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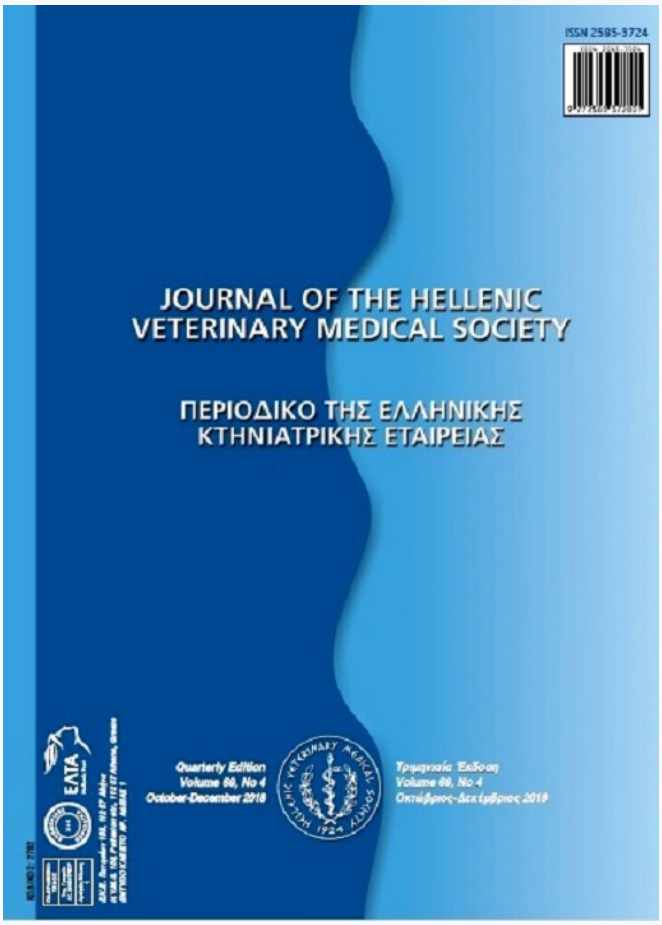

Τοξίκωση με ιώδιο σε βοοειδή στην Τουρκία - Κλινική, Αιματολογική και Βιοχημική Αξιολόγηση

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Research article
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Iodine Intoxication in Beef Cattle in Turkey - Clinical, Hematological and Biochemical Evaluation

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ABSTRACT. Iodine is an essential trace element for humans and animals. The incidence of iodine poisoning in cattle is low. In the present study, we evaluated the clinical findings, serum glucose and cholesterol, thyroid hormone and urine iodine levels in cattle exposed to excess iodine. All of the clinical data were determined following the addition of potassium iodide to the drinking water. Inappetence, cough, and hyperthermia were notable clinical findings. We detected a very high iodine level (470 µg /L) in an analysis of the drinking water samples. A biochemical analysis revealed that the serum cholesterol levels in the affected cattle were significantly lower ($p<0.05$) than in healthy cattle. However, the serum glucose in the affected cattle was significantly higher ($p<0.05$) compared to healthy cattle. The iodine concentration in the urine of the affected animals was also significantly higher ($p<0.05$) than in the healthy animals. Importantly, a hematological analysis indicated leukocytosis with neutrophilia. Several clinical signs, including hyperthermia, tachycardia, alopecia, and a naso-oral discharge, based on suspected history can suggest iodine intoxication. In addition, biochemical parameters, such as urine iodine, serum glucose and cholesterol levels, were observed to be different between healthy and affected cattle. The thyroid function in affected cattle should also be studied.

Keywords: iodine toxicity, beef cattle

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INTRODUCTION

Iodine is an essential trace element that is primarily obtained from plants and is involved in the structure of thyroid hormones. Thyroid hormones are extremely important in cell and tissue growth and development (Hetzel and Dunn, 1989). In addition, thyroid hormones are necessary for many metabolic processes, such as lipolysis, glucose metabolism and erythrocyte production (Brent, 2012; Bustad and Fuller, 1970). The recommended iodine levels for a mature lactating dairy cow in the ration dry matter have been set in a range from 0.6 ppm (National Research Council, 2001) to 0.8 ppm (British Agricultural Research Council, 1965), which is equivalent to 9 to 12 mg for a 500 kg cow that consumes 20-25 kg dry matter daily. Bustad and Fuller (1970) estimate that on the basis of the thyroxine secretion rate (TSR) and radioiodine metabolism data, the daily iodine requirement for a 500 kg cow would be 5.5 to 11 mg.

