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Effect of Intermittent Feed Deprivation on Plasma Insulin-Like Growth Factor-I and Tibial Dyschondroplasia in Broiler Chicks*

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Abstract: Two experiments were conducted to evaluate dietary manipulation of growth rate and the subsequent incidence of tibial dyschondroplasia (TD) in broiler chicks. A corn-soybean meal diet which contained 1.15 % calcium and approximately 0.6 % available phosphorus (aP) was fed. In Experiment 1, birds were fed *ad libitum* or deprived of feed for 8 h during the night either three times per week on Monday, Wednesday and Friday or twice a week on Monday and Friday starting at d 5. In the second experiment, birds were full fed vs depriving feed for 8 h during the day every third day beginning at d 6. Feed deprivation decreased 20-d BW only in Experiment 1 when feed was deprived three times per week. Gain:feed was decreased in both experiments when the birds were restricted fed. The incidence of TD was decreased by 25 to 33 % and the number of severe TD lesions was decreased by 50 to 80 % when feeding time was restricted. Bone ash was not affected in Experiment 1, but was increased in Experiment 2 by feed deprivation. Plasma insulin-like growth factor-I (IGF-I) was decreased by feed deprivation, and returned to control levels after feed was returned. The results indicate that feed deprivation for eight hours at various daily intervals will attenuate the incidence of TD in birds fed a Ca:aP ratio of 2:1. This may be related to temporary reductions in circulating levels of IGF-I.

Key Words: Broiler, feed deprivation, insulin-like growth factor-I, tibial dyschondroplasia

Introduction

Levels of insulin-like growth factor-I (IGF-I), also known as Somatomedin-C, decrease in the blood when an animal is deprived of feed. This effect has been demonstrated in humans (Clemmons *et al.*, 1981), rats (Phillips and Young, 1976), and chickens (Huybrechts *et al.*, 1985). Salmon and Daughaday (1957) reported that a serum sulfation factor, called somatomedin, was necessary for the incorporation of sulfate onto the glycosaminoglycan side chains of proteoglycans in the organic matrix of cartilage. Phillips and Young (1976) observed a decrease in sulfation of cartilage 6 h following a decrease in somatomedin activity in feed-deprived rats. Somatomedin activity and cartilage growth were stimulated after refeeding the animals.

Tibial dyschondroplasia (TD) is a common leg aberrance in broilers, which is caused by an abnormality in cartilage growth and maturation (Hargest *et al.*, 1985). The TD lesion is characterized by a white mass of unvascularized and uncalcified cartilage in the proximal metaphysis of the tibia. Intermittent feed deprivation has been shown to be effective for reducing TD incidence and severity (Edwards and Sorenson, 1987; Elliot and Edwards, 1994). Feed deprivation for 8 h every fourth day during the starter period was an effective method for ameliorating TD. A TD-inducing diet containing low calcium and high phosphorus and chloride was used in those studies. Feed deprivation has also been shown to increase mineralization of the tibia as evidenced by higher bone ash (Edwards and Sorensen, 1987; Elliot and Edwards, 1994).

The objective of this study was to determine the extent of an effect of intermittent 8-h periods of feed deprivation on plasma IGF-I in broiler chicks and the concomitant TD incidence in broilers fed a diet with a calcium:available phosphorus ratio of approximately 2:1.

Materials and Methods

Animals and Diets: A total of 480 male and female chicks (Arbor Acres X Arbor Acres) were housed in electrically heated battery-brooders (Petersime Incubator Co., Gettysburg, OH 45328) with raised wire floors and continuous lighting for each experiment. Ten chicks were placed in each pen and the chicks were wing feather sexed to provide equivalent males and females in each pen. The basal diet was calculated to contain 1.00 % calcium (analyzed at 1.15%) and 0.60 % available phosphorus (Table 1). The diets were fed for either *ad libitum* consumption or chicks were deprived of feed for 8 h by removing the feeders from the battery-brooders.

