The Impact of Blood Ammonia on Animal Health (Postprint)

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Abstract

Ammonia generated during amino acid metabolism in various tissues of the organism, along with ammonia produced by intestinal microbial decomposition that is subsequently absorbed, can both enter the bloodstream to form blood ammonia. Excessively high concentrations of blood ammonia can seriously endanger animal health and have gradually emerged as a concern in the livestock industry. This review summarizes the metabolic characteristics of blood ammonia and its effects on animal health, with the aim of providing data references for blood ammonia detection in practical livestock production.

Full Text

Effects of Blood Ammonia on Animal Health

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Abstract

Ammonia produced from amino acid metabolism in various tissues and generated by gastrointestinal microbiota can be absorbed into the bloodstream, forming blood ammonia. Excessively high blood ammonia concentrations severely endanger animal health and have gradually become a concern in animal husbandry. This review summarizes the metabolic characteristics of blood ammonia and its effects on animal health, providing a data reference for blood ammonia detection in practical livestock production.

Keywords: blood ammonia; blood ammonia concentration; preventive measures

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Blood ammonia primarily originates from ammonia produced through the deamination of dietary protein and amino acids in the body, with its main elimination pathway being transport to the liver for urea synthesis via the urea cycle, followed by excretion in urine via the kidneys. Increased sources or decreased elimination of blood ammonia can lead to elevated concentrations. High blood ammonia poses numerous hazards to animals, and changes in blood ammonia concentration have gradually attracted attention. This review will examine blood ammonia metabolism, concentration ranges in different animals, potential causes and effects of hyperammonemia, and preventive measures, providing a reference for hyperammonemia control in practical production.

1. Blood Ammonia Metabolism

Blood ammonia sources include endogenous and exogenous pathways. Endogenous ammonia mainly comes from transamination and deamination of amino acids, with small amounts from purine and pyrimidine decomposition and adenylate deamination [1]. Renal distal tubular epithelial cells also produce ammonia through glutaminase-catalyzed glutamine hydrolysis. Exogenous ammonia primarily derives from undigested dietary protein and amino acids in the digestive tract, which release ammonia under bacterial action and are absorbed into circulation. In ruminants, dietary non-protein nitrogen sources such as ammoniated straw and urea can be rapidly degraded by rumen microbial urease, with the resulting ammonia absorbed through the rumen wall into the bloodstream.

Absorbed ammonia enters the peripheral venous blood of the digestive tract, converges with peripheral venous blood from visceral organs, and is transported via the portal vein to the liver [2]. Additionally, ammonia produced in other tissues (e.g., brain tissue) can combine with glutamate via glutamine synthetase to form non-toxic glutamine, which is transported to the kidneys for metabolism [3]. The primary elimination pathway for blood ammonia is conversion to non-toxic urea via the urea cycle in the liver, followed by transport through the bloodstream to the kidneys for urinary excretion.

2. Blood Ammonia Concentrations in Animals

To date, numerous studies have investigated blood ammonia concentrations in humans. Research indicates that healthy adult venous blood ammonia concentration is 30 mol/L, generally not exceeding 59 mol/L [4]. The following sections present reported blood ammonia values from published literature, organized by animal species and sampling site to facilitate further research.

2.1 Ruminants

As shown in Table 1 , blood ammonia concentrations vary significantly across different sampling sites in the same animal. In sheep, hepatic vein ammonia concentration is the lowest, portal vein concentration is the highest, while arterial and jugular vein concentrations are intermediate. This likely occurs because the portal vein converges ammonia from the digestive tract and peripheral tissues before transporting it to the liver, where ammonia enters hepatocytes and is converted to non-toxic urea via the urea cycle. Based on statistical data for sheep in Table 1, arterial blood ammonia concentration ranges from 40–150 mol/L, jugular vein from 40–110 mol/L, portal vein from 200–500 mol/L, and hepatic vein from 30–135 mol/L.

Blood ammonia concentrations in dairy and beef cattle are typically measured from jugular and tail vein samples. Table 1 lists concentrations for beef cattle and dairy cows during dry and lactating periods. The data show that blood ammonia concentration is highest in peak-lactation dairy cows, with lactating cows having higher concentrations than dry cows and unbred heifers. Holstein bulls and finishing cattle have blood ammonia concentrations below 100 mol/L. When dairy cows are fed non-protein nitrogen such as urea, blood ammonia concentration rises rapidly. Davidovich et al. [5] administered urea directly into the rumen of steers at 0.5 g/kg BW; rumen bacterial urease rapidly hydrolyzed urea to carbon dioxide and ammonia, causing carotid artery ammonia concentration to increase from 76.5 mol/L to 100.0 mol/L within 5 minutes, and jugular vein ammonia concentration to surge from 64.7 mol/L to 252.9 mol/L.

