Iodine toxicity in ruminants

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ABSTRACT: The inadequate intake of iodine is still a topical problem, because it contributes to a reduction in performance through the disturbed health of adult animals and their offspring. The necessity of iodine is frequently described in association with hypothyroidal state. In our work we want to assign the hidden risk of prolonged iodine feeding in ruminants. We discuss the possible sources of iodine intoxication, the clinical signs of the intoxication, its effects on production, reproduction, and thyroid functions; animal susceptibility to intoxication; laboratory and necropsy findings; diagnostic, and therapeutic possibilities.

Keywords: iodine; intoxication; cattle; sheep; goats

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1. Introduction

The role of iodine deficiency in thyroid disorders, especially that of endemic goitre, has been known for two hundred years. Nowadays, over one thousand million people have an inadequate iodine intake (Maberly, 1994).

As with the human population, so too the occurrence of functional thyroid disorders has been increasing in animals, especially in new-born calves and lambs (Körber et al., 1985; Kursa et al., 1996; Bíreš et al., 1996; Sargison et al., 1998).

Iodine is the essential element used by the thyroid for the biosynthesis of thyroid hormones (Thilly et al., 1992). Through these hormones, iodine is involved in controlling metabolism, cell growth and maturation, and the development and growth of tissues (Hertzel, 1989). Iodine deficiency during pregnancy has particularly adverse effects – retardation of foetus development, its death, dead or weak neonates with hyperplastic thyroid – goitre. These findings were reported in cattle (Kursa et al., 1996; Herzig and Suchý, 1996), sheep (Radostits et al., 1994), and goats (Radostits et al., 1994; Bíreš et al., 1996). Importance of iodine for cell mediated immune function has not been confirmed by Šlosarková et al. (2002).

As a mineral element, iodine cannot be synthesized in the body. Soil and consequently plants are the primary sources of iodine. Because the iodine concentrations of soils in Central Europe (and so in Slovakia) are relatively low (Anke et al., 1993), the foodstuffs cannot supply an adequate iodine intake for animals. The Slovak region thus belongs to these regions where iodine deficiency disorders occur, both in the human population and farm animals, particularly in sheep and goats (Bíreš et al., 1993, 1996). Substitution and utilization of iodine in pigs and cattle were studied by Herzig et al. (1999, 2000, 2001a, 2001b).
The literature reports mostly concern the aforementioned disorders associated with an inadequate iodine intake. However, from the practical point of view, it is important to mention conditions when the iodine acts as a poison to the body. In humans, Pennington (1990) describes six types of excessive iodine intake – thyroiditis, goitre, hypothyroidism, hyperthyroidism, hypersensitiveness, and acute responses. Urinary iodine levels can be used as indicator of iodine intake in cattle (Herzig et al., 1996).

In this work we want to indicate comparable clinical signs in ruminants after prolonged excessive iodine intake.

In some people, prolonged iodine intake at a dose over 10 times of the daily requirement may lead to goitre or thyrotoxicosis (Wolf, 1969; Braverman et al., 1971). In ruminants, iodine intoxication is a less frequent clinical problem because the toxic doses in these species are very high.

2. The toxic doses of iodine in ruminants

Severe or fatal intoxication in calves occurs after the prolonged administration of iodine at a dose of 10 mg/kg per day. Intoxications with marked and mild clinical manifestations are induced by daily iodine doses of 2.2 mg/kg and 0.4 mg/kg, respectively (Mangkoewidjojo et al., 1980). These doses are about 500, 100, 20 times higher than the daily requirement of iodine (approximately 0.02 mg/kg b.w. – NRC, 1978). In adult cows weighing about 600 kg, the daily iodine requirement for synthesis of thyroid hormones is approximately 10 mg (Convey et al., 1978), i.e. 0.016 mg/kg b.w. In practice, intoxication results from the prolonged intake of higher iodine doses ranging from 70 to 600 mg per animal and day (McCauley et al., 1972; Wallace, 1975; Hillman and Curtis, 1980; Olson et al., 1984). In a dairy cow weighing 600 kg this represents 0.12 up to 1.0 mg of iodine per kg of body weight daily. This amount is between 7.5 and 63 times higher than the daily requirement. Sheep are probably less sensitive to iodine intoxication than cattle (Forbes et al., 1932). Clinical disease with a fatal course in lambs weighing on average 30 kg was manifested after an intake of at least 562 mg of iodine in the form of EDDI (ethylenediamine dihydroiodide) or 393 mg of potassium iodide for 3 weeks (McCauley et al., 1973). These doses represent 18.7 and 13.1 mg of iodine per kg b.w. and day, respectively.

