The impact of high iodine intake on thyroid function in ewes and lambs

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Abstract

OBJECTIVES: The objective of the study was to assess the metabolic risk of excessive dietary iodine intake in ewes and neonatal lambs.

DESIGN: Pregnant Šumava ewes received an experimental diet containing 3.1 mg iodine per kg of dietary dry matter in Group A (control, n=13, 6 ewes and 7 lambs) and 5.1 mg iodine per kg of dietary dry matter in Group B (experimental, n=12, 6 ewes, 6 lambs) for eight months. Iodine was administered to ewes as calcium iodate. TSH in blood serum; TT₃, TT₄, fT₃, and fT₄ in blood plasma were examined in both groups of ewes and lambs to assess the risks of iodine intake above the permitted limit, as it applies to thyroid gland activity.

RESULTS: Group B ewes showed a significant increase in TSH and TT₄ only on day 1 after parturition. The highest values of TT₄, TT₃, and fT₃ in lambs were recorded on day 1 after birth. The lowest values of fT₃ and fT₄ in lambs were measured on day 60 after birth with no differences observed between the groups. In lambs of Group B the lower concentration of TSH until day 3 after birth was followed by a significant increase from day 10 after birth.

CONCLUSION: Our results indicate a risk of postnatal hypothyroidism among lambs from pregnant and lactating ewes having a high iodine intake.

Abbreviations:

Cal - calcium iodate
fT₃ - free triiodothyronine
fT₄ - free tetraiodothyronine (thyroxine-prohormone)
ICCIDD - International Council for the Control of Iodine Deficiency Disorders
TH - thyroid hormones
TSH - thyroid stimulating hormone
TT₃ - total triiodothyronine
TT₄ - total tetraiodothyronine (thyroxine-prohormone)
INTRODUCTION

Widespread supplementation of iodine in feed of farm animals in the Czech Republic (Kursa et al. 2000) has significantly contributed to elimination of goiter. With increasing iodine supplementation, goitrogenic risks from excessive iodine are currently increasing, as reported by the International Council for the Control of Iodine Deficiency Disorders (IDD) newsletter on Iodine Deficiency Disorders (IDD Newsletter). High iodine intake from marine algae or through a high concentration of iodine in iodized table salt has increased risk of goiter in humans in some countries (Teng et al. 2006). Sang et al. (2012) reported an increased concentration of TSH and subclinical hypothyroidism and/or autoimmune thyroiditis. With acute iodine excess, its incorporation into organic compounds decreases while thyro-stimulating hormone increases. The primary function of thyroid hormones is enhancement of basal metabolism and glucose utilization in cells (Todini et al. 2006; 2007). According to Radetti et al. (2006) extreme doses of iodine in pregnancy do not markedly influence the level of thyroid hormones in ewes. Boland et al. (2008) investigated iodine supplementation in pregnant ewes and in lambs and concluded that high iodine intake in ewes decreased IgG concentration in lamb blood serum. Acute excess iodine decreases iodine transport, intrathyroidal organification, and release of thyroid hormones from the thyroid gland (Dayan & Panicker 2009).

The objective of the present study was to assess the risk of metabolic dysfunction with excessive dietary intake of iodine in ewes and newborn lambs.

MATERIALS AND METHODS

Experimental design

Twelve pregnant Šumava ewes in their 5th lactation weighing 53–60 kg and their neonatal lambs (n = 13) were used in this study. Environmental conditions such as feed, housing conditions, and temperature before and during experimentation were similar. Prior to the start of the experiment, the ewes were randomly divided into two groups: Group A (control) comprised 6 ewes and their 7 lambs (3 female and 4 male) while Group B (experimental) consisted of 6 ewes and their 6 lambs (4 female and 2 male). Group A feed was supplemented with calcium iodate at 3 mg iodine per kg of dietary dry matter (DM). The diet of Group B was enriched with calcium iodate at 5 mg iodine per kg of dietary dry matter (DM). Lambs were fed only maternal milk. The formulation of the daily feed ration in the 2 month period before the experiment was identical in the groups. In the experimental period (from 1–2 months of gestation to 60 days after parturition) the feed ration differed only in iodine content of the mineral supplement. The content of iodine in the basal diet of ewes was 0.10 mg/kg. Water was supplied ad libitum to all sheep.

To assess iodine intake, its concentration in blood plasma was determined by the Sandell–Kolthoff colorimetric method.