The incidence of iodine poisoning in cattle is seen less frequently compared to iodine deficiency. Thyroiditis, goiter, hypothyroidism, hyperthyroidism and hypersensitivity may follow excess iodine intake in humans (Pennington, 1990). In iodine intoxicated cattle, cough, hyperthermia, depression, tachycardia, alopecia, dermatitis, exophthalmus and susceptibility to infectious diseases may be observed (Olson et al., 1984; Paulíková et al., 2002). Changes in serum biochemical parameters, such as hypocholesterolemia and hyperglycemia, and changes in hematological parameters, such as leukocytosis, may occur in cattle with iodine intoxication (Paulíková, 2002). The best method to detect an iodine deficiency or an iodine excess is to measure the urine iodine level (Herzig et al., 1996). In a study by Hilman and Curtis (1980), the urine iodine levels in healthy and intoxicated cattle have been reported as 1.87 ppm and 6.81 ppm, respectively.

Iodine deficiency is a well-known issue, but limited knowledge exists regarding excess iodine intake in cattle, which causes systemic toxicity. Thus, the aim of this study was to evaluate the clinical symptoms of excess iodine intake and changes in the serum glucose and cholesterol levels and in the thyroid hormones and the urine iodine levels following iodine exposure in the drinking water.

MATERIALS AND METHODS

The study was conducted on a Simmental breeding farm consisting of 600 cattle near the town of Luleburgaz in Edirne, Turkey. Potassium iodide was added by a local farmer to the drinking water of only one paddock (n: 100) that included two different age groups because of an erroneous belief that this could be helpful against respiratory diseases. The potassium iodide was added once, and the duration of the iodated water consumption was 7 days. A farm owner and a local practitioner said that 35 kg of potassium iodide was added to 100 tons of drinking water. However, the amount of iodine that the affected animals received with their food is unknown. Clinical signs were apparent 3 days after the animals consumed the iodine-containing drinking water. A detailed clinical examination of animals showing tachypnea and mental depression in the paddock (n:100) was performed in a cattle crush.

The detailed clinical examination included body temperature, heart rate and respiration rates, the peripheral pulse quality (4- Bounding, 3-Increased 2-Normal 1-Weak 0-Absent or nonpalpable-using the coccygeal artery) and the mental status, which was scored as 0: clinically normal, 1: mild signs of depression (standing), 3:moderate signs of depression (able to stand but with a dull status) 4: severe (recumbent with no alertness) (Modified from Walker et al., 1998). The ages of the affected animals ranged from 4 to 22 months old. These animals included fattening beef cattle aged 4 to 8 months and pregnant heifers which were in their 7^{th} – 8^{th} month of gestation.

Healthy animals were determined by a clinical examination and selected (Simmental beef cattle, 6 – 22 months of ages) (n=10) randomly via a lottery of the herd list of different groups.

Blood samples were collected for the measurement of the biochemical parameters from the coccygeal vessels using plain vacuum tubes, (Becton Dickinson and Company, Franklin Lakes, NJ) from healthy animals (n:10) and from animals showing clinical signs (n:10). One hemolyzed sample was excluded from the study. Urine samples were also collected from healthy animals (n:10, showing clinical signs (n:10, 8M-2F) using a urine catheter. The serum was collected from blood samples (15 minutes at 1000 g) that were centrifuged on the farm. Water samples

for iodine analysis were collected in 100-mL deiodinated plastic tubes. Blood and urine samples were sent to the laboratory on dry ice (Düzen laboratory, Ankara, Turkey). The biochemical parameters were determined by a reflectance photometry method using a commercially available blood biochemical measurement device (Reflotron Plus System, Roche Diagnostics®, Switzerland). The iodine concentration in the water and in the urine was measured with an ion chromatography device (ICS 3000, Dionex Corp., USA). The urine specimens were sent to the laboratory immediately after they were taken.

