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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; TT_3, TT_4, fT_3, and fT_4 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 TT_4 only on day 1 after parturition. The highest values of TT_4, TT_3, and fT_3 in lambs were recorded on day 1 after birth. The lowest values of fT_3 and fT_4 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:

CaI	- calcium iodate
fT_3	- free trijodothyronine
fT_4	- free tetraiodothyroxine (thyroxine-prohormone)
ICCIDD	- International Council for the Control of Iodine Deficiency Disorders
TH	- thyroid hormones
TSH	- thyroid stimulating hormone
TT_3	- total trijodothyronine
TT_4	- total tetraiodothyroxine (thyroxine-prohormone)

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ORIGINAL ARTICLE

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 (ICCIDD) in the newsletter of 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 of ewes 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 TT_3, TT_4, fT_3 and fT_4 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.

Tab 1. The formulation of daily feed ration in the experimental period of control and experimental groups of ewes.

Dietary component	Number
meadow hay	1 500 g
oat groats	270 g
lucerne granules	240 g
mineral supplement[b]	9 g

[b]supplied per kg diet: 3 mg of I in Group A, 5 mg of I in Group B, 20.0 mg of Co, 6 000 mg of Zn, 30.0 mg of Se, 1 000 mg of Cu, 5 100 mg of Mn, 900 000 I.U. of vit. A, 110 000 I.U. of vit. D3, 1 500 mg of vit. E

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.

TT_3, TT_4, free T_3 and free T_4 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, TT_3, TT_4, fT_3, and fT_4 concentrations. Values of $p<0.05$ were considered significant. The results are expressed in mean values ± standard deviations.

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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.

TT_3, TT_4, free T_3 and free T_4 plasma concentrations in ewes (Table 3)

- **30–50 days before parturition (Table 3)**
  There were no differences in the concentrations of TT_3, TT_4, fT_3, and fT4 between Groups A and B.

TT_3 plasma concentrations

- **1–60 days after parturition (Table 3)**
  There were no differences in the concentrations of TT_3 between Groups A and B.

TT_4 plasma concentrations

- **1 day after parturition (Table 3)**
  Concentration of TT_4 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 TT_4 between Groups A and B. On day 30 after parturition a pronounced increase was observed in TT_4 concentration in both groups of ewes, while, on day 60, the concentration of TT_4 in both groups of ewes decreased ($p<0.05$) to the values recorded 30 days before parturition.

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

Variable	Before experiment*	
	A	B
TSH (ng/ml) blood serum	0.55±0.13	0.91±0.46
TT_3 (nmol/l) blood plasma	2.4±0.3	2.4±0.2
TT_4 (nmol/l) blood plasma	75.6±14.6	69.2±9.2
FT_3 (pmol/l) blood plasma	4.7±0.7	4.2±0.6
FT_4 (pmol/l) blood plasma	13.6±3.3	12.5±3.1

* mean from 2 consumptions

Free T_3 plasma concentrations

- **30 days after parturition (Table 3)**
  Concentration of fT_3 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 fT_3 between Groups A and B.

Free T_4 plasma concentrations

- **1–60 days after parturition (Table 3)**
  There were no differences in the concentrations of fT_4 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 3. Hormones in ewes during iodine supplementation before and after parturition.

Variable	Before parturition		Days after parturition 1		10		30		60	
Group	A	B	A	B	A	B	A	B	A	B
TSH^1	0.59±0.13	0.88±0.27	$0.54±0.12^t$	$0.75±0.13^u$	0.58±0.03	0.99±0.39	0.64±0.22	0.64±0.09	0.68±0.19	0.77±0.25
$TT_3{}^2$	2.2±0.3	2.3±0.4	$2.0±0.1^c$	2.8±1.2	$2.5±0.3^d$	2.4±0.7	2.3±0.3	2.3±0.2	2.2±0.1	2.0±0.4
$TT_4{}^2$	56.6±11.8	62.1±12.1	$47.8±6.8^e$	$78.2±11.7^f$	$61.7±7.4^g$	64.7±13.7	$94.7±20.4^j$	$91.0±17.5^l$	$54.1±7.6^k$	$62.0±9.6^m$
$FT_3{}^3$	3.8±0.4	3.5±0.4	4.4±0.3	4.2±1.1	4.0±0.5	3.6±0.3	$4.2±0.3^n$	$3.6±0.3^o$	$3.0±0.1^p$	$2.7±0.3^q$
$FT_4{}^3$	13.4±3.5	12.22.9	12.0±1.8	$13.1±1.6^h$	10.9±2.8	$9.9±0.7^i$	13.8±1.8	$13.6±1.3^r$	12.3±1.5	$11.9±0.4^s$