Table 1: Composition of the basal diet

Ingredients	%
Ground yellow corn	53.10
Soybean meal (48.5% CP)	40.00
Vegetable oil[1]	2.00
Dicalcium phosphate	2.50
Limestone	1.50
Salt	0.50
DL-methionine	0.28
Vitamin premix[2]	0.10
$MnSO_4$-H_2O	0.02
Analyzed composition	
Calcium	1.15
Phosphorus, total	0.82
Copper, ppm	7
Calculated composition	
CP	24.00
ME, kcal/kg	2,931
Phosphorus, available	0.60
Chloride	0.34

[1]Wesson Oil, Beatrice/Hunt Wesson, Inc., Fullerton, CA 92834
[2]Vitamin premix provides per kilogram of diet: retinyl acetate, 3,000 IU; cholecalciferol, 400 ICU, DL-alpha-tocopherol acetate, 20 mg; menadione sodium bisulfite, 1.06 mg; thiamine HCl, 3.6 mg; riboflavin, 7.2 mg; D-calcium pantothenate, 20 mg; niacin, 54 mg; biotin, .2 mg; folic acid, 1.1 mg; pyridoxine HCl, 6 mg; and vitamin B_{12}, 18 μg.

The feed deprivation treatments began at 5 d of age in Experiment

*The use of trade names in this publication does not imply endorsement by the North Carolina Agricultural Research Service of the products named nor criticism of similar ones not mentioned

Table 2: Effect of feed deprivation on growth performance, bone ash and development of tibial dyschondroplasia in broiler chicks

Feed Deprivation	20-d BW[1] (g)	Gain:feed[1] (g:g)	Bone ash[2] (%)	Tibial dyschondroplasia incidence[1] (%)	Tibial dyschondroplasia score[1] (%)	No. 3[3] (%)
Experiment 1 (days/week)						
0	579[a]	0.687[a]	50.5	54[a]	1.86	16[a]
2	556[ab]	0.630[b]	51.3	27[b]	1.81	7[ab]
3	546[b]	0.630[b]	51.2	21[b]	1.18	3[b]
Pooled SEM	7	0.010	0.9	5	0.22	3
Treatment effects	P values					
	0.008	0.001	0.629	0.001	0.069	0.007
Experiment 2						
No	504	0.634[a]	46.4[b]	76[a]	2.30	38[a]
Yes	490	0.607[b]	49.0[a]	51[b]	2.10	20[b]
Pooled SEM	7	0.004	0.9	3	0.08	3
Treatment effects	P values					
	0.167	0.001	0.041	0.001	0.089	0.001

[a-b]Means within each column with no common superscript differ significantly($P < 0.05$).
[1]Means of 12 pens of 10 chicks per pen in Experiment 1 and 24 pens of 10 chicks per pen in Experiment 2.
[2]Means of 12 pens of two bones/pen in Experiment 1 and 24 pens of 1 bone/pen in Experiment 2.
[3]Percentage of birds that were scored 3 (severe lesion) at the end of the experiment.

1 and 6 d of age in Experiment 2. The chicks were grown to 20 d of age in both experiments. In Experiment 1, feeders were removed from 0030 to 0830 h. The chicks that were deprived of feed three times per wk had feeders removed on Monday, Wednesday and Friday whereas chicks deprived of feed twice a wk had feeders removed on Monday and Friday. There were 12 replications of each treatment in Experiment 1. In Experiment 2, the chicks were deprived of feed from 0800 to 1600 h every third day of the trial after the initial 6 d. Treatments were replicated 24 times in this experiment.

