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Original article

Influence of lipoic acid on lipid metabolism and β-adrenergic response to intravenous or oral administration of clenbuterol in broiler chickens

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Abstract — The effects of lipoic acid (LA) on muscle growth, metabolic response and hepatic respiration in broilers treated with or without clenbuterol (CLE) were examined. In 4-week-old chickens, dietary LA administration (100 $mg \cdot kg^{-1}$) enhanced the β-adrenergic response of plasma nonesterified fatty acid with an intravenous injection of CLE (50 $\mu g \cdot kg^{-1}$, estimated from the response area for 120 min (–7860 vs. 874 $\mu mol \cdot L^{-1} \cdot min$ in control and LA-treated groups, respectively; $P < 0.05$). When chickens received long-term oral administration of CLE (0.25 $mg \cdot kg^{-1}$) for 30 d, LA interfered with the repartitioning action of CLE, decreased abdominal fat weight ($P < 0.05$) and increased protein concentration of the breast muscle ($P < 0.05$), in 7-week-old chickens. In addition, the LA supplementation alone increased both plasma nonesterified fatty acid ($P < 0.05$) and triacylglycerol ($P < 0.05$), whereas these effects were not associated with CLE administration. These findings suggest that the dietary LA level used stimulates rapid lipolytic response of plasma nonesterified fatty acid to CLE injection and fatty acid turnover between adipose tissue and the liver, but does not facilitate the repartitioning action of CLE during long-term treatment in broilers.

lipoic acid / clenbuterol / triacylglycerol / lipolysis / chicken

1. INTRODUCTION

Generally, α-lipoic acid (LA), a vitamin-like substance, is known to function as a cofactor in enzyme systems involved in the oxidative decarboxylation of α-keto acids [4]. In recent studies, treatment with this compound has been found to stimulate insulin action and glucose oxidation in the skeletal muscle of diabetic rats [11, 13, 18]. In lipid metabolism, LA supplementation reduces serum levels of total cholesterol and β-lipoproteins in rabbits with experimental atherosclerosis [12]. Segermann

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et al. [17] also demonstrated that the serum triacylglycerol (TAG) level of rats is lowered by intraperitoneal injection of LA. These metabolic effects of LA on energy metabolism may be available and beneficial to energy redistribution and the control of adipose tissue accretion in meat-producing animals. However, there has been little investigation of the effect on growth performance or metabolic response in domestic animals. Hence, the author examined the effect on weight gain, adipose tissue accretion and plasma metabolite concentrations in broiler chickens. Body weight (BW) gain, abdominal fat weight or breast muscle weight was not affected by the dietary LA feeding [9]. On the contrary, dietary LA supplementation enhanced the plasma nonesterified fatty acid (NEFA) level and the rate of in vitro hepatic oxygen consumption and decreased plasma TAG in the chicken, although the effects were dependent upon the dose level and age-related metabolic state [9]. A recent study has also confirmed a decrease in plasma total cholesterol with LA feeding [10]. Moreover, when its administration level is higher than previously used (5 or 50 mg·kg diet^{-1}) [9, 10], whether the response of chicken performance and lipid metabolism to dietary LA is facilitated or different is currently unclear.

In relation to hormonal action, the author demonstrated that the dietary administration of LA facilitates the response of plasma glucose and NEFA to intravenous infusion of a non-selective β-adrenergic agonist, isoproterenol, in broilers [9, 10]. In domestic animals, clenbuterol (CLE), a selective β_2-adrenergic agonist, is well known to be a potent growth promoter that increases muscle mass and protein deposition or decreases adipose tissue accretion [3, 5, 15, 16, 20]. Moreover, recent studies have reported that this repartitioning action is dependent upon nutritional states such as dietary protein level [2, 6, 7]. With regard to vitamins, thiamine supplementation enhances the lipolytic response of broiler chicks to CLE administration [8]. Likewise, LA acting as a cofactor may also facilitate the repartitioning action induced by CLE. However, whether the CLE-inducing muscle hypertrophy or fat accretion reduction during long-term administration accelerates with LA supplementation remains uncertain. Therefore, this study was conducted to examine: (1) the rapid β-adrenergic response of LA-fed chickens to CLE injection; and (2) the growth performance and metabolic response to dietary LA at a higher level (100 mg·kg^{-1}) in broiler chickens receiving long-term administration of CLE.