The hematological parameters, including the total white blood cell count (WBC), hematocrit (HCT), hemoglobin (Hgb), erythrocyte (RBC) and platelet counts (PLT), were measured by an automatic hemogram analyzer (Vetscan HM5 Abaxis®, USA). In addition, a serum hormonal profile analyses included triiodothyronine (T3), and thyroxine (T4) measured with a commercial kit (Immulite 2000 Total T3/ L2KT36; Immulite 2000 Total T4/L2KT46; Siemens, Italy).

The affected animals were provided with a supply of fresh water. Ascorbic acid (25 mg/kg, IV, for 3 days), vitamin E + selenium (single dose, 4 to 8 cc, IM), acetyl cysteine (1200 to 2400 mg/per animal, IV, for 3 days) and ceftiofur (2.2 mg/kg, IM for 5 days) were also given.

All data passed a normality test. Differences between cattle suffering from iodine intoxication and healthy cattle were analyzed by Student's t-test for each parameter. The results were expressed as the mean ± standard deviation (SE), and a P-value less than 0.05 was considered to be statistically significant.

RESULTS

Water iodine analysis

The water analysis showed that the level of iodine was very high (47 µg/L).

Clinical signs

In animals considered intoxicated (n:10), clinical signs, including inappetence, hyperthermia (39.5-41.6 C), naso-ocular discharge, cough, increased heart rate (110-148/beats/minute), increased respiratory rate (52-68 breaths /minute), hypersalivation, severe mental depression and decreased ruminal movements, were observed in varying degrees (Table 1).

Serum biochemical results and urine iodine analysis

The serum biochemical results and the iodine level (Mean±SE) in the urine are presented in Table 2. The serum cholesterol concentration in the iodine intoxicated cattle was significantly lower ($p<0.05$) than

Table 1. Clinical findings in 10 cattle with Potassium iodide toxicity

Variable	Finding	Number of cattle (n:10)	Reference range
Appetite	Decreased	3	
	Absent	7	
Ruminal motility	Reduced	2	
	Absent	8	
Salivation	Severe	7	
	Mild	3	
Alopecia	Mild	2	
	Marked	2	
	Absent	6	
Cough	Mild	3	
	Persistent-severe	7	
Naso-ocular discharge	Mild	3	
Body temperature	Normal	0	37.8 - 39.2°C
	High	10	
	Low	0	
Heart Rateb (reference range:	Normal	0	60 -80/beats/ minute)
	Bradycardia	0	
	Tachycardia	10	
Respiratory Rate	High	10	10 - 30 breaths/ minute)
Mental depression	Severe	10	
Exophthalmos	Present	2	
	Absent	8	

Table 2: Biochemical and urine iodine results in healthy and cattle affected by potassium iodine toxicity

Parameters	Cattle with KI toxicity (n=10) (Mean±SE)	Healthy Cattle (n=10) (Mean±SE)
Cholesterol (mg/dL)	43.0±4.8^{A}	139.1±15.1^{B*}
Triglyceride (mg/dL)	16.1±1.4	20.0±1.8
Potassium (mEq/L)	4.6±0.2	4.3±0.9
BUN (mg/dL)	17.9±3.9	10.1±0.4
Glucose (mg/dL)	88.7±2.6^{A}	74.4±3.7^{B*}
Triiodo thyronine (**T3**)	1.6±0.1	1.5±0.1
Thyroxine (**T4**)	7.2±0.8	6.9±0.1
Urine iodine (μg/dL)	45.7±13^{A}	12.0±0.8^{B*}

*$p<0.05$
A, B: define statistically importance within a row
KI: Potassium iodide

in healthy cattle (Table 2). We also detected an elevated serum glucose concentration (75.4-104.1 mg/dL) in iodine intoxicated cattle compared to healthy animals ($p<0.05$). More importantly, the urine iodine concentration (13.4-113.8 μg/dL) in the intoxicated animals was significantly higher ($p<0.05$) compared to healthy animals, and the BUN values (31.3-38.3 mg/dL) of three animals were observed to be high. No statistically significant differences were found in the remaining biochemical parameters between animals exposed to potassium iodide (n:10) and healthy animals (n:10) (Table 2).