Data expressed as mean ± SE (Group A, n=6, Group B, n=6).
$^{e:g;\ l:m;\ n:o;\ r:s;\ t:u}$ $p<0.05$; $^{c:d;\ e:f;\ h:i;\ n:p;\ a:p;\ j:k;\ o:q}$ $p<0.01$
^{1}(ng/ml), ^{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

TT_3 plasma concentrations in lambs (Figure 2)

- **1, 30, and 60 days postnatal**

There were no differences in the concentration of TT_3 between lambs of Groups A and B. Within 60 days after parturition there was a significant decrease in TT_3 in both groups ($p<0.05$).

- **3 and 10 days postnatal**

Concentration of TT_3 in Group B was significantly higher than in Group A ($p<0.05$).

TT_4 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 TT_4 between lambs in Groups A and B. A gradual decrease in TT_4 from day 1 was significant in Group A on day 3 ($p<0.01$) and day 6 ($p<0.05$) after birth.

Free T_3 plasma concentrations (Figure 4)

- **1 day after birth**

The concentration of fT_3 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 fT_3 between Groups A and B. A gradual decrease in fT_3 from day 1 was significant only in Group A on day 30 ($p<0.05$) and day 60 ($p<0.01$) after birth.

Free T_4 plasma concentrations (Figure 5)

- **1 day after birth**

The concentration of fT_4 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 fT_4 among Groups A and B. A gradual decrease in fT_4 from day 1 was significant only in Group A on day 10 ($p<0.05$) after birth.

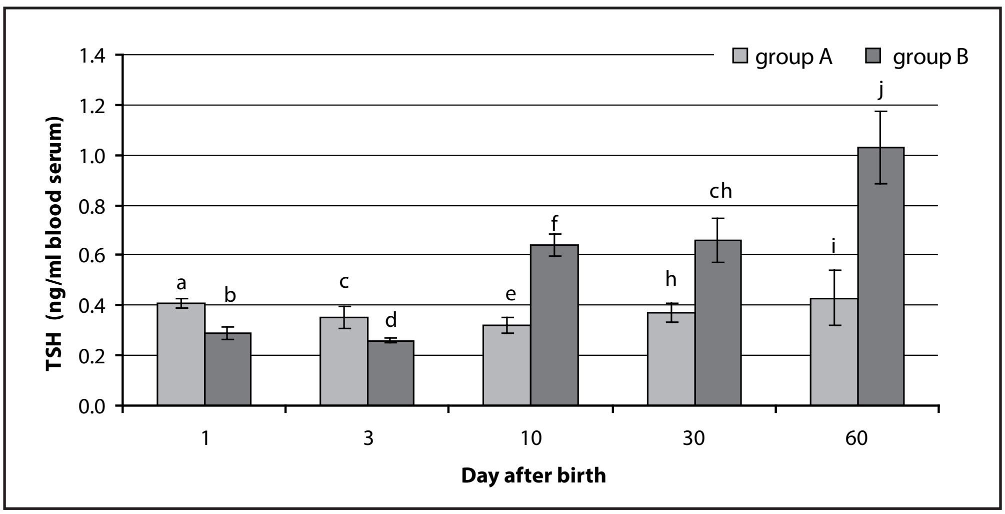

Fig. 1. TSH concentrations in lambs after birth. Data expressed as mean ± SE (Group A, n=7, Group B, n=6). a:b; e:f; h:ch $p<0.01$; j:a,b,c,d,e,h,i $p<0.001$; j:f,ch; c:d; ch:e,b,d; f:b,d $p<0.05$.