2. MATERIALS AND METHODS

2.1. Animals and diets

One-day-old female broiler chicks (*Ross*) were initially housed in battery cages until 2 weeks of age. A commercial starter diet containing 23% crude protein and 3050 kcal of metabolizable energy·kg^{-1} until 3 weeks of age and, then, a commercial finishing diet containing 18% crude protein and 3150 kcal of metabolizable energy·kg^{-1} were given ad libitum as basal diets.

2.2. Experiment 1: Metabolic response of LA-fed chickens to CLE challenge

To determine the dietary LA effect on rapid metabolic response to CLE injection, 76 female broiler chicks (5 d of age) were housed in battery cages of 19 birds each. Half were assigned to the LA treatment group, and the remainder were used for controls. LA (Sigma, St. Louis, MO, USA) was added to the diets at the level of 100 mg·kg^{-1}. At 28 d of age, chickens (n = 30 per treatment group) were randomly selected for blood sampling. Blood was taken from a wing vein, using a heparinized syringe, and centrifuged (2000 g) to obtain plasma. Plasma samples were stored at –20 °C until chemical analyses for glucose, NEFA and

TAG concentrations. Furthermore, 29-d-old chickens randomly selected from each treatment group (n = 6) were used for CLE challenge. A medical cannula (i.d. 0.48 mm, o.d. 0.68 mm, Nipro, Osaka, Japan) was inserted into a wing vein under general anaesthesia (pentobarbital sodium, Nembutal Injection®, Abbott Laboratories, North Chicago, IL, USA). After 30 min, blood was taken as a pre-injection sample (0 min). Then, CLE (Sigma) dissolved in saline (9 g NaCl·L^{-1}) was injected into the cannula at the dosage of 50 μg·kg^{-1} (solution volume of 1 mL·kg^{-1}); control birds received an injection of saline alone. Blood (1 mL) was sampled with a heparinized syringe at post-injection times of 10, 20, 30, 60 and 120 min. Plasma samples containing an anticoagulant, heparin, were stored at –20 °C and were used for chemical analyses of glucose and NEFA.

2.3. Experiment 2: Combined effects of dietary LA and CLE on growth performance and plasma metabolite concentrations

To examine the effects of LA on the dietary CLE-inducing repartitioning action, 2-week-old chicks were assigned to 20 wire cages (120 × 75 × 75 cm), with 6 birds per cage and were used for a 2 × 2 factorial experimental design (30 birds in 5 cages per treatment group). The first group was fed a basal diet. The second and the third groups were fed a diet containing LA at the level of 100 mg·kg^{-1} and CLE at the level of 0.25 mg·kg^{-1}, respectively. The fourth group was fed a diet containing both LA and CLE. The experimental diets were given to each group for 30 d in a continuously lighted room maintained at a temperature of 25 °C. At 44 d of age, live body weights of all chickens were measured, and 3 birds per cage were randomly selected for blood and tissue sampling. A blood sample was taken from a wing vein using a heparinized syringe; then, pentobarbital sodium was injected into a wing vein to kill the chickens. Plasma samples containing an anticoagulant, heparin, were obtained from centrifuged blood (2000 g) and stored at –20 °C until chemical analyses for glucose, NEFA and TAG (n = 10 per group). The left side of the breast muscle and abdominal fat pad were removed and weighed (n = 15 per group). The breast muscle was stored at –20 °C until protein determination (n = 10 per group). In addition, 45-d-old chickens (n = 5 per group) were randomly selected and used for measurement of hepatic oxygen consumption.