Hematological analysis

A hematological examination revealed leukocytosis 19.8±1.6 x 10^9/L (reference range 4.0 to 12.0 x 10^9/L) together with neutrophilia 16.4±0.1 x 10^9/L (reference range 0.7 to 6.0 x 10^9/L) associated with a suppurative infection, which might have been related to a previous respiratory infection.

DISCUSSION

Many researchers have described the clinical signs of iodine intoxication, including a persistent cough, hyperthermia, naso-ocular discharge, inappetence, depression, dermatitis, alopecia, tachycardia, nervousness, weight loss, exophthalmos, susceptibility to infectious diseases, respiratory stress and death (Olson et al., 1984; Döcke et al., 1994). The clinical signs of iodine toxicity in ruminants observed in the present study except for nervousness were consistent with those in previously reported studies.

The most appropriate method to detect an iodine deficiency or an iodine excess is to determine the urine iodine level (Herzig et al., 1996). Renal iodine clearance is related to the glomerular filtration rate (GFR) or creatinine clearance, the sex and pregnancy (Soldin, 2002; Stilwell et al., 2008). Stilwell et al. (2008) reported that urine iodine excretion was increased during early lactation and that excretion decreased in subsequent stages of lactation In a study conducted by Herzig et al. (1996), the urine iodine levels in 672 dairy cows from 22 herds were determined. They reported that the urine iodine levels were less than 2 μg/dL, 2 to 5 μg/dL, 5 to 10 μg/dL and more than 10 μg/dL in 27.5, 24.6, 16.8, and 31.3% of the cows, respectively. The same authors reported that the mean urine iodine concentration was 9.48 μg/dL at the peak of the lactation period and 2.3 μg/dL immediately before drying off. To the best of our knowledge, no study of urine iodine levels in beef cattle has been conducted. In a study reported by Meyer et al. (1996), the mean serum iodine level was 15.3 mg/dL in cattle fed a ration with 0.5 mg iodine per kg dry matter added.

In our study, the mean urine iodine concentration in healthy cattle was 12.0 ± 0.8 μg/dL, while in cattle suffering from iodine intoxication, it was 45.7 ± 13 μg/dL. Moreover, the BUN levels were within the reference limits for healthy and intoxicated animals,

but were numerically higher in the latter than in the former.

The daily iodine requirements of beef cattle should be 0.4 mg/kg dry matter (NRC, 2001 In this study, 35 kg of potassium iodide was added to 100 tons of water. Furthermore, it is not known how much iodine the affected animals received via the feed. Technical problems prevented an analysis of the amount of iodine in the diet. However, high concentrations of urine iodine in the affected animals indicate that they received excessive amounts of iodine. The iodine level in the drinking water in Turkey varies geographically. The mean iodine level in the drinking water in the Aydın region in Turkey was 270 μg/L (Özkan, 2008). Compared to that study, the amount of iodine in the drinking water in our study (470 μg/L) was very high. These results indicate that the drinking water was the source of the iodine poisoning.

Biochemical and hematological changes may occur in animals subjected to iodine poisoning. Hillman and Curtis (1980) noted that the serum glucose and BUN values were increased, but on the contrary, the serum cholesterol concentration was decreased. In the present study, the serum cholesterol values in cattle affected by potassium iodine toxicity was significantly lower ($p<0.05$) than in healthy cattle (Table 2). These results are in agreement with Hillman and Curtis (1980) and Paulíková (2002), who reported hypocholesterolemia. Thyroid hormones induce triglyceride mobilization from the adipose tissue for lipolysis and are responsible for the decrease in the blood cholesterol level. Additionally, iodine-induced thyroid hormones activate LDL clearance in the serum and reduce intestinal absorption (Shin et al.,2003; Galman et al., 2008). In the presence of thyroid hormone, an increase in NEFA and glycerol levels is also observed (Nikitin and Babenko, 1989; Pucci et al., 2000). In the present study, the serum glucose level in cattle affected by potassium iodine toxicity was significantly higher (88.7±2.6 mg/dL) than in healthy cows (74.4±3.7 mg/dL) ($p<0.05$). This effect may explain the decreased serum cholesterol level in mammals affected by iodine intoxication.

