

## Effect of long-term oral administration of thyroxine on morphology of the gastrointestinal tract in broiler breeder hens

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**Abstract** Published data on 4-week-long administration of extra thyroxine (T<sub>4</sub>) in broiler breeder hens to alleviate the cold-induced ascites in their offspring suggested that long-term maternal hyperthyroidism would affect the gastrointestinal tract morphology. Broiler breeder hens (n=70) were reared in individual cages and allotted to control and hyperthyroid groups (five replicates of seven hens each). Thyroxine, dissolved in water, was orally administered to the hyperthyroid group (0.3 mg T<sub>4</sub>/bird/day) for 100 days and the control group received an equal volume of drinking water. At the end of the experiment (64 week of age), two birds per replicate (20 hens in total) were selected for histological evaluation of the gastrointestinal tract. Thyroxine treatment resulted in an increase in plasma concentration of T<sub>4</sub>; however, triiodothyronine (T<sub>3</sub>) level was not affected. The results of this study showed that long-term administration of T<sub>4</sub> had no adverse effects on the gastrointestinal morphology in broiler breeder hens; therefore, long-term maternal T<sub>4</sub> administration may be recommended as a treatment to reduce the ascites incidence in the progeny. However, further studies are needed to confirm this recommendation as a preventative treatment in reducing the ascites incidence.

**Keywords:** ascites, gastrointestinal morphology, thyroxine

*Received:* 13 Oct. 2018, *accepted:* 21 May. 2019, *published online:* 14 Oct. 2019

### Introduction

Thyroid hormones play vital roles in various physiological functions such as intestinal development (Black, 1988; Suvarna et al., 1993). The gastrointestinal tract requires a large amount of O<sub>2</sub> (Yen et al., 1989), which may reduce O<sub>2</sub> flow to other organs during hypoxemia as seen in the ascites disorder. The ascites syndrome is pulmonary hypertension which happens in broilers and is exacerbated by hypoxemia (Luger et al., 2001). Despite raising the mortality rate, ascites causes reduced weight gain in broilers (Julian, 1993). Several methods have been proposed to reduce ascites incidence including; feed restriction (Acar et al., 1995), intermittent lighting (Buys et al., 1998), genetic selection (Pavlidis et al., 2007), and potassium bicarbonate administration (Shlosberg et al., 1998). Thyroid hormone administration has also been suggested as a method to reduce the ascites syndrome. More recently, it was reported that short-term (4 weeks) administration of thyroxine (T<sub>4</sub>) to broiler breeder hens reduced the ascites incidence in their chicks (Akhlaghi et al., 2012). The role of thyroid hormones in reducing the ascites has been attributed to the development of the pulmonary system and greater

efficiency in O<sub>2</sub> and CO<sub>2</sub> exchange (Akhlaghi et al., 2012). Because thyroid hormones were reported to impact on the intestine, a high oxygen-requesting organ (Akhlaghi et al., 2013); the objective of the current study was to determine whether the ascites-reducing effect of long-term hyperthyroidism could affect the histomorphologic characteristics of the gastrointestinal tract in broiler breeder hens.

### Materials and methods

All animal procedures were carried out as recommended by the Animal Care and Welfare Committee of Shiraz University, Shiraz, Iran. The Cobb 500 breeder hens (47-week-old) were allotted into two equal (n= 35 birds) groups (five replicates of seven hens each), namely; the control and hyperthyroid. The hyperthyroid group received thyroxine (T<sub>4</sub>) (0.3 mg/bird/d) for 100 days (Saemi et al., 2018a). The birds, reared under the same conditions, were fed a corn-soybean based diet (2700 kcal metabolizable energy/kg, and 14%, 2.99% and 0.36% crude protein, calcium and phosphorus, respectively). At the end of the experiment (64 week of age),

two birds per replicate (20 hens in total) were sacrificed and the gastrointestinal tracts (GIT) were dissected and rinsed in normal saline. Small pieces of the GIT were fixed in 10% buffered formalin and hematoxylin-eosin-stained sections were evaluated qualitatively and quantitatively (Saemi et al., 2018b).

*Statistical analysis*

This study was carried out as a completely randomized design. The data were analyzed for normality (SAS , 2004). Data were subjected to the GLM procedure. Differences between means were compared by the least squares means procedure and the level of significance was set at  $P \leq 0.05$ .