3. Possibilities of iodine intoxication in cattle and sheep

Land-locked European countries, including Slovakia, are deficient in iodine to some extent (Delange, 1995; Langer, 1995). However, under certain conditions daily iodine intake may exceed the daily requirement, even several times. This may be caused by:

– the long-term consumption of a diet containing several components supplemented with iodine
– the incorrect management of mineral feed admixtures over a long time
– the use of iodine compounds over long periods of time as a feed additive for the therapy and prevention of infectious pododermatitis, a complex of respiratory diseases, actinomycosis, mastitis, and infertility.

These possibilities of iodism in cattle and sheep were reported by several authors (Forbes et al., 1932; Blaxter, 1946, 1948; Miller and Swanson, 1973; McCauley et al., 1972, 1973; Wallace, 1975; Buck et al., 1976; Fish and Swanson, 1979; Hillman and Curtis, 1980; Olson et al., 1984) both in experimental and field conditions.

4. Clinical signs of the intoxication

Iodism in cattle is manifested by a persistent cough, hyperthermia, naso-ocular discharge, inappetency, depression, dermatitis, and alopecia (Forbes et al., 1932; Blaxter, 1944, 1946; Schmidt et al., 1971; McCauley et al., 1972; Newton et al., 1974; Wallace, 1975; Hillman and Curtis, 1980; Mangkoewidjojo et al., 1980; Olson et al., 1984; Radostits et al., 1994; White, 1998). In dairy cows, Döcke (1994) described tachycardia, nervousness, loss of weight, and a high level of metabolism. Other reported signs included the occurrence of exophthalmos (Blaxter, 1946; Hillman and Curtis, 1980; Radostits et al., 1994) and infectious diseases, especially diseases of the respiratory system (Forbes et al., 1932; Blaxter, 1946; McCauley and Johnson, 1972; McCauley et al., 1972; Wallace, 1975; Mangkoewidjojo et al., 1980; Olson et al., 1984), in some cases death (Mangkoewidjojo et al., 1980) and an increased mortality of the offspring from such dams (Thomas and Moore, 1953; Olson et al., 1984).

In sheep, depression, anorexia, hyperthermia, cough, changes in the respiratory system, and
sometimes death were reported (Forbes et al., 1932; Blaxter, 1948; McCauley et al., 1973). Lacrimation, salivation, and skin lesions were not observed (Blaxter, 1948).

Some clinical and laboratory findings of iodine intoxication of cattle and sheep are summarized in Table 1.

5. The effects on production and reproduction

– a decrease in milk yield and an increase in reproduction disorders (Thomas and Moore, 1953; Schmidt et al., 1971; McCauley et al., 1972; Wallace, 1975; Hillman and Curtis, 1980; Olson et al., 1984; Radostits et al., 1994)

Table 1. Clinical and laboratory findings of intoxication caused by various iodine doses in cattle and sheep