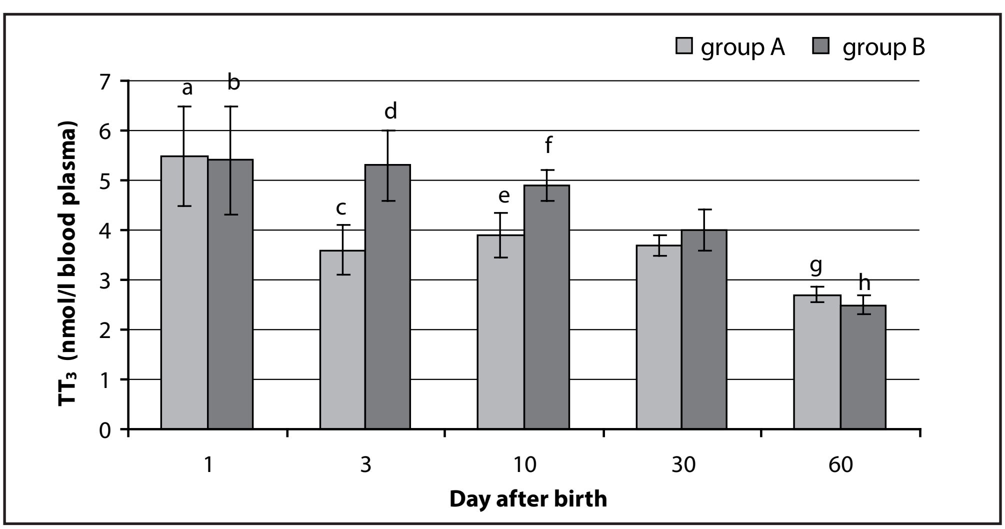

Fig. 2. TT_3 concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). a:g; b:h; c:d, e:f $p<0.05$.

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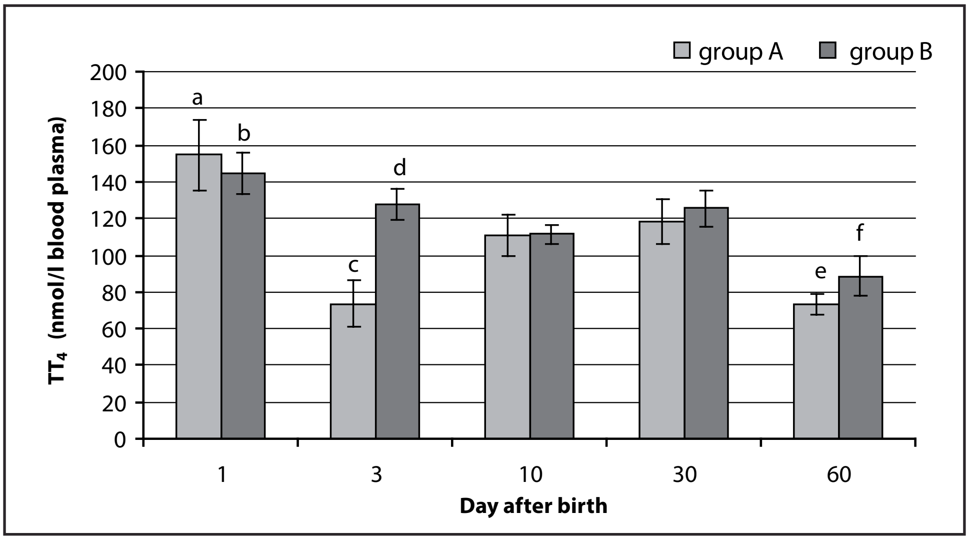

Fig. 3. TT_4 concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). $^{a:c,\ c:d}$ $p<0.01$; $^{c:b,\ b:e,\ a:e,f}$ $p<0.05$