2.4. Analyses

Plasma glucose was assayed with an automatic analyzer using pyranose oxidase (M110, Sakura Co., Tokyo, Japan). Enzymatic assay kits were used in the determinations of plasma TAG (Sanko Chemical, Tokyo, Japan) and NEFA (Kyowa Medex, Tokyo, Japan). Protein concentration in the breast muscle was determined with the modified Lowry method using bovine serum albumin as the standard [14]. Preparation of liver slices and the monitoring method for the hepatic oxygen consumption were performed as previously reported using an oxygen electrode assembly with a Clark-type probe [8]. In the present study, the rate of oxygen consumption was expressed per mg protein measured using the modified Lowry method [14].

2.5. Statistics

All data were statistically analyzed with computer software (StatView, Abacus Concepts Inc., Berkeley, CA, USA). In the CLE challenge experiment, basal concentrations of plasma metabolites and the response area under the curve and above the baseline in the LA-fed chickens were compared with those of controls using a t test. In the experiment of the response to dietary LA and CLE, data were analyzed with a two-way

ANOVA. When a significant interaction between LA and CLE treatments was detected in any analysis, the CLE effect was tested separately in each LA group using a *t*-test.

3. RESULTS

3.1. Metabolic responses of LA-fed chickens to the CLE challenge

The effect of LA (100 mg·kg^{-1}) on plasma metabolites in broiler chickens is shown in Table I. When the chickens were fed dietary LA from 5 to 21 d of age, a 13% decrease in plasma glucose was observed ($P < 0.001$) in the LA-treated chickens. LA did not affect plasma NEFA, but it decreased ($P < 0.001$) plasma TAG by 42%.

With regard to the relationship of LA to β-adrenergic responsiveness, changes in plasma glucose level following CLE injection are shown in Figure 1. Although basal concentrations of plasma glucose were different between the control and the LA-fed group, the intravenous injection of CLE increased the plasma glucose level in both control and LA-fed chickens. The increased plasma glucose was maximal at 60 min post-injection and remained high 120 min after injection. However, the response areas of controls and the LA-fed group, which were 170.1 mmol·L^{-1}·min and 217.0 mmol·L^{-1}·min (SEM = 15.9), respectively, had no significant difference ($P > 0.05$). Plasma NEFA concentration also changed in response to the CLE injection in both controls and the LA-fed group (Fig. 2). Initially, plasma NEFA rose rapidly and reached its maximum

Table I. Effects of LA on plasma glucose, NEFA and TAG in broilers (experiment 1).

Treatment group	Control	LA	SEM[b]
Plasma concentration[a]			
Glucose, mmol·L^{-1}	11.9	10.4***	0.1
NEFA, μmol·L^{-1}	573	570	17
TAG, μmol·L^{-1}	475	276***	17

[a] The values represent means for 30 birds per treatment group.
[b] Pooled standard error of the means; *** $P < 0.001$.

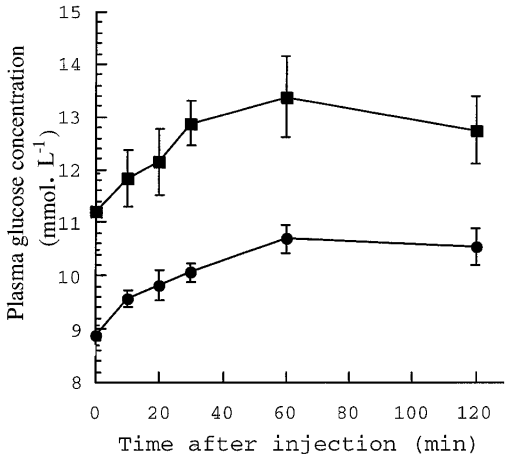

Figure 1. Changes in plasma glucose concentration following CLE injection in broiler chickens treated with or without LA. Values are means for 6 birds with SE represented by vertical bars (●, control; ■, LA-fed group). Response area calculated under the curve and above the baseline during 120 min was 170.1 and 217.0 mmol·L^{-1}·min (SEM = 15.9) in the control and the LA-fed group, respectively ($P > 0.1$).