**Results and discussion**

Regarding the role of thyroid hormones in regulation of the gastrointestinal tract (Black, 1988; Suvarna et al., 1993), we hypothesized that thyroid hormones might affect the gastrointestinal tract morphology in broiler bre-

eder hens. Thyroxine concentration was higher in the hyperthyroid group as compared with the control one (27.08vs.10.24 ng/mL;  $P=0.003$ ). Plasma  $T_3$  concentration was not affected by  $T_4$  treatment which can be explained by the transformation of extra thyroxine to inactive  $T_3$  ( $rT_3$ ) (Decuypere et al., 1987). The histomorphometrical values of different parts of the gastrointestinal tract were not affected by long-term  $T_4$  administration (Tables 1-6).

There are reports on decreased intestinal growth and distorted intestinal morphology and function in stressed birds (Mitchell and Carlisle, 1992; Hansen et al., 2004). Although glucocorticoid levels were not measured in the present study, it has been reported that stress induced by corticosterone, decreased the height of villi and crypt depth in the epithelium of the small intestinal epithelial cells (Hu and Guo, 2008), with the lower villus height resulting in decreased absorptive capacity (Hangalapura et al., 2003). No differences in plasma  $T_3$  concentration between the control and hyperthyroid groups were found which exclude the systemic path of  $T_3$  function as

**Table 1.** Effect of long-term hyperthyroidism on histomorphometric measurements of the proventriculus (Ls mean  $\pm$  SE) in breeder hens<sup>1</sup>

Parameter ( $\mu$ m)	Control	Hyperthyroid	P
Epithelial thickness	624.5 $\pm$ 62.58	561.8 $\pm$ 69.96	NS
Submucosal thickness	4598.9 $\pm$ 324.76	4528.5 $\pm$ 314.56	NS
Mucosal thickness	5223.4 $\pm$ 412.59	5087.5 $\pm$ 461.29	NS
Tunica muscularis thickness	706.7 $\pm$ 118.63	426.5 $\pm$ 132.63	NS
Serosal thickness	305.6 $\pm$ 51.96	246.5 $\pm$ 58.09	NS

<sup>1</sup>Thyroxine ( $T_4$ ) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age.  
NS: Not significant.

**Table 2.** Effect of long-term hyperthyroidism on histomorphometric measurements of the gizzard (Ls mean  $\pm$  SE) in breeder hens<sup>1</sup>

Parameter ( $\mu$ m)	Control	Hyperthyroid	P
Height of gland	506.7 $\pm$ 62.55	501.7 $\pm$ 62.55	NS
Submucosal thickness	259.9 $\pm$ 43.19	246.7 $\pm$ 43.19	NS
Mucosal thickness	768.8 $\pm$ 102.63	654.5 $\pm$ 102.63	NS
Tunica muscularis thickness	6937.2 $\pm$ 1054.45	5949.5 $\pm$ 1054.45	NS

<sup>1</sup>Thyroxine ( $T_4$ ) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age.  
NS: Not significant.

**Table 3.** Effect of long-term hyperthyroidism on histomorphometric measurements of the duodenum (Ls mean  $\pm$  SE) in breeder hens<sup>1</sup>

Parameter ( $\mu$ m)	Control	Hyperthyroid	P
Villus height	1332.8 $\pm$ 150.71	1611.1 $\pm$ 168.50	NS
Villus width	155.6 $\pm$ 20.48	218.8 $\pm$ 22.90	NS
Crypt depth	1038.3 $\pm$ 130.53	1302.8 $\pm$ 145.94	NS
Villus : crypt ratio	1.30 $\pm$ 0.04	1.20 $\pm$ 0.04	NS
Epithelial thickness	1738.7 $\pm$ 225.85	2163.1 $\pm$ 252.51	NS

<sup>1</sup>Thyroxine ( $T_4$ ) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age.  
NS: Not significant.

**Table 4.** Effect of long-term hyperthyroidism on histomorphometric measurements of the jejunum (Ls mean ± SE) in breeder hens<sup>1</sup>

Parameter (µm)	Control	Hyperthyroid	P
Villus height	155.4 ± 78.69	163.3 ± 78.69	NS
Villus width	197.8 ± 17.94	180.1 ± 17.94	NS
Crypt depth	1440.8 ± 66.97	1419.8 ± 66.97	NS
Villus : crypt ratio	1.1 ± 0.06	1.1 ± 0.06	NS
Epithelial thickness	2002.8 ± 157.6	2205.9 ± 157.6	NS

<sup>1</sup>Thyroxine (T<sub>4</sub>) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age. NS: Not significant.