Blood: Blood samples were obtained by cardiac puncture from 1 chick/pen (12/treatment) in the morning following an 8 h feed deprivation period in Experiment 1. Blood samples were taken from 12 chicks/treatment immediately before and after the feed deprivation period and 64 h after refeeding in Experiment 2. Ethylenediamine-tetraacetate (EDTA) was used as an anticoagulant to obtain plasma samples. Plasma IGF-I was measured by a double antibody radioimmunoassay after acid-ethanol extraction of the IGF-I binding protein. A kit (Nichols Institute Diagnostics, San Juan Capistrano, CA 92675) used to measure human IGF-I was effective for this purpose. Control samples of human plasma were provided to verify the accuracy of the assay. Huybrechts *et al.* (1985) reported plasma somatomedin-C concentrations in Leghorn chicks using a heterologous radioimmunoassay using recombinant human somatomedin-C. Ballard *et al.* (1990) found that IGF-I in acid-ethanol extracts of chicken plasma produced parallel dose-response curves to pure chick IGF-I and human IGF-I.

Bone: Chicks were killed by cervical dislocation at 20 d of age and the right tibia was examined for the incidence and scored for severity of TD as described by Edwards and Veltmann (1983). Objectivity was increased in the scoring index by measuring the lesion from the lower edge of normal epiphyseal growth plate cartilage to the deepest penetration of the lesion in the metaphysis of the bone. A mild lesion was scored as a 1 and was less than 3 mm deep. A moderate lesion was scored as a 2 and was 3 to 5.9 mm in depth. A severe lesion was scored as a 3 and was 6 mm or greater. The absence of a lesion was scored as zero.
The left tibia was removed from two birds per pen in Experiment 1 and one bird per pen in Experiment 2. Each bird was selected on the basis of its weight being near the average weight of the chicks in that pen. The bones cleaned and ashed after fat extraction by ethanol as described by the AOAC (1984). The articular cartilage was removed from the bones before fat extraction.

Statistical Analysis: Data were analyzed by PROC GLM of SAS (1985) using pen as the experimental unit and treatment means were separated by the Bonferroni t-test. A contrast analysis was conducted on the plasma IGF-I levels to test differences between birds that had been fed *ad libitum* or deprived of feed at 8 h intervals in Experiment 1.

Results

There was a decrease ($P = 0.008$) in 20-d body weight due to feed deprivation three times per wk in Experiment 1 (Table 2), but not when birds were deprived feed for 8 h two times per wk compared to the *ad libitum* fed controls. There was also no difference in body weight when birds were given an 8-h feed deprivation period every third day in Experiment 2. Feed efficiency was decreased ($P = 0.001$) in both experiments when birds were subjected to periods of feed deprivation regardless of the feeding schedule.
The incidence of TD was decreased ($P = 0.001$) in both experiments due to feed deprivation. Relative to *ad libitum* feeding, the incidence of severe TD lesions (No. 3 scores) was reduced by about 50% by 8-h feed deprivation periods twice per wk in Experiment 1 and was reduced 50% further by depriving feed three times per wk. Feed deprivation three times per week resulted in a significant decrease ($P = 0.007$) in No. 3 scores compared with the control treatment. The incidence of severe lesions was also decreased ($P = 0.001$) by 8 h feed deprivation periods every third day in Experiment 2 in which the incidence was also reduced by about 50%. Overall severity scores were not significantly affected by treatment. Bone ash was not affected by feed deprivation in Experiment 1, but was increased ($P = 0.041$) by feed deprivation periods in Experiment 2.
Plasma IGF-I was decreased ($P < 0.003$) by feed deprivation in both experiments (Table 3) except at d 15 of Experiment 1, in which the difference was significant at ($P = 0.065$). On average, the level of IGF-I in the plasma was decreased by approximately one-third after an 8-h feed deprivation period.