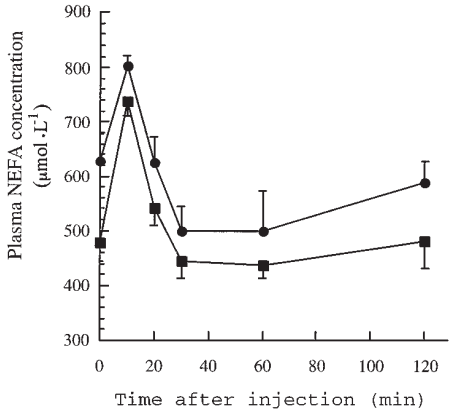

Figure 2. Changes in plasma NEFA concentration following CLE injection in broiler chickens treated with or without LA. Values are means for 6 birds with SE represented by vertical bars (●, control; ■, LA-fed group). Response area calculated under the curve and above the baseline during 120 min was –7860 and 874 μmol·L^{-1}·min (SEM = 2191) in the control and the LA-fed group, respectively ($P < 0.05$).

at 10 min post-injection time, but it subsequently fell to basal levels or below. In an absolute responsiveness to the CLE injection, the response area of plasma NEFA in the LA-fed chickens was significantly greater ($P < 0.05$) than that of the controls (–7860 μmol·L^{-1}·min vs. 874 μmol·L^{-1}·min; SEM = 2191).

3.2. Combined effects of dietary LA and CLE on growth performance and plasma metabolite concentrations

The effects of LA and CLE on BW gain and tissue weights in the chickens are shown in Table II. Dietary LA supplementation had no effect on weight gain or tissue weight. The treatment with CLE resulted in decreased final BW and BW gain ($P < 0.05$), regardless of the LA administration. The absolute mass of the left breast muscle was unchanged in the chickens fed either CLE or LA, but this muscle weight as a proportion of BW (g·kg BW^{-1}) was 5% heavier ($P < 0.05$) in the CLE-fed chickens than in the untreated birds. The absolute mass of the abdominal fat weight showed a significant interaction between LA and CLE treatments ($P < 0.05$). When chickens were not treated with LA, the CLE administration decreased the

Table II. Effects of LA and CLE on BW gain and tissue weight in broiler chickens (experiment 2).

LA, mg·kg diet^{-1}	0		100			Significance		
CLE, mg·kg diet^{-1}	0	0.25	0	0.25	SEM[c]	LA	CLE	LA × CLE
Final BW[a], g·bird^{-1}	2209	2138	2237	2195	14	NS	*	NS
BW gain[a], g·bird^{-1}·d^{-1}	62	59	62	61	1	NS	*	NS
Tissue weight[b], g·bird^{-1}								
Breast muscle	140	144	143	147	2	NS	NS	NS
Abdominal fat	60.5[d]	48.8[e]	54.2	57.2	1.9	NS	NS	*
Tissue composition[b], g·kg^{-1}								
Breast muscle	62.2	66.7	64.4	66.0	0.7	NS	*	NS
Abdominal fat	26.8	22.6	24.3	25.4	0.8	NS	NS	NS

[a] The values represent means for 5 replicates of 6 birds.
[b] The values represent means for 15 birds per treatment group.
[c] Pooled standard error of the means.
[d,e] Mean values with different superscript letters in each CLE-treated group were significantly different, $P < 0.05$; * $P < 0.05$, NS = no significance.

Table III. Effects of LA and CLE on protein accretion in the breast muscle of broiler chickens (experiment 2).

LA, mg·kg diet^{-1}	0		100			Significance		
CLE, mg·kg diet^{-1}	0	0.25	0	0.25	SEM[c]	LA	CLE	LA × CLE
Breast muscle protein[a]								
Concentration, mg·g^{-1}	213[c]	242[d]	222	234	3	NS	***	*
Absolute mass, *g*	29.5	35.1	32.4	34.4	0.8	NS	*	NS

[a] Values represent means for 10 birds per treatment group.
[b] Pooled standard error of means.
[c,d] Mean values with different superscript letters in each CLE-treated group were significantly different, $P < 0.05$; *** $P < 0.001$; * $P < 0.05$; NS = no significance.