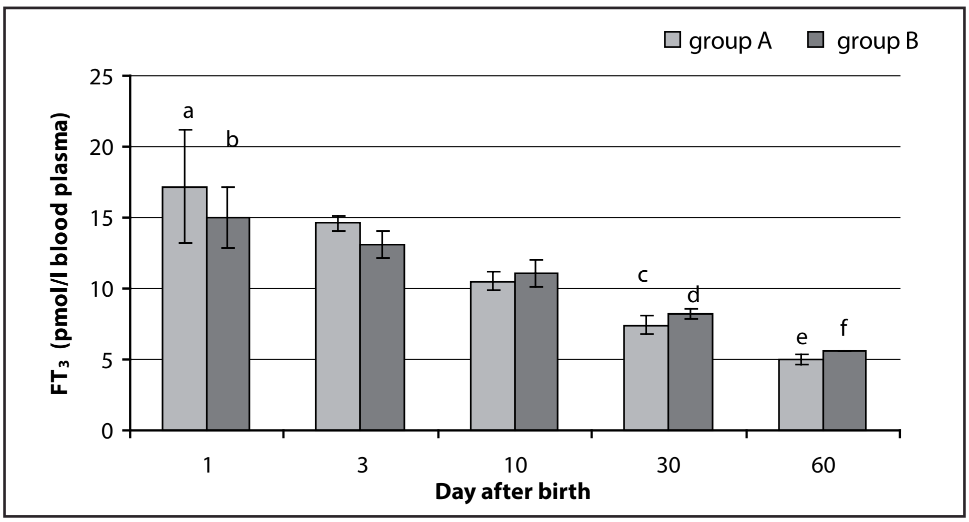

Fig. 4. FT_3 concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). $^{a:e,f}$ $p<0.01$; $^{a:b,c,d,\ b:e}$ $p<0.05$

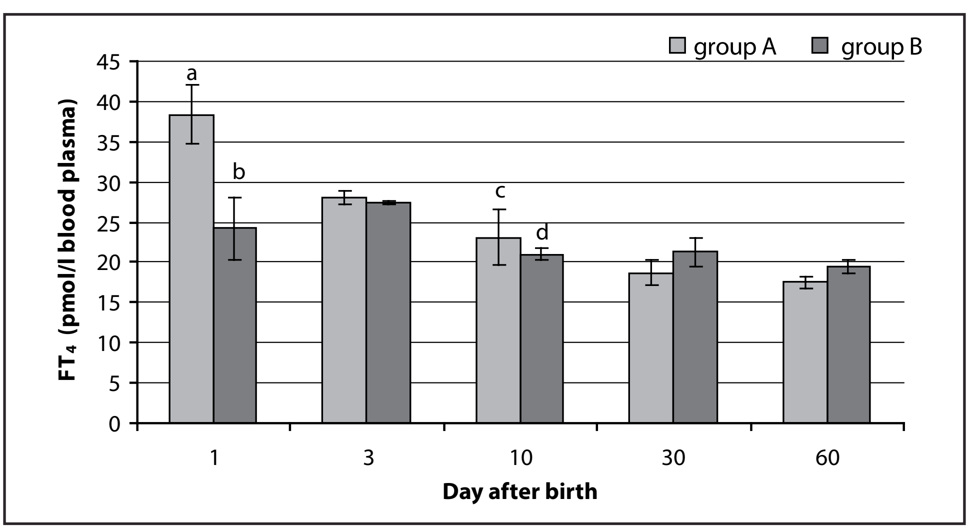

Fig. 5. FT_4 concentrations in lambs after birth (Data expressed as mean ± SE (Group A, n=7, Group B, n=6). $^{a:b}$ $p<0.01$; $^{a:c}$ $p<0.05$; $^{a:d}$ $p<0.001$

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 (Burikhanov & Matsuzaki 2000). Our results differed from those of Guyot *et al.* (2011), who found markedly higher TSH concentration in cows (2.5 ng/ml in a group without supplemental iodine), decreasing to 1.5 ng/ml following 120-day iodine supplementation. 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 T_4 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 T_4 concetrations measured 14 days before parturition, 10 days after parturition and at the weaning (Baňoch *et al.* 2011). Aumont *et al.* (1989) reported decreasing T_4 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 TT_3 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 TT_3 concentration in Group B was lower but not significant following parturition (except day 1) (Table 3).

With the exception of day 30 *post-partum*, TT_4 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 TT_4 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 TT_4 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 TT_4 concentration in non-pregnant adult sheep without iodine supplementation compared to our results. The permanently higher level of fT_3 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 fT_4 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 T_3 and T_4 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, TT_4 increased consistently until day 30 *post-partum* in Group B, while fT_3 showed a decrease after day 10 *post-partum*. The lowest values in fT_3 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 fT_3 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 FT_4 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 TT_3 and TT_4 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 fT_3 concentration (Figure 4) recorded in lambs of both groups was higher than reported by Eshratkhah *et al.*

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(2010) in Iranian Moghani lambs. A gradual decrease in fT_3 and fT_4 (Figures 4, 5) in both groups of lambs from day 1 to day 60 after birth was significant in Group A. The decrease in fT_3 in lambs (Figure 4) was more pronounced from 10 days of age than the decrease in fT_4 (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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REFERENCES

1 Antunović Z, Novoselec J, Sauerwein H, Vegara M, Veranda M (2010). Blood metabolit hormones and leptin in growing lambs. Poljoprivreda **16:** 29–34.