<table>
<thead>
<tr>
<th>Animals</th>
<th>Toxic dose(s)</th>
<th>Clinical and laboratory findings</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calves</td>
<td>50–10 mg/kg of dry matter of diet for up to 112 days</td>
<td>decrease in food intake, coughing, nasal discharge</td>
<td>Newton et al., 1974</td>
</tr>
<tr>
<td></td>
<td>250–1 250 mg of iodine (EDDI) per calf and day for 6 months</td>
<td>mucopurulent nasal discharge, seromucous ocular discharge, hypersalivation, thick scaly skin, rough hair, alopecia, pneumonia with the severity apparently dose-related</td>
<td>Mangkoewidjojo et al., 1980</td>
</tr>
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<td></td>
<td>1 250 mg of iodine (EDDI) daily for 6 months</td>
<td>decrease in persistence of antibody titres to Brucella and Leptospira organisms after vaccination, decreased lymphocyte mitotic activity, phagocytosis by WBC, and WBC counts</td>
<td>Haggard et al., 1980</td>
</tr>
<tr>
<td></td>
<td>0.625–5.0 mg of iodine per kg of b.w. (EDDI)</td>
<td>nasal discharge, occasional lacrimation, moderate coughing</td>
<td>Fish and Swanson, 1982</td>
</tr>
<tr>
<td>Dairy cows</td>
<td>164 mg of EDDI for 3 weeks</td>
<td>lacrimation, coryza, conjunctivitis, coughing, hair loss, scaly dermatitis, exophthalmos</td>
<td>Hillman and Curtis, 1980</td>
</tr>
<tr>
<td></td>
<td>440 mg of EDDI for 1 month</td>
<td>milk production reduced by 15%, coughing</td>
<td>Olson et al., 1984</td>
</tr>
<tr>
<td></td>
<td>300–600 mg of EDDI for 4 years</td>
<td>coughing, naso-ocular discharge, salivation, dry coat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>600 mg of EDDI for 7 years</td>
<td>pneumonia in calves with 50% mortality, decreased milk production</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300–600 mg of EDDI for 2 years</td>
<td>pneumonia in calves, decreased milk production, naso-ocular discharge</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;68 mg of EDDI for 1 year</td>
<td>cows with injured hocks not responding to therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>250–785 mg of EDDI for 3 years</td>
<td>naso-ocular discharge, increased calving interval</td>
<td></td>
</tr>
<tr>
<td>Lambs</td>
<td>94–785 mg of iodine in EDDI or potassium iodide for 3 weeks</td>
<td>lethargy, decreased food intake, retarded growth, hyperthermia, coughing, at larger doses death due to bronchopneumonia</td>
<td>McCauley et al., 1973</td>
</tr>
</tbody>
</table>

EDDI = ethylenediamine dihydroiodide
– the loss of body weight in adult animals (Blaxter et al., 1944, 1946; Schmidt et al., 1971; McCauley et al., 1972; Hillman and Curtis, 1980)
– a decrease in weight gain in calves (Forbes et al., 1932; McCauley and Johnson, 1972; Herrick, 1972; Newton et al., 1974; Leung et al., 1980; Fish and Swanson, 1982).
In sheep, neither the loss of weight in adults (Blaxter, 1948) nor the decreased weight gain in lambs (Forbes et al., 1932; McCauley et al., 1973) were observed.

6. The effects on thyroid functions

A study of the effects of excessive iodine intake on thyroid functions showed more distinct results. Thyroid functions were not altered even after prolonged increased iodine intake in common farm conditions (Convey et al., 1977; Hillman and Curtis, 1980). The same was observed in experimentally-induced iodine toxicosis with the use of 200 up to 300 times higher dose than the daily requirement. In calves, the altered synthesis of thyroid hormones was recorded only after long-term supplementation of an iodine dose 500 times higher than their daily requirement (Leung et al., 1980). An inhibitory effect of excessive iodine intake on the synthesis of thyroid hormones was observed in humans (Nagataki, 1974) and horses (Baker and Lindsey, 1969). Nagataki (1974) suggested that such effects depend not only on the amount and time of iodine exposure, but also on the functional state of the thyroid and species or individual genetic potential. According to Leirer et al. (1983), a very high intake of iodine may consequently cause a blockage of thyroid function with a reduction in iodine incorporation into thyrosine residue, leading thus to a hypothyroidal state.