Table IV. Effects of LA and CLE on plasma metabolites and hepatic oxygen consumption in broiler chickens (experiment 2).

LA, mg·kg diet^{-1}	0		100			Significance		
CLE, mg·kg diet^{-1}	0	0.25	0	0.25	SEM[c]	LA	CLE	LA × CLE
Plasma concentration[a]								
Glucose, mmol·L^{-1}	10.4	10.4	11.0	10.7	0.2	NS	NS	NS
NEFA, μmol·L^{-1}	577	652	669	804	32	*	NS	NS
TAG, μmol·L^{-1}	599	368	743	507	35	*	***	NS
Hepatic oxygen uptake[b]								
μL·mg protein^{-1}	2.03	2.51	1.87	2.96	0.13	NS	***	NS

[a] The values represent means for 10 birds per treated group.
[b] The values represent means for 5 birds per treated group.
[c] Pooled standard error of means.
*** $P < 0.001$; * $P < 0.05$; NS = no significance.

abdominal fat weight by 19%. However, the effect of CLE on the abdominal fat weight disappeared in the LA-fed chickens. Likewise, a tendency for LA to hamper the reduction of the adipose tissue accretion in the CLE-fed chickens was observed for abdominal fat weight as a proportion of BW ($P < 0.1$). Concentration and absolute mass of protein in the breast muscle are shown in Table III. Protein concentration in the muscle showed a significant interaction between LA and CLE ($P < 0.05$). A 14% increase in the muscle protein concentration was observed in the CLE-treated chickens without the LA feeding ($P < 0.05$), but the magnitude of this response was numerically slight ($P > 0.05$) in the chickens when fed LA. The absolute mass of the muscle protein also increased by 12% ($P < 0.05$) with the CLE feeding, whereas a significant interaction with LA in this response was not detected.

The effects of LA on plasma metabolite concentrations (Tab. IV) were different from those shown in the CLE challenge (experiment 1). Although neither LA nor CLE affected plasma glucose, significant

differences were detected in plasma lipid concentrations. A 20% increase in plasma NEFA occurred with the LA feeding, as compared to the untreated chickens ($P < 0.05$). In the CLE-fed chickens, plasma NEFA was 17% higher than in the controls ($P < 0.1$), but the effect of CLE on plasma NEFA had no significant interaction with the LA administration. The plasma TAG level was increased by 29% ($P < 0.05$) with the LA feeding, in contrast with the result from the CLE challenge experiment. On the contrary, CLE supplementation decreased the plasma TAG level by 35% ($P < 0.001$), but its response had no significant interaction with LA. With regard to the hepatic respiration, the rate of O_2 consumption was 40% higher ($P < 0.001$) than in the controls only in the CLE-fed chickens, whereas LA administration did not affect O_2 consumption (Tab. IV).

4. DISCUSSION

4.1. Metabolic responses of LA-fed chickens to CLE challenge

Recent studies have found that LA treatment decreases hyperglycemia and enhances glucose uptake, a result of stimulated insulin action, in skeletal muscle of obese rats [11, 18]. Likewise, in this experiment, a decrease in plasma glucose that might be attributable to enhanced glucose uptake by peripheral tissue was observed in the LA-treated chickens. This was statistically significant, but the magnitude of the difference was numerically slight. Thus, the LA effect on plasma glucose level, including the results of experiment 2, was thought to be weak in broilers. With regard to plasma lipids, LA decreased only plasma TAG by 42%, and this effect would result from lowered neutral fat transport (lipoprotein) or reduced fat synthesis in the liver. LA has also been reported to decrease serum β-lipoproteins in rabbits with experimental atherosclerosis [12]. In addition, a similar reduction of plasma TAG has been previously observed in 6-week-old broiler chickens with LA (50 $mg \cdot kg^{-1}$) but not in 4-week-old birds [9, 10]. Taken together with this previous finding, unless dietary LA is administered at a higher level to 4-week-old birds, a distinctive effect of LA on plasma metabolites could not be confirmed. Therefore, metabolic responsiveness to LA in the growing period of chickens might be insensitive, although the aim of the present study was not to determine the interrelationship of LA action with chicken age.