2 Aumont G, Levieux D, Lamand M, Tressol JC (1989). Iodine nutrition in ewes: II. Effect of low to high iodine intake by ewes on iodine content of biological fluids and plasma immunoglobulins G in newborn lambs. Reprod Nutr Develop. **29:** 203–217.

3 Badiei K, Nikghadam P, Mostaghni K (2009). Effect of cadmium on thyroid fuction in sheep. Comp Clin Pathol. **17:** 259–262.

4 Badiei K, Mostaghni K, Gorjizadeh E (2008). Effect off manganese on thyroid fuction in sheep. Comp Clin Pathol. **18:** 255–259.

5 Badiei K, Mostaghni K, Nikghadam P, Pourjafar M (2010). The effect of mercury on thyroid function in sheep. Int J Vet Res. **4:** 277–281.

6 Baňoch T, Fajt Z, Kuta J, Kotrbáček V, Konečný R, Trávníček J, Svoboda M (2011). Utilisation of iodine from different sources by sows and their progeny. Neuroendocrinol Lett. **32**: 510 – 517.

7 Bekeova E, Elecko J, Krajnicakova M, Hendrichovsky V, Maracek I (1991). Dynamics of changes in concentrations of cholesterol and thyroid and ovarian hormones in blood-serum during postparturient period of ewes. Vet Med-Czech **36:** 673–684.

8 Bekeová E, Krajnicáková M, Hendrichovský V, Maracek I (1995). Thyroid and ovarian hormones in ewes treated with gestagens and PMSG in the spring season. Vet Med-Czech **40:** 345–352.

9 Benjaminsen E (1981). Plasma prolactin in the sow with emphasis on variation in resumption of ovarian activity after weaning. Acta Vet Scand. **22:** 67.

10 Boland TM, Hayes L, Sweeney T, Callan JJ, Baird AW, Keely S, Crosby TF (2008). The effects of cobalt and iodine supplementation of the pregnant ewe diet on immunoglobulin G, vitamin E, T3 and T4 levels in the progeny. Animal **2**: 197–206.

11 Braverman LE (2009). Environmental perchlorate: perhaps much ado about nothing. Endocr Pract. **15:** 50–52.

12 Burikhanov RB, Matsuzaki S (2000). Excess iodine induces apoptosis in the thyroid of goitrogen-pretreated rats in vivo. Thyroid **10:**123–129.

13 Dayan CM, Panicker V (2009). Interpretation of thyroid function tests and their relationship to iodine nutrition: Changes in TSH, free T4, and free T3 resulting from iodine deficiency and iodine excess. In: Preedy VR, Burrow GN, Watson RR: Comprehensive Handbook of Iodine: Nutritional, Biochemical, Pathological and Therapeutic Aspects. Academic Press, N. Y., 887–896.

14 EU standard (2005). Commission Regulation /EC/ No. 1459/2005 of 8 September amending the conditions for authorization of a number of feed additives belonging to the group of trace elements, OEJU **233:** 8–10.

15 Eshratkhah B (2012). Comparative study on determination of plasma thyroid hormones using the three immunoassay methods in sheep. J Comp Clin Path Res. **1:** 9–16.

16 Eshratkhah B, Sadaghian M, Eshratkhah S, Pourrabbi S, Najafian K (2010). Relationship between the blood thyroid hormones and lipid profile in Moghani sheep; influence of age and sex.Com Clin Pathol. **19:** 15–20.

17 Gordon CJ, Becker P, Padnos B (2000). Comparison of heat and cold stress to assess thermoregulatory dysfunction in hypothyroid rats. AJP - Regu Physiol. **279**: 2066–2071.

18 Guyot H, de Oliveira LA, Ramery E, Beckers JF, Rollin F (2011). Effect of a combined iodine and selenium supplementation on I and Se status of cows and their calves. J Trace Elem Med Biol. **25:**118–124.

19 Huszenica GY, Kulcsar M, Nikoli JA, Schmidt J, Korodi P, Katai L (2001). Plasma leptin concentration and its interrelation with some blood metabolites, metabolic hormones and the resumption of cyclic ovarian function in postpartum dairy cows supplemented with monensin or inert fat in feed. Br Soc Anim Sci. **2:** 405–409.