7. Susceptibility to intoxication

Different responsiveness to iodine intoxication was found not only between the animal species (NRC, 1978), but also within the same ruminant species (McCauley et al., 1973; Newton et al., 1974; Mangkoewidjojo et al., 1980; Fish and Swanson, 1982).

Perhaps, this may explain cases of excessive iodine intake in cattle with no clinical signs, or manifested only by a mild cough and slight naso-ocular discharge (Long et al., 1953, 1956; Kuebler, 1957; Buck et al., 1976; Fish and Swanson, 1982), which may be attributed to the expectorant effect of iodine (Beckman, 1961). According to some authors, the development of clinical iodine toxicosis in cattle (Olson et al., 1984) and sheep (McCauley et al., 1973) depends, apart from the amount and exposure time, on such factors as stress, concomitant diseases, and nutritional disorders. The different severity of clinical manifestation may also depend on the type of iodine compound. This was recorded in laboratory animals (Webster et al., 1957), calves (Newton et al., 1974; Fish and Swanson, 1982), and lambs (McCauley et al., 1973). A higher tolerance was observed with an organic iodine compound (EDDI) compared with inorganic iodine substances (calcium iodate, potassium iodate). However, the biological efficacy of organic and inorganic iodine compounds at normal doses is almost the same (Miller and Swanson, 1973). Risk of iodine intoxication appears when the EDDI is used for the therapy and prevention of infectious pododermatitis, because recommended doses per animal and day (400–500 mg for 2–3 weeks, or 50–100 mg continually for a longer time) (Harris, 1978) are several times higher than the nutritional requirements. A decrease in body weight or weight gain is preceded by a decrease in food intake, which was observed in dairy cows (McCauley et al., 1972), sheep (Blaxter, 1948), calves (Forbes et al., 1932; McCauley and Johnson, 1972; Newton et al., 1974), and lambs (Forbes et al., 1932; McCauley et al., 1973). The cause of decreased food intake is not well known. Studies with iodine administration by means of gelatinous capsules (McCauley et al., 1973) or oral tube (Leung et al., 1980) indicate that, in addition to the reduced palatability of the food (Newton et al., 1974; Fish and Swanson, 1982), some unknown factors are involved.

8. Laboratory findings in iodine intoxication

During iodine toxicosis some changes in biochemical indices are found. Hillman and Curtis (1980) reported significant increase in serum glucose, AST, and blood urea nitrogen. A significant decrease in serum cholesterol and urinary creatinine was also observed (Long et al., 1953; Hillman and Curtis, 1980). However, other authors (Olson et al., 1984) did not confirm these findings. On the other hand, there was evidence that increased iodine intake correlates with increase in iodine concentrations in the blood serum of dairy cows.
(Long et al., 1953, 1956; Kuebler, 1957; Harris, 1978; Hemken, 1979; Olson et al., 1984; Maas et al., 1989), calves (Newton et al., 1974; Fish and Swanson, 1982), and lambs (McCauley et al., 1973), and also in the milk and urine of dairy cows (Convey et al., 1977; Harris, 1978; Binnerts, 1979; Hillman and Curtis, 1980; Hemken, 1979).

Alterations in the immune system occur during the continuous administration of the EDDI form of iodine at the daily dose of 50 mg, which is the dose commonly used for the prevention of infectious pododermatitis in cattle (Harris, 1978). In animals, changes in the quantity and functional state of leukocytes and other components of the immune system were found. These changes resulted in lymphopenia, neutrophilia (Hillman and Curtis, 1980), leukopenia, a decrease in lymphocyte blastogenic response to T and B cellular mitogens, depressed phagocytic capacity, and a shortening of the persistence of the antibody titre in response to bacterial mitogens (Haggard et al., 1980). These findings clearly indicate suppression of cellular and humoral immunity, possibly with inadequate response to infectious agents. This may explain the field observations of the increased occurrence of refractory infectious diseases in animals fed foods supplemented with excessive amounts of iodine (McCauley and Johnson, 1972; McCauley et al., 1972; Wallace, 1975; McCauley et al., 1973; Olson et al., 1984).