In β-adrenergic response, CLE increased plasma glucose in both controls and the LA-fed chickens, but this responsiveness, estimated from the response area, was not affected by the LA feeding. The plasma glucose increment following CLE injection possibly resulted from the stimulated glycogenolysis in the liver [20]. A previous study confirmed that LA stimulated plasma glucose increases when birds receive a continuous infusion of isoproterenol [9]. Consequently, the CLE-stimulated glycogenolytic response was not associated with LA, although the β-adrenergic response of plasma glucose is thought to be even more sensitive in the CLE challenge than in the case of a single injection of isoproterenol [10]. Therefore, the present result indicates that LA possesses a possible effect leading to reduced blood glucose but does not affect the CLE-induced rapid glycogenolysis responsible for hyperglycemia in chickens.

With regard to fatty acid mobilization, plasma NEFA is generally considered as an index of adipose tissue lipolysis. A lipolytic response to the β-agonist in adipose tissue is well known in mammalian species [1, 20], but this effect is thought to be weak in chickens [19, 20]. An injection of thiamine, which acts as a cofactor similar to LA, elicits the β-adrenergic stimulation of plasma NEFA release in the CLE-treated broiler chicks [8]. The present study also confirmed that CLE injection led to a transient increase in plasma NEFA, and its responsiveness in the

LA-fed chickens was significantly greater than that in the controls. A possible effect of constant CLE-induced lipolysis would be inhibited under a hyperglycemic state in this study. If the enhanced plasma glucose level returns immediately to its basal level following isoproterenol injection, a rise in plasma NEFA in response to β-adrenergic stimulation occurs continuously in the LA-fed chickens [10]. Thus, to assess the in vivo sensitivity of rapid β-adrenergic lipolysis from a change in plasma NEFA, the correlation of plasma glucose level to the regulation of energy mobilization should be considered. Therefore, this study suggests that LA is a possible facilitator for rapid CLE-induced lipolysis in the adipose tissue of chickens while the adrenergic response of glycogenolysis just prior to the fatty acid mobilization is sensitive.

4.2. Combined effects of dietary LA and CLE on growth performance and plasma metabolite concentrations

A previous study observed no effect on BW gain or tissue weight in broilers fed 5 or 50 $mg \cdot kg^{-1}$ [9]. The present experiment also indicates that LA does not affect body growth or tissue mass even when chickens are fed dietary LA at the higher level of 100 $mg \cdot kg^{-1}$. The effect on feed intake and feed efficiency still remains to be examined because this study focused mainly on body composition and metabolic response. While the dietary CLE administration retarded BW gain regardless of the LA feeding, the absolute mass of adipose tissue decreased in the CLE-fed chickens. However, its response was inhibited by the LA feeding. A similar tendency was also observed in the adipose tissue weight per kg live BW. Thus, this alteration of the adipose tissue accretion would result from different modes of action of CLE and LA as to fatty acid metabolism, as described below. In addition, the CLE feeding stimulated muscle protein accretion with increased muscle weight per kg live BW. Many studies have noted that the muscle protein deposition induced by the β-agonist is attributable to a lowered fractional rate of protein degradation rather than to a stimulated fractional protein synthesis [6, 15, 16, 20]. LA supplementation, however, had no effect on the CLE-induced muscle protein accretion. The present data suggest that LA does not affect the repartitioning action of CLE that leads to muscle hypertrophy and adipose tissue accretion reduction.