Blood samples were taken from ewes 30 and 60 days prior to experimentation (Table 1), 30–50 days before parturition and on days 1, 10, 30, and 60 after parturition. Blood samples from lambs were collected on 1, 3, 10, 30, and 60 days of age. Blood samples were collected from ewes and lambs between 07.00 and 09.00 (1–2 h after morning feeding) from the vena jugularis into tubes containing heparin (for assessment of TT3, TT4, fT3 and fT4 from blood plasma) and without heparin (for assessment of TSH from blood serum) and centrifuged for 10 min. Blood serum and plasma were collected in sterile tubes and frozen at –20°C until analysis. The experiment was conducted in accordance with principles of the Anti Animal Cruelty Commission at the Agricultural Faculty of the University of South Bohemia in České Budějovice.

TSH analysis

TSH concentration in blood serum was determined immune-enzymatically using commercial kits from ELISA Development. Immuno-enzymatic determination of TSH is a sandwich-type technique in two steps and based on the interaction of a specific polyclonal antibody with the ovine hormone TSH.

TT3, TT4, free T3 and free T4 analysis

Concentrations of free and total thyroid hormone in blood plasma were determined by radio-immunoanalysis using commercial kits from IMMUNOTECH (Praha).

Statistical analysis

Data were analyzed using Statistica 6.0 Cz software. The non-parametric Tukey test was used for TSH, TT3, TT4, fT3, and fT4 concentrations. Values of p<0.05 were considered significant. The results are expressed in mean values ± standard deviations.
RESULTS

EWES

TSH serum concentrations in ewes (Table 3)

- 30–50 days before parturition (Table 3)
  There were no differences in the concentrations of TSH between Groups A and B.
- 1 day post-parturition (Table 3)
  Group B TSH concentration was significantly higher than Group A ($p<0.05$).
- 10, 30, and 60 days after post-parturition (Table 3)
  There were no differences in the concentrations of TSH between Groups A and B.

TT3, TT4, free T3 and free T4 plasma concentrations in ewes (Table 3)

- 30–50 days before parturition (Table 3)
  There were no differences in the concentrations of TT3, TT4, fT3, and fT4 between Groups A and B.

TT3 plasma concentrations

- 1–60 days after parturition (Table 3)
  There were no differences in the concentrations of TT3 between Groups A and B.

TT4 plasma concentrations

- 1 day after parturition (Table 3)
  Concentration of TT4 was significantly higher in Group B than in Group A ($p<0.01$).
- 10, 30, and 60 days after parturition (Table 3)
  There were no differences in the concentration of TT4 between Groups A and B. On day 30 after parturition a pronounced increase was observed in TT4 concentration in both groups of ewes, while, on day 60, the concentration of TT4 in both groups of ewes decreased ($p<0.05$) to the values recorded 30 days before parturition.

Free T3 plasma concentrations

- 30 days after parturition (Table 3)
  Concentration of fT3 in Group A was significantly higher than in Group B ($p<0.05$).
- 1, 10, and 60 days after parturition (Table 3)
  There were no differences in the concentration of fT3 between Groups A and B.

Free T4 plasma concentrations

- 1–60 days after parturition (Table 3)
  There were no differences in the concentrations of fT4 between Groups A and B.

LAMBS

TSH serum concentrations in lambs (Figure 1)

- 1 and 3 days postnatal
  Concentration of TSH in Group B was significantly lower than in Group A ($p<0.05$).
- 10, 30, and 60 days postnatal
  Concentration of TSH was significantly higher in Group B than in Group A ($p<0.01$).

Tab 2. Hormones in ewes before experiment without iodine supplementation. Data expressed as mean ± SE (Group A, n=12, Group B, n=12).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before experiment*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>TSH (ng/ml blood serum)</td>
<td>0.55±0.13</td>
</tr>
<tr>
<td>TT3 (nmol/l blood plasma)</td>
<td>2.4±0.3</td>
</tr>
<tr>
<td>TT4 (nmol/l blood plasma)</td>
<td>75.6±14.6</td>
</tr>
<tr>
<td>FT3 (pmol/l blood plasma)</td>
<td>4.7±0.7</td>
</tr>
<tr>
<td>FT4 (pmol/l blood plasma)</td>
<td>13.6±3.3</td>
</tr>
</tbody>
</table>

* mean from 2 consumptions

Tab 3. Hormones in ewes during iodine supplementation before and after parturition.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before parturition</th>
<th>Days after parturition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>TSH1</td>
<td>0.59±0.13</td>
<td>0.88±0.27</td>
</tr>
<tr>
<td>TT32</td>
<td>2.2±0.3</td>
<td>2.3±0.4</td>
</tr>
<tr>
<td>TT42</td>
<td>56.6±11.8</td>
<td>62.1±12.1</td>
</tr>
<tr>
<td>FT33</td>
<td>3.8±0.4</td>
<td>3.5±0.4</td>
</tr>
<tr>
<td>FT43</td>
<td>13.4±3.5</td>
<td>12.2±2.9</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SE (Group A, n=6, Group B, n=6).