In a study by Minelli et al., (1997), iodine was given to humans with hepatitis B and C who had previously received interferon-alpha. In the study, the thyroid hormone levels varied, either increasing, decreasing or normal. This variation may have been caused by cytokines (Minelli, et al., 1997). In our study, a concurrent respiratory disease may have caused the release of cytokines which might have resulted in normal thyroid levels (Minelli et al., 1997). In our study, some samples from intoxicated animals had high thyroid levels. Furthermore, a surge in the thyroid hormone level may also be related to the blood collection time and the variance in the samples, differently than implied by the above explanation. We assumed that repeated blood analysis can remove the variability of thyroid hormone levels in future studies. High thyroid hormone levels increase glucose concentration in the blood and trigger hepatic insulin resistance (Klieverik et al., 2009; Ferrannini et al., 2017). In a study conducted by Hillman and Curtis (1980), no difference was found between the thyroid hormone concentrations in cows fed a high or normal iodine diet ((32.66 ± 3.3 ng/ml vs 32.29 ±2.0 ng/ml). In the same study, it was concluded that the serum glucose and cholesterol levels in cattle intoxicated with iodine were respectively elevated or decreased.

In the present study, the serum T3 and T4 levels were observed to be numerically higher in animals affected by iodine intoxication compared to healthy animals, although these results were not statistically significant. However, cholesterol levels were significantly lower (43.0±4.8 mg/dL) in cattle intoxicated with iodine than in healthy animals (139.1±15.1 mg/dL). High levels of thyroid hormones induce lipolysis from adipose tissue. Increased lipolysis promotes hepatic insulin resistance (Brent, 2012; Rachel et al., 2014). It can be interpreted that the increase in the serum glucose concentration in sick animals may be related to hepatic insulin resistance in accordance with the high thyroid hormone levels.

Derscheid et al. reported that the use of potassium iodide decreased the severity of a BRSV infection in the cattle *in vivo* (Derscheid et al., 2014). In our study, KI was used against respiratory problems by a practitioner. However, it has been observed that respiratory system infections were much more severe in cows affected by iodine toxicity. In the present study, neutrophilic leukocytosis was detected in cattle affected by iodine intoxication. These results are comparable with those reported by Hillman and Cur-

tis (1980) and might be related to the suppression of cellular and humoral activity caused by an excessive iodine uptake (Olson et al., 1984). An excessive iodine intake may also cause lymphopenia, and neutrophilia along with the dysfunction of the T and B lymphocytes, as well as a decrease in the phagocytic function of macrophages (Haggard et al., 1980). In addition, changes in the hemogram may be related to respiratory problems.

The thyroid gland has a limited capacity for iodine storage. In humans, excessive iodine uptake caused differences in the thyroid function. Excessive iodine intake may cause increased thyroid hormone synthesis and its release to the circulation in humans (Koukkou et al., 2017). As a result, excess iodine supplementation can cause hyperthyroidism in susceptible humans. (Leung and Braverman, 2014). Another study (Schnur, 2015) reported that excessive amounts of dietary iodine intake led to hyperthyroidism associated with autoimmune changes in the thyroid. Contrarily, Hillman and Curtis (1980) have reported that long-term iodine uptake did not lead to changes in the thyroid function in animals. However, changes in the thyroid function were observed when a 500-fold excess of the daily amount of normal iodine required by calves was given (Leung et al., 1980). Excess iodine can lead to iodopeptid formation, which might be related to the transient blocking of enzyme reactions and protein synthesis in the thyroid gland (Leung and Braverman, 2014; Koukkou et al., 2017). In the present study, clinical signs associated with hyperthyroidism, such as exophthalmos, tachycardia, and an increased respiratory rate, were also identified. In addition, we detected an increase in serum cholesterol level and a rise in the glucose level. In conclusion, the determination of the iodine level in the urine of an animal showing signs of iodine intoxication will be decisive for diagnosis. Future studies might also evaluate the urine iodine concentration together with the urine creatinine clearance or the GFR ratio. In addition, future detailed studies are necessary to reveal the effect of excessive iodine exposure on the thyroid function.

Iodine intoxication should be considered in the cattle with clinical signs that include respiratory problems, hyperthermia, tachycardia, dermatitis, alopecia, coughing, and naso-oral discharge following excessive iodine supplementation.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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