Neither LA nor CLE affected plasma glucose. The changes in plasma lipids due to LA supplementation in this experiment were distinct from the results of experiment 1. The increased plasma NEFA, probably resulting from stimulated adipose tissue lipolysis, has also been observed in 6-week-old chickens that received LA at the level of 50 $mg \cdot kg\ diet^{-1}$, together with reduced plasma TAG [9]. Thus, the lipolytic response of adipose tissue to LA was relatively sensitive in the finisher period (7 weeks of age) rather than in younger chickens, as discussed above. However, the enhanced plasma NEFA level in the LA-fed chickens might not necessarily be due to stimulated lipolysis in adipose tissue. An increase in blood NEFA will also occur when the rate of fatty acid utilization or uptake in peripheral tissue is below the releasing rate of NEFA with lipolysis. Hepatic energy expenditure, estimated from in vitro oxygen consumption, was not affected by LA. This result was similar to a previous report that hepatic oxygen consumption in LA-fed chickens increases at 4 weeks of age, but its effect disappears at 6 weeks of age [9]. Even though LA stimulated fatty acid mobilization constantly in the present study, most of the increased fuel of free fatty acid would not necessarily be oxidized in the peripheral tissues, especially in the liver. In addition, the increased plasma TAG of the LA-fed chickens observed in this experiment was an interesting result and would be attributable to enhanced hepatic TAG synthesis or lipoprotein release,

in contrast with the response in the CLE challenge experiment. The present data were scarcely able to explain the apparent cause of this observation, whereas LA action in the liver is thought to be variable in relation to the age-related metabolic state and dose response. How LA affects fatty acid metabolism in the liver, as a specific action, might be considered as follows: as a hypothesis, the availability of acetyl-CoA, which is oxidized completely in the Krebs cycle and incompletely in the ketone body production pathway, was probably limited in the livers of the LA-fed chickens. Consequently, the metabolic rate for re-esterification of fatty acid (acyl-CoA), the TAG-synthesis pathway, in the liver might be accelerated by LA. Thus, the present study suggests merely that dietary LA possesses a stimulatory effect on fatty acid turnover between adipose tissue and the liver.

In relation to CLE supplementation, the lowered plasma TAG and the slight enhancement of plasma NEFA in this study would be responsible for the decreased fat deposition. The reduced plasma TAG level has been suggested to be a main response to a β-agonist for fat accretion reduction in chickens, since most fat synthesis in avian species occurs in the liver [19]. Moreover, the increased hepatic O_2 consumption of the CLE-fed chickens might also be associated with fatty acid mobilization resulting from stimulated lipolysis because plasma NEFA tends to increase in the β-adrenergic response to CLE. However, the present data indicates that LA does not interact with lipid metabolism in chickens that received long-term administration of CLE.

4.3. Conclusions

The metabolic response of plasma lipids to LA administration varies in relation to chicken age and was thought to be more sensitive in the finisher period of growing chickens (experiment 2) than in the grower period (experiment 1). In particular, LA not only led to lowered plasma TAG, but also had an interesting ability to increase this lipid level when chickens were fed dietary LA at a level of 100 mg·kg diet^{-1}. Its variable LA action could be associated with fatty acid metabolism in the liver. In the lipolytic response of adipose tissue, LA was certainly able to elevate plasma NEFA, but this effect was not responsible for adipose tissue accretion reduction. Hence, the present study suggests that LA affects fatty acid turnover between adipose tissue and the liver and lowers hepatic fatty acid mobilization. Together with age-related and dose-dependent response, further experiments that focus on LA-inducing fatty acid metabolism in the liver are required if LA function is to be applied to fat deposition control. Moreover, in β-adrenergic action, this study concluded that LA facilitates the rapid response of CLE-induced adipose tissue lipolysis but does not necessarily aid the repartitioning actions of CLE such as muscle hypertrophy and reducing fat deposition in broilers.

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REFERENCES

[1] Adeola O., McBride B.W., Young L.G., Metabolic responses induced by isoproterenol in ractopamine-fed pigs, J. Nutr. 122 (1992) 1280–1286.

[2] Bracher-Jakob A., Blum J.W., Effects of a β-adrenergic agonist on growth performance, body composition and nutrient retention in finishing pigs fed normal or low amounts of protein, Anim. Prod. 51 (1990) 601–611.

[3] Buyse J., Decuypere E., Huyghebaert G., Herremans M., The effects of clenbuterol supplementation on growth performance and on plasma hormone and metabolite levels of broilers, Poultry Sci. 70 (1991) 993–1002.