eg: 1(mg/kg); 2(nmol/l); 3(pmol/l)

1 blood serum; 2, 3 blood plasma
A - control Group supplementation 3 mg I/kg DM of diet
B - experimental Group supplementation 5 mg I/kg DM of diet

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TT3 plasma concentrations in lambs (Figure 2)

- 1, 30, and 60 days postnatal
  There were no differences in the concentration of TT3 between lambs of Groups A and B. Within 60 days after parturition there was a significant decrease in TT3 in both groups (p<0.05).
- 3 and 10 days postnatal
  Concentration of TT3 in Group B was significantly higher than in Group A (p<0.05).

TT4 plasma concentrations (Figure 3)

- 3 days postnatal
  Concentration of TT4 in Group B was significantly higher than in Group A (p<0.01).
- 1, 10, 30, and 60 days postnatal
  There were no differences in the concentrations of TT4 between lambs in Groups A and B. A gradual decrease in TT4 from day 1 was significant in Group A on day 3 (p<0.01) and day 6 (p<0.05) after birth.

Free T3 plasma concentrations (Figure 4)

- 1 day after birth
  The concentration of fT3 in Group B was significantly lower than in Group A (p<0.05).
- 3, 10, 30, and 60 days postnatal
  There were no differences in the concentrations of fT3 between Groups A and B. A gradual decrease in fT3 from day 1 was significant only in Group A on day 30 (p<0.05) and day 60 (p<0.01) after birth.

Free T4 plasma concentrations (Figure 5)

- 1 day after birth
  The concentration of fT4 in Group B was significantly lower than in Group A (p<0.01).
- 3, 10, 30, and 60 days postnatal
  There were no differences in the concentration of fT4 among Groups A and B. A gradual decrease in fT4 from day 1 was significant only in Group A on day 10 (p<0.05) after birth.
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Fig. 3. TT₄ concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). a,c,d p<0.01; b,e,f p<0.05

Fig. 4. FT₃ concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). a,f p<0.01; a,b,c,d,f p<0.05

Fig. 5. FT₄ concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). a,b p<0.01; a,c p<0.001; a,d p<0.001
DISCUSSION

Iodine intake in the control Group A was 3.1 mg/kg DM while in the experimental Group B it exceeded the maximum limit set by EU standards (2005) of 5 mg/kg of 88% dietary DM. Only the free hormone is responsible for the biological activity of thyroid hormones and available to tissue (Todini 2007). Concentrations of thyroid hormones are influenced by such factors as age, breed, nutrition, season, physiological conditions, method of measurement, and use of a fat- or starch-enriched diet (Todini et al. 2005, 2006; Eshratkhah et al. 2010). The other factors such as selenium status can also play an important role in thyroid hormone metabolism (Sewerynek et al. 2006).

Assessment of the results of our study is complex, due to a wide variation in the levels of thyroid hormones, confirming reports by Todini et al. (2007). The level of serum TSH in the ewes before the trial (Table 2) and before parturition (Table 3) was similar in both groups. The TSH concentration in Group B receiving 5.1 mg/kg DM was significantly higher on day 1 after parturition than in Group A, indicating a potential risk. TSH concentration (Table 3) reached the highest average value on day 10 (0.99±0.39 ng/ml) after parturition in Group B, representing a goitrogenic risk (Burikha et al. 2011). In agreement with the findings of Badiei et al. (2009, 2010) in non-pregnant sheep and Eshratkhah et al. (2010) in Moghani sheep, our results are consistent with the findings of Badiei et al. (2009), who recorded similar TSH concentration in Iranian sheep. Badiei et al. (2010) reported lower TSH concentration in 1 year old sheep without supplementation, at 0.07 ng/ml.

The level of plasma TH hormones (Table 2) in our ewes decreased as gestation progressed. Yildiz et al. (2005) also reported that T4 concentration was highest during early pregnancy and gradually decreased, with the lowest values measured at the end of gestation and post-parturition. The experiments in sows indicate same tendency of decrease of T4 concentrations measured 14 days before parturition, 10 days after parturition and at the weaning (Baňoch et al. 2011). Aumont et al. (1989) reported decreasing T4 concentration during pregnancy. Manalu et al. (1997) suggested that the decrease in the level of thyroid hormones during pregnancy can be explained by the consumption of iodine by the thyroid gland of the fetus.