**Table 5.** Effect of long-term hyperthyroidism on histomorphometric measurements of the ileum (Ls mean ± SE) in breeder hens<sup>1</sup>

Parameter (µm)	Control	Hyperthyroid	P
Villus height	973.9 ± 103.78	853.3 ± 103.78	NS
Villus width	159.9 ± 13.76	153.9 ± 13.76	NS
Crypt depth	785.5 ± 81.63	659.4 ± 81.63	NS
Villus : crypt ratio	1.2 ± 0.04	1.3 ± 0.04	NS
Epithelial thickness	126.75 ± 118.29	118.05 ± 118.29	NS

<sup>1</sup>Thyroxine (T<sub>4</sub>) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age. NS: Not significant.

**Table 6.** Effect of long-term hyperthyroidism on histomorphometric measurements of the cecum (Ls mean ± SE) in breeder hens<sup>1</sup>

Parameter (µm)	Control	Hyperthyroid	P
Circular fold height	861.6 ± 169.66	1187.7 ± 169.66	NS
Circular fold width	135.8 ± 0.083	862.2 ± 135.80	NS

<sup>1</sup>Thyroxine (T<sub>4</sub>) was orally administered to the hyperthyroid group (0.3 mg/bird/day) for 100 days and the control group received the drinking water only during 47 to 64 wk of age. NS: Not significant.

a causal mechanism for changes in histomorphometry of the gastrointestinal tract such as duodenal and jejunal villus height and crypt depth in the hyperthyroid group (Akhlaghi et al., 2013). These findings might be as a result of locally-produced T<sub>3</sub> in the intestine via intra-intestinal de-iodination of thyroxine (Van der Geyten et al.2002). As shown in Tables 1 to 6, long-term induced hyperthyroidism had no apparent adverse effect on gastrointestinal morphometric values. It could be suggested the commercial use of thyroid hormones, as far as it relates to the gastrointestinal morphology, to reduce the incidence of ascites in progeny chicks might be a potentially applicable approach. However, the effects of long-term hyperthyroidism on hatchability and performance in progeny chicks needs to be clarified before making a final conclusion on the use of this preventative treatment in reducing the ascites incidence.

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**Communicating editor:**

## تأثیر درازمدت تجویز خوراکی تیروکسین بر ویژگی‌های ریخت‌شناسی دستگاه گوارش مرغ‌های مادر گوشتی

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**چکیده** داده‌های منتشر شده در مورد تجویز ۴ هفته‌ای تیروکسین در مرغ‌های مادر گوشتی که سبب کاهش آسیت ناشی از سرما در فرزندان آنها شد پیشنهاد می‌دهد که پرکاری درازمدت تیروئید مادر ممکن است بر ویژگی‌های ریخت‌شناسی دستگاه گوارش مرغ‌های مادر گوشتی اثر بگذارد. هفتاد قطعه پرنده در قفس‌های فردی و به دو گروه تیمار (۵ تکرار و ۷ پرنده در هر تکرار)، شامل کنترل و پرکار تیروئید دسته بندی شدند. تیروکسین حل شده در آب برای ۱۰۰ روز به شیوه دهانی به گروه پرکار تیروئید (۰/۳ میلی گرم به ازای هر پرنده در روز) و همزمان به گروه کنترل، همان حجم آب آشامیدنی خورانده شد. در پایان آزمایش (۶۴ هفتگی)، دو پرنده از هر تکرار (۲۰ مرغ) کشتار شدند و ویژگی‌های کمی و کیفی بافتهای دستگاه گوارش بررسی شد. تجویز تیروکسین سبب افزایش غلظت پلاسمایی تیروکسین شد اما غلظت  $T_3$  تحت‌تأثیر قرار نگرفت. نتایج این پژوهش نشان داد که پرکاری درازمدت تیروئید بر ریخت‌شناسی دستگاه گوارش مرغ‌های مادر گوشتی اثری نداشت. ممکن است ایجاد پرکاری درازمدت تیروئید مادری بتواند برای کاهش بروز آسیت در فرزندان کاربردی شود. با این وجود، نتیجه‌گیری قطعی نیازمند پژوهش‌های بیشتری است.