[4] Christensen K., Vitamins, in: Riis P.M. (Ed.), Dynamic biochemistry of animal production, Elsevier Science, Amsterdam, 1983, pp. 215–272.

[5] Dalrymple R.H., Baker P.K., Gingher P.E., Engle D.L., Pensack J.M., Ricks C.A., A repartitioning agent to improve performance and carcass composition of broilers, Poult. Sci. 63 (1984) 2376–2383.

[6] Hamano Y., Kobayashi S., Terashima Y., Effects of β-adrenergic agonist (clenbuterol) on skeletal muscle protein turnover in broiler chicks fed either low or adequate protein diet, Anim. Sci. Technol. (Jpn.) 65 (1994) 1105–1110.

[7] Hamano Y., Kume K., Yamazaki S., Kobayashi S., Terashima Y., Combined effects of clenbuterol and various concentrations of protein on performance of broiler chickens, Br. Poult. Sci. 39 (1998) 117–122.

[8] Hamano Y., Okada S., Tanaka T., Effects of thiamine and clenbuterol on plasma metabolites and hepatic oxygen consumption in broiler chicks, Br. Poult. Sci. 40 (1999) 127–130.

[9] Hamano Y., Sugawara S., Kamota Y., Nagai E., Involvement of lipoic acid in plasma metabolites, hepatic oxygen consumption, and metabolic response to a β-agonist in broiler chickens, Br. J. Nutr. 82 (1999) 497–503.

[10] Hamano Y., Kamota Y., Sugawara S., Effects of lipoic acid on plasma metabolites and metabolic response to intravenous injection of isoproterenol in broilers, Asian-Aus. J. Anim. Sci. 13 (2000) 653–658.

[11] Henriksen E.J., Jacob S., Streeper R.S., Fogt D.L., Hokama J.Y., Tritschler H.J., Stimulation by α-lipoic acid of glucose transport activity in skeletal muscle of lean and obese Zucker rats, Life Sci. 61 (1997) 805–812.

[12] Ivanov V.N., Effect of lipoic acid on tissue respiration in rabbits with experimental atherosclerosis, Cor Vasa 16 (1974) 141–150.

[13] Khamaisi M., Potashnik R., Tirosh A., Demshchak E., Rudich A., Tritschler H., Wessel K., Bashan N., Lipoic acid reduces glycemia and increases muscle GLUT4 content in streptozotocin-diabetic rats, Metabolism 46 (1997) 763–768.

[14] Markwell M.A.K., Haas S.M., Bieber L.L., Tolbert N.E., A modification of Lowry procedure to simplify protein determination in membrane and lipoprotein samples, Anal. Biochem. 87 (1978) 206–210.

[15] Morgan J.B., Jones S.J., Calkins C.R., Muscle protein turnover and tenderness in broiler chickens fed cimaterol, J. Anim. Sci. 67 (1989) 2646–2654.

[16] Muramatsu T., Kakita M., Aoyagi Y., Okumura J., β-Adrenergic agonist effects on liver and breast muscle protein synthesis in female chicks, Poultry Sci. 70 (1990) 1630–1632.

[17] Segermann J., Hotze A., Ulrich H., Rao G.S., Effect of α-lipoic acid on the peripheral conversion of thyroxine to triiodothyronine and on serum lipid-, protein- and glucose levels, Arzneim. Forsch. Drug Res. 41 (1991) 1294–1298.

[18] Streeper R.S., Henriksen E.J., Jacob S., Hokama J.Y., Fogt D.L., Tritschler H.J., Differential effects of lipoic acid stereoisomers on glucose metabolism in insulin-resistant skeletal muscle, Am. J. Physiol. 273 (1997) E185–E191.

[19] Wellenreiter R.H., β-Adrenergic agonists for poultry, Crit. Rev. Poult. Biol. 3 (1991) 229–237.

[20] Yang Y.T., McElligott M.A., Multiple actions of β-adrenergic agonists on skeletal muscle and adipose tissue, Biochem. J. 261 (1989) 1–10.