9. Necropsy findings

The majority of pathological changes are related to the respiratory system, in some cases to the thyroid and adrenal glands. The severity of the lesions depends strongly on the amount of iodine intake. In cattle, gross findings in the respiratory system are characteristically tracheitis, bronchopneumonia, and pleurisy (Mangkoewidjojo et al., 1980). Enlargement and hyperaemia of the mediastinal lymphnodes are observed in some cases. In the lung tissue, there is exudative inflammation at the centres of the affected areas, hypertrophy of the bronchial mucosal membrane, necrosis in the bronchioles, and fibrinous exudate in the alveoli. Microscopical findings may consist of changes in the tracheal mucosal membrane (squamous metaplasia), loss of cilia, and slight lymphocytic and neutrophilic infiltration of the lamina propria. At the lumen and the wall of the bronchi, bronchioles, and alveoli, inflammatory infiltration was found with the presence of neutrophils, lymphocytes, and macrophages. Peribronchial lymphatic follicles are hyperplastic, lymph vessels are dilated or spastic. Squamous metaplasia of the salivary glands was observed after excessive EDDI intake (Mangkoewidjojo et al., 1980).

McCauley et al. (1973) observed suppurative bronchopneumonia and fibrinous pneumonia in sheep intoxicated with iodine.

The evidence for thyroid alteration by increased iodine intake in cattle and sheep was not conclusive (McCauley et al., 1973). While some authors (Convey et al., 1978) did not report thyroid enlargement in dairy cows even with an iodine intake about 200 to 400 times higher than their daily requirement, Wallace (1975) observed thyroid hypertrophy in dairy cows with an iodine intake only 10 times higher (107 mg per day) than their daily requirement. Similar findings were also observed in calves. While Newton et al. (1974) described some cases of increased thyroid weight with a 25–200 times higher intake, others (Leung et al., 1980) did not find thyroid hypertrophy even with an iodine intake 500 times higher than their requirement. Increase in thyroid weight after excessive iodine intake was also described in horses (Baker and Lindsey, 1969) and pigs (Newton and Clawson, 1974), as well as in humans (Suzuki et al., 1965; Wolf, 1969).

Similarly, different findings were recorded in the relation between iodism and the adrenal glands. Wallace (1975) reported the hyperplasia of adrenal glands in lactating cows with estimated iodine intake of 107 mg per day. Newton et al. (1974) found an increased weight of adrenal glands in calves fed iodine at a dose of 25 to 100 mg/kg. These authors suggested that hyperplasia of this endocrine gland may be the result of stress caused by consuming a diet with high content of iodine. However, the significance of these observations is questionable because Newton et al. (1974) in another experiment within their work did not confirm the previous findings. The adverse effect on the weight of adrenal glands and on serum glucocorticoid levels in calves fed up to 1 250 mg of iodine daily was also reported by other authors (Leung et al., 1980).

10. Diagnosis

It is impossible to make a diagnosis of chronic intoxication without laboratory examinations. Except
for the analysis of iodine concentrations in the blood serum, milk, and urine, indices of metabolic profile have no diagnostic value. Confirmation of the diagnosis in suspect herds requires the determination of iodine in the aforementioned samples completed by examination of the diet (Olson et al., 1984). Only in this way, may we clarify the basic problem.

11. Therapeutic possibilities

No specific antidotes against iodism are available. Remission of the problem requires the elimination of iodine sources. This will lead to a gradual decrease in iodine body levels and a reduction in the clinical manifestation of iodine toxicosis (Olson et al., 1984).

12. REFERENCES


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