The concentrations of TT3 in ewes during the experiment correspond to the values reported in sheep by Trávníček et al. (2001), Nazifi et al. (2008), and by Qin et al. (2011) in goats. In contradiction, higher values were determined in sheep by Badiei et al. (2010), Bekeová et al. (1995), and Eshratkhah (2012) and in cows by Guyot et al. (2011). In the present study, the TT3 concentration in Group B was lower but not significant following parturition (except day 1) (Table 3).

With the exception of day 30 post-partum, TT4 concentrations (Table 3) were lower in both groups of ewes than those reported by Nazifi et al. (2008) in adult non-supplemented sheep, 91.60 ± 2.95 nmol/l. On day 30 post-partum (Table 3) our value of TT4 exceeded those reported by Badiei et al. (2008) and Bekeová et al. (1995) in sheep without iodine supplementation and in those receiving simultaneous supplementation of iodine and selenium (Trávníček et al. 2001). The polyfactorial influence of TT4 and the relatively limited usefulness of this variable are demonstrated by results of Badiei et al. (2010) and Eshratkhah et al. (2012), who reported higher TT4 concentration in non-pregnant adult sheep without iodine supplementation compared to our results. The permanently higher level of fT3 in Moghani sheep in Iran (Nazifi et al. 2008, Badiei et al. 2009, 2010, Eshratkhah et al. 2010) in comparison with the values of the Šumava ewes used in our experiment in the Czech Republic suggests a potential influence of temperature of the area (Gordon et al. 2000) in which the trial was conducted that makes comparison of experimental results difficult. For a comparison of results of assessments of thyroid gland activity it is necessary to standardize rearing conditions under which the studies were conducted.

The level of plasma fT3 in our ewes was lower during the trial than that reported by Nazifi et al. (2008), Badiei et al. (2009, 2010) in non-pregnant sheep and Eshratkhah et al. (2010) in Moghani sheep.

From the aspect of metabolic demands, a pronounced influence of the onset of lactation after parturition can be assumed. The concentration of T3 and T4 was lowest in ewes on day 1 post-partum in Group A and subsequently gradually increased, which corresponds to metabolic demands of lactation and the observations of Bekeová et al. (1991), Huszenica et al. (2001), and Antunović et al. (2010). In our trial, TT4 increased consistently until day 30 post-partum in Group B, while fT3 showed a decrease after day 10 post-partum. The lowest values in fT3 concentration for both Groups A and B were recorded in the period 30–50 days before parturition (Table 3). On day 3 the levels of fT3 was slightly increased from day 1 post-partum, while from day 10 there was a decreasing trend to a minimum of 3.0 pmol/l in Group A and 2.7 pmol/l in Group B. The lowest values of fT4 were measured on day 10 post-parturition. According to Benjaminsen (1981) and Riis & Madsen (1985) the concentration of thyroid hormones decreases during lactation.

The trend of decrease in TT3 and TT4 until 60 days of age in lambs, which was significant in Group A (Figures 2 and 3), corresponds to ontogenetic changes in metabolism regardless of the level of iodine intake from milk (Todini et al. 2005, 2006; Todini 2007). The fT3 concentration (Figure 4) recorded in lambs of both groups was higher than reported by Eshratkhah et al.
(2010) in Iranian Moghani lambs. A gradual decrease in fT3 and fT4 (Figures 4, 5) in both groups of lambs from day 1 to day 60 after birth was significant in Group A. The decrease in fT3 in lambs (Figure 4) was more pronounced from 10 days of age than the decrease in fT4 (Figure 5), suggesting a high level of metabolism in growing lambs irrespective of the influence of higher iodine intake from mother’s milk in Group B.

The significantly higher TSH concentration (Figure 1) from day 3 after birth in lambs of ewes with iodine intake of 3.1 mg/kg DM paradoxically corresponds to findings of insufficient iodine intake (Zamrazil et al. 1996), although, according to EU standards (2005), the load of iodine in lambs before and after birth was high, particularly in Group B. In general, these findings correspond to values reported by Guyot et al. (2011) in calves whose mothers received high dietary doses of iodine.

Significantly higher values of TSH (Figure 1) from day 10 to day 60 in Group B lambs having mothers receiving iodine at 5.1 mg/kg is associated with, according to Teng et al. (2006), to findings connected with hypothyroidism. The above-mentioned significant differences demonstrate potential risks of the prenatal and postnatal iodine load in lambs with mothers having high iodine intake during pregnancy and lactation. Rose et al. (2007), Boland et al. (2008) and Guyot et al. (2011) also emphasized the not yet fully explained problem of an undesirable effect of high iodine in pregnancy.

According to Utiger (2006), excessive iodine intake is accompanied by a decrease in TSH, while its increase is indicative of iodine deficiency. Our results document the goitrogenic risks of high iodine intake (5.1 mg/kg dietary dry matter) in ewes and in their lambs.

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