20 Kursa J, Trávníček J, Rambeck WA, Kroupová V, Vítovec J (2000). Goitrogenic effects of extracted rapeseed meal and nitrates in sheep and their progeny. Vet Med - Czech **45:** 129–140.

21 Manalu W, Sumaryadi MY, Kusumorini N (1997). Maternal serum concentrations of total triiodothyronine, tetraiodothyronine and cortisol indifferent status of pregnancy during late pregnancy in Ettawah-cross does. Asian-Aust J Anim Sci.**10:** 385–390.

22 Nazifi S, Saeb M, Abangah E, Karimi T (2008). Studies on the relationship between thyroid hormones and some trace elements in the blood serum of Iranian fat-tailed sheep. Vet Arch. **78:** 159–165.

23 Qin F, Zhu X, Zhang W, Zhou J, Zhang S, Jia Z (2011). Effects of dietary iodine and selenium on nutrient digestibility, serum thyroid hormones, and antioxidant status of Liaoning cashmere goats. Biol Trace Elem Res. **143:** 31480–31488.

24 Radetti G, Gottardi E, Bona G, Corrias A, Salardi S, Loche S (2006). Study group for thyroid diseases of the Italian society for pediatric endocrinology and diabetes. The natural history of euthyroid Hashimoto's thyroiditis in children. J Pediatr. **149**:827–832.

25 Riis PM, Madsen A (1985). Thyroxine concentration and secretion rates in relation to pregnancy, lactation and energy balance in goats. J Endocrinol. **107:** 421–427.
26 Rose MT, Wolf BT, Haresign W (2007). Effect of the level of iodine in the diet of pregnant ewes on the concentration of immunoglobulin G in the plasma of neonatal lambs following the consumption of colostrum. Br J Nutr. **97:** 315–320.
27 Sang Z, Wang PP, Yao Z, Shen J, Halfyard B, Tan L *et al.* (2012). Exploration of the safe upper level of iodine intake in euthyroid Chinese adults: a randomized double – blind trial[1,2,3] . J Am Clin Nutr. **95:** 367–373.
28 Sewerynek E, Dabrowska K, Stuss M, Wiktorska JA, Gromadzinska J, Wasowicz W (2006). Potassium iodide changes the levels of thyroid hormones in goitrogenic rats on selenium deficient diet. Neuroendocrinol Lett. 27: 631–638.
29 Teng W, Shan Z, Teng X, Guan H, Li Y, Teng D *et al.* (2006). Effect of iodine intake on thyroid diseases in China. N Engl J Med. **354:** 2783–2793.
30 Todini L (2007). Thyroid hormones in small ruminants: effects of endogenous, environmental and nutritional factors. Animal **1:** 997–1008.
31 Todini L, Delgadillo JA, Debenedetti A, Chemineau P (2006). Plasma total T3 and T4 concentrations in bucks as affected by photoperiod. Small Rum Res. **65:** 8–13.
32 Todini L, Malfatti A, Barbato O, Trabalza-Marinucci M, Acuti G, Antonini Debenedetti A (2005). Plasma thyroid hormones, fibre characteristics and hair follicle activity in angora kids: effects of supplementation with horse bean *(Vicia faba minor)*. Atti SIS Vet. **59:** 39–40.
33 Todini L, Malfatti A, Valbonesi A, Trabalza-Marinucci M and Debenedetti A (2007). Plasma total T3 and T4 concentrations in goats at different physiological stages, as affected by the energy intake. Small Rum Res. **68:** 285–290.
34 Trávníček J, Kroupová V, Kursa J, Illek J, Thér R (2001). Effects of rapeseed meal and nitrates on thyroid functions in sheep. Czech J Anim Sci. **46:** 1–10.
35 Utiger R (2006). Iodine Nutrition - More Is Better. New England J Med. **354:** 2819–2821.
36 Yildiz A, Balikci E, Gurdogan F (2005). Changes in some serum hormonal profiles during pregnancy in single- and twin-foetus-bearing Akkaraman sheep. Med Wet - Pl. **61:** 1138–1141.
37 Zamrazil V, Čeřovská J, Dvořáková M, *et al.* (1996). Iodine deficiency in Czech Republic. In: Neve J, *et al.* (eds.). Therapeutic uses of Trace Elements. Plenum Press, New York, London, 329–332.

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