2.2 Poultry

Currently, research on blood ammonia in poultry is limited and primarily focused on broilers. Table 2 presents blood ammonia concentrations in broilers at different ages. Blood ammonia concentration ranges from 87.9–188.0 mol/L in 0–3 week-old broilers and 121.7–211.0 mol/L in 4–6 week-old broilers. Zha Qiaochu et al. [22] measured blood ammonia concentration in 19-week-old laying hens, with an average value of 133.8 mol/L.

2.3 Pigs

For monogastric pigs, blood ammonia is an important blood biochemical indicator. Table 3 lists blood ammonia concentrations at different stages and sampling sites. Generally, portal vein ammonia concentration is higher than arterial concentration, similar to the pattern observed in ruminants. Additionally, concentrations at the same sampling site vary considerably, likely due to differences in dietary composition. Further research is needed on blood ammonia concentration changes in pigs.

3. Possible Causes and Hazards of Hyperammonemia

In humans, a blood ammonia concentration of 100 mol/L indicates nitrogen metabolism disorders, while concentrations exceeding 1,000 mol/L result in acute hyperammonemia [4]. Due to limited research on blood ammonia in animals, there is no clear definition of hyperammonemia in animals; this review primarily refers to abnormally elevated blood ammonia concentrations under non-physiological conditions.

3.1 Causes of Hyperammonemia

Human hyperammonemia mainly results from genetic factors or urea cycle enzyme deficiencies, such as N-acetylglutamate synthetase defects and ornithine transcarbamylase deficiency [39]. In animals, besides these genetic factors, hyperammonemia can also be caused by liver or kidney dysfunction, unreasonable dietary protein composition, and high environmental ammonia concentrations. Ammonia absorbed from the intestine accounts for 27–51% of total ammonia entering the hepatic portal vein [40]. When liver function is impaired, the capacity for urea synthesis and ammonia clearance decreases, allowing intestinal ammonia to enter systemic circulation without hepatic detoxification [3], resulting in elevated blood ammonia concentration. When kidney function is compromised, metabolic products cannot be efficiently excreted, causing urea nitrogen concentration to rise sharply. Urea can enter the intestinal lumen and gastrointestinal tract, where intestinal bacterial urease decomposes it to produce ammonia, which upon absorption further increases blood ammonia concentration [41].

For monogastric animals and poultry, when dietary protein composition is unreasonable or protein levels are excessive, surplus amino acids undergo deamination in the liver to be converted to glucose and fat, simultaneously generating ammonia. In poultry, the absence of a urea cycle means ammonia can only be excreted as uric acid. Excessive blood uric acid tends to precipitate as urate crystals on joints, thoracic and abdominal cavities, and various organ surfaces, causing gout. Additionally, high stocking density in poultry houses facilitates accumulation of harmful gases, particularly ammonia, endangering poultry health. Song Yi et al. [25] found that as environmental ammonia concentration increased, blood ammonia concentration in broilers gradually rose, with red blood cell count, hematocrit, and mean corpuscular volume also showing upward trends. High ammonia concentrations in housing (80 mg/kg) may also induce ascites syndrome in broilers.

Ruminant diets often include non-protein nitrogen to provide nitrogen sources for rumen microbial protein synthesis, thereby supplementing dietary protein. Literature reports indicate that urea can generally replace 30% of crude protein in ruminant diets, but when adequate dietary crude protein is present, urea addition may cause ammonia toxicity [42]. Furthermore, urea is completely degraded in the rumen within a short time, producing large amounts of readily absorbable ammonia that rumen microbes cannot rapidly utilize, allowing

substantial ammonia to enter the bloodstream through the rumen wall. Research has shown that supplementing steers with ammonium chloride (NH4Cl) via mesenteric vessels caused a sharp increase in hepatic vein blood ammonia concentration after 3 hours [43], while adding urea at 0.5 g/kg BW to healthy bulls resulted in blood ammonia concentration reaching 782.0 mol/L after 41 minutes [44-45].

