuretic was studied 65 years ago. This changed almost overnight in 2007 when the pet food scandal broke out. Later in 2008, the much more serious melamine-adulterated milk powder scandal occurred in China. Ingestion of melamine-adulterated milk and other animal products could lead to fatal renal failure and even death. Melamine is an organic nitrogenous compound used in the production of plastics, dyes, fertilizers, and fabrics. It has a high nitrogen content of 667g/kg, which may correspond to a crude protein (CP) level of 4168.75 g/kg (N x 6.25). Hence, melamine is added intentionally to protein foods such as wheat gluten, corn gluten, rice protein, soya and fishmeal to falsely increase their apparent protein content, which are used for making livestock and poultry feed. The toxic effects of melamine, include nephroliths, chronic nephritis and bladder carcinoma in animals. Feeding of melamine contaminated diets to broiler chicken resulted in mortality and other production losses like reduced weight gain, increased feed conversion ratio (FCR) and tissue residues mainly in muscles of birds.

Key words: Broilers, FCR, Feed additives, Melamine, Nephrotoxicity.

Melamine (1,3,5-triazine-2,4,6-triamine; C3H6N6; MEL) is an organic compound and a trimer of cyanamide utilised in a variety of industrial applications such as plastics, coatings, leather, paints, laminates, flame-retarding agent and table-tops (China Chemical Reporter, 2006). The first serious concerns regarding the inclusion of MEL in food became evident in the 2006/2007 pet food scandal. More than 1000 dogs and cats died in various countries due to renal failure caused by accumulated kidney stones (WHO, 2008). The second appalling MEL scandal emerged in 2008 after it became known that six babies died and 294000 became ill after drinking MEL-tainted infant formula. More than 50000 of the infants were reported to be hospitalized with dysfunctional urinary symptoms caused by renal tube blockages and kidney stones (WHO, 2008). It is commercially synthesized from urea (Hau et al., 2009) and has a high melting point of 345°C, which explains why some plastic wares melt only after high heat exposure (Van der Merwe and Smith, 1991). In the feed industry the crude protein value for feedstuffs can be obtained by determining the nitrogen (N) value of the ingredient multiplied by 6.25 (Van der Merwe and Smith 1991). The N content of pure MEL is 667g/kg (Ogasawara et al. 1995) which corresponds to a crude protein value of 4168.75 g/kg. This value is substantially higher than that of pure urea (2917 g/kg). Generally, the inclusion of MEL as a fraudulent protein in feed seemed to be an alluring substitute for the more costly protein supplements.

Toxicokinetics of melamine: MEL is not metabolized by animals and greater than 90% is eliminated in urine within 24 hrs (Bhalla et al., 2009). The elimination half-life of melamine was from 2.7 to 4.04 h in laboratory animals like rats, mice guinea pig. The MEL concentration was similar in blood, liver and plasma. Lipschitz and Stokey (1945) found that fifty per cent of a single oral dose of 250 mg/kg b. w. melamine was recovered from the urine of rats within 6 h. Worzalla et al. (1974) observed that the s-triazine ring of MEL is very stable and does not cleave in vivo, including MEL was recovered after administration of hexamethylmelamine to rat. Baynes et al. (2008) studied the pharmacokinetics of MEL in the pig following a single intravenous dose of 6.13 mg/kg. The volume of distribution was 0.61 ± 0.04 L/kg, the half-life was 4.04 ± 0.37 h and a renal clearance of 0.11 ± 0.01 L/h/kg (approximately 27 ml/min). The study also confirmed that melamine was readily cleared by the kidney and there was unlikely to deposit in organs like liver, spleen and muscles.

Toxicodynamics of melamine: When MEL is absorbed into the blood stream, it combines with uric acid, phosphate or cyanuric acids, these complexes concentrates and interacts in the urine-filled renal microtubules, and crystallize to form large number of round, yellow crystals, which in turn block and damage the renal cells that line the tubules, causing renal malfunction (Merck, 2001). Proximal convoluted tubule (PCT) is prone to any toxin based injury due to a comparable loose epithelia, as toxins can easily enter. Owing to active

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tubular secretion of H+ ions, the pH in PCT reduce from 7.4 (glomerular filtrate) to 5.5 or below and at such a low pH, crystallization and deposition of crystals can occur. Once the crystals are deposited in PCT, they hinder and reduce the blood supply leading to hypoxic injury. Further insult may lead to necrosis and regeneration in tubular epithelium, and fibrosis and inflammation in the renal interstitium (Reimschuessel, et al. 2008).