3.2 Hazards of High Blood Ammonia Concentration

Excessively high blood ammonia concentration, particularly arterial ammonia, substantially increases ammonia uptake by brain tissue. Large amounts of ammonia entering brain tissue combine with -ketoglutarate to form glutamate, which further combines with ammonia to produce glutamine, consuming large quantities of ATP in the process. Excessive ammonia depletes -ketoglutarate in brain tissue, slowing the tricarboxylic acid cycle. Combined with substantial ATP consumption, this can lead to insufficient energy supply to brain cells, impairing normal physiological function and potentially causing coma or even death in severe cases. High ammonia concentration can also alter concentrations of neurotransmitters such as acetylcholine, -aminobutyric acid, and serotonin in the brain, interfering with normal neurotransmission and causing central nervous system dysfunction.

Unreasonable dietary protein composition or high-protein diets increase deamination in the liver and excretion by the kidneys, significantly elevating blood ammonia concentration. Long-term consumption can easily lead to liver and kidney diseases. Feeding hybrid bulls urea at 0.5 g/kg BW caused rapid blood ammonia elevation due to rumen bacterial urease activity. At jugular vein ammonia concentrations of 558.8 mol/L, bulls exhibited muscle twitching and other ammonia toxicity symptoms, and when concentration reached 1,632 mol/L, bulls showed coma and even asphyxiation [44].

Long-term exposure to low ammonia concentrations in livestock housing can also cause chronic ammonia poisoning, manifested as decreased resistance, increased morbidity, and reduced feed intake, daily gain, and reproductive performance. Generally, poultry are most sensitive to environmental ammonia in livestock housing, with monogastric animals being more sensitive than ruminants. Ammonia in poultry, similar to mammals, originates from amino acid deamination, purine and pyrimidine deamination, and intestinal absorption. The absence of a urea cycle in poultry means ammonia is not easily excreted, so blood ammonia concentration should not be excessively high. High dietary protein or high environmental ammonia causing elevated blood ammonia concentration can affect metabolism in brain and muscle cells, significantly reducing feed intake and daily gain in broilers [46].

4. Preventive Measures for Hyperammonemia

Diets should be formulated according to the nutritional requirements of animals at different stages to improve protein utilization and increase dietary nitrogen absorption, thereby reducing unreasonable deamination of protein and amino acids and decreasing ammonia production at the source. Currently, using low-protein, amino acid-balanced diets has become a trend for improving dietary protein utilization. Lu Ning et al. [47] compared the feeding effects of a low-protein (14%), amino acid-balanced diet versus a normal diet (18% protein) on 15 kg castrated male pigs, finding that the low-protein, amino acid-balanced diet did not affect growth performance while significantly reducing urinary and fecal nitrogen excretion. Additionally, adding additives that promote the urea cycle [such as N-carbamylglutamate (NCG)] to diets can improve conversion of ammonia compounds and enhance dietary protein utilization. NCG is a structural analog of N-acetylglutamate (NAG) that can activate carbamoyl phosphate synthetase-I and promote urea cycle progression to accelerate ammonia conversion. Liu Xingda et al. [35] added 0.08% NCG to sow diets and found reduced blood urea nitrogen and ammonia concentrations while improving dietary nitrogen utilization.

For ruminants, when feeding urea, it must be thoroughly mixed with other feed ingredients while providing sufficient readily fermentable carbohydrates to supply necessary energy and carbon skeletons for rumen microbes. Additionally, urea is not recommended for calves under 3 months of age, as their rumen is not fully developed and urea cannot serve as a high-quality protein source.

Most livestock live in housing where animal feces and bedding decompose via microbial fermentation to produce ammonia. Poor ventilation allows ammonia to accumulate. Ammonia production can be reduced at the source by removing feces from housing, or ammonia concentration can be decreased by increasing ventilation to exhaust ammonia. Research indicates that for safe ammonia levels in poultry housing, concentration should not exceed 13 mg/kg for 0–3 week-old broilers and 20 mg/kg for 4–6 week-old broilers [28]. Livestock farm environmental quality standards specify that ammonia concentration in livestock housing air should not exceed 20.0 mg/m^3, and ammonia concentration in poultry housing should not exceed 15.0 mg/m^3 [48].

Unless animals exhibit hyperammonemia toxicity symptoms, high blood ammonia concentration is not easily detected visually. Given the hazards of hyperammonemia, blood ammonia concentration changes should be monitored using blood ammonia analyzers to take necessary measures and avoid economic losses from reduced animal performance.

5. Conclusion

As large-scale, high-density intensive farming models develop in animal husbandry, blood ammonia concentration changes have gradually become an important indicator for monitoring animal health status. Timely and accurate

understanding of blood ammonia concentration changes helps predict whether dietary formulation is reasonable, housing environment is suitable, and animals are in good health, enabling targeted prevention and control measures to better promote healthy animal growth and improve farmers' economic benefits.

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Note: Figure translations are in progress. See original paper for figures.