**Toxicity of melamine in broiler chickens:** MEL toxicity came to our attention in 2008 because of an outbreak of urinary stones in children who consumed melamine-contaminated milk in China. An outbreak of pet food associated renal failure, affecting an estimated 6000 dogs, occurred in Asia in 2004 (Lipschitz and Stokey 1945). In 2007, large numbers of dogs and cats in North America developed acute renal failure (ARF) associated with ingestion of certain brands of pet food (Brown, et al., 2007).

**Clinical observation and mortality in broiler chicken:** According to Lu et al. (2009), there was no change in the feed intake (FI), body weight gain (BWG) and mortality in broiler chickens fed MEL up to 1,000 mg/kg of diet. Basson et al. (2011) concluded that dietary MEL level of up to 500 mg/kg did not have any adverse effect on mortality, FI and BWG in broiler chick. But Brand et al. (2011) reported that FI and BWG decreased linearly with increasing dietary concentration of melamine in broiler chicks fed ≥1.0% melamine. They also observed 16 to 36% mortality in birds fed ≥2% melamine, and 75% of the mortality occurred by Day 10. Apart from this Sirilaophaisan et al. (2010) noted in a 42 day study. Arber Acres broiler chicks fed on melamine had a linear decrease effect on BWG. As the level of melamine in the diet increased, the greatest decrease in BWG was in birds fed ≥0.75% melamine.

**Gross pathology:** Brand et al. (2009) reported pale and enlarged kidneys in turkeys fed 2 - 3% MEL. In MEL fed broilers, Ledoux et al. (2009) noted enlarged pale kidney and gall bladder containing opaque bile. In broilers fed 2.0, 2.5 and 3.0% MEL that died early in the experiment, Brand et al. (2011) noted enlarged, pale kidneys and the gall bladder with brown to green opaque bile and no gross lesions in the liver.

**Histopathology:** Reimschuessel (2008) mentioned that chickens fed only MEL could develop spherulite crystals containing uric acid, a normal excretion product in chicken. Moreover, Bai et al. (2010) examined the kidney samples from laying hens given MEL at 8.6-140.9 mg/kg of BW/d for 34 days. There were crystals in one of three kidneys in hens given MEL at either 62.6 or 140.9 mg/kg. There was “spoke wheel” shaped macroscopic and microscopic crystals in the liver, kidney and spleen of broiler chicks fed 0.5% MEL in the diet (Sirilaophaisan et al. 2010).

Similarly, Brand et al. (2011) reported accumulation of eosinophilic to basophilic casts in the collecting ducts and tubules with an associated moderate heterophil infiltration of the collecting ducts and tubules of broilers. Wang et al. (2011) observed fatty degeneration in the liver of Cobb 500 broiler birds that received alone 100 mg of MEL/kg of feed as well as combination of 33.3 mg and 50 mg of CYA (Cyromazine)/kg of feed with 100 mg of MEL/kg of feed. Moreover, the kidneys of birds receiving 100 mg of MEL/kg of feed and 33.3 and 50 mg of CYA/kg of feed with 100 mg of MEL/kg of feed had dilated renal tubules and expanded small blood vessel.

**Diagnosis:** The diagnosis of MEL toxicosis can be done by observation through clinical signs, post-mortem examination and histopathology and by detecting the presence of melamine and its derivatives in food articles. Staining of melamine crystals requires special stains like Oil red O-72 h (ORO 72h). United States Food and Drug Administration (US FDA) has approved six methods for melamine detection: UHPLC–UV (with UV detection), HPLC-UV (with UV detection), LC-MS, GC-MS, ELISA, Infrared spectroscopy and chemiluminescence.

**CONCLUSIONS**

During the past decade, the illegal inclusion of the organic chemical, MEL, was detected in infant formula, pet food and certain other food products. Since MEL has no nutritional value and is nephrotoxic, it should not be present in any food product. Even though MEL adulteration could be banned from society, environmental MEL could still surface in food products, including poultry, meat, and eggs.

MEL toxicosis now warrants the attention of veterinarians, physicians and the environmentalists. There is a global effort to control the MEL adulteration in the human and animal food chain by governments and food manufactures to ensure safe food.

**REFERENCES**