Discussion

The results indicate that 8 h of feed deprivation at various daily intervals during the starter period will decrease 20-d BW by 3 to 6 percent when a calcium:available phosphorus ratio of approximately 2:1 is fed. Edwards and Sorenson (1987) observed a decrease in BW of up to 15 percent in chicks deprived of feed for 8 h every day of the starter period in one experiment, but did not observe this effect in two other experiments. However, when chicks were deprived of feed every 2 or 4 d there was no effect on 20-d BW.
Feed deprivation decreased feed efficiency by 4 to 8 percent in the

Table 3: Effect of an 8 h feed deprivation period on plasma insulin-like growth factor-I (IGF-I) in broiler chicks[1]

	Age (d)				
Treatment	5	6	9	12	15
			(ng/ml)		
Experiment 1					
Ad libitum	16.06		23.96[a]		26.83
Feed Deprived	---------		18.04[b]		20.80
Pooled SEM	0.40		0.87		2.05
Treatment effect	P values				
			0.001		0.065
Experiment 2					
Ad libitum		10.25[a]	17.27[a]	20.74[a]	32.02[a]
Refed		11.95[a]	16.69[a]	25.38[a]	25.06[b]
Feed Deprived		6.40[b]	9.84[b]	14.37[b]	12.42[c]
Pooled SEM		0.75	1.20	1.46	1.92
Treatment effects	P values				
		0.002	0.001	0.001	0.001

[a-c]Means within columns with no common superscripts differ significantly ($P < 0.05$).
[1]Means represent approximately 12 pens of 1 bird/pen.

present experiments. A similar response was observed by Edwards and Sorensen (1987) when chicks were deprived of feed for 8 h every d, but not when the birds were deprived feed less often. Elliot and Edwards (1994) did not observe a feed deprivation effect on feed efficiency when chicks were deprived of feed 8 h each day. In our studies, feed deprived chicks attacked the feed with such vigor when refed that feed spillage was increased which may have accounted for some of the decrease in feed efficiency.

The results of feed deprivation on TD agree with Edwards and Sorensen (1987) and Elliot and Edwards (1994). Although TD was decreased by feed deprivation, the incidence was high in Experiment 1 and very high in Experiment 2. Dietary phosphorus and chloride levels were high as was fed in previous studies in which TD was induced (Edwards and Veltmann, 1983; Edwards and Sorensen, 1987; Elliot and Edwards, 1994). However, calcium was fed at a level that would decrease the effect of high phosphorus and chloride on TD incidence by reducing anionic imbalance in the diet (Sauveur and Mongin, 1978).

There were obviously other factors that may have contributed to the high incidence of TD in this study. The level of cholecalciferol fed in this study was twice the NRC (1994) requirement of 5 μg/kg , but was apparently too low. Edwards *et al.* (1994) reported that broilers fed 10 μg/kg cholecalciferol had a rickets incidence of 35 and 77% in separate experiments. When ultraviolet light was blocked, 20 μg/kg cholecalciferol was needed to prevent rickets. However, Elliot and Edwards (1997) did not observe a decrease in TD incidence when cholecalciferol was added to a cholecalciferol deficient diet. High dietary calcium (1.50-1.92%) will reduce the incidence of TD when broilers are fed a low level of cholecalciferol (Roberson *et al.*, 1993). There was also no copper added to the diet in this study and the diet was analyzed to contain 7 ppm copper. The NRC (1994) requirement for copper is listed as 8 ppm. Copper deficiency has been reported to be a cause or method of inducing TD (Wu *et al.*, 1990; Rosselot *et al.*, 1994).

Other researchers have observed that feed deprivation consistently increased bone ash (Edwards and Sorensen, 1987; Elliot and Edwards, 1994). Feed deprivation may have resulted in more retention of calcium in the bone. A more consistent response of bone ash to feed deprivation in the studies of Edwards and Sorensen (1987) and Elliot and Edwards (1994) may have been due to the lower bone ash values observed when the articular cartilage is left on the ends of the tibia before ashing. These reseachers also used a low calcium diet to induce TD in their studies. A greater response of bone ash would be expected when a low calcium diet is fed which was used in.

The decrease in plasma IGF-I after feed deprivation observed in this study agrees with the results of other studies using rats (Phillips and Young, 1976), humans (Clemmons *et al.*, 1981), and chickens (Huybrechts *et al.*, 1985). Phillips and Young (1976) observed that short term feed deprivation decreased serum somatomedin activity and cartilage growth in rat costal cartilage. Binz *et al.* (1989) illustrated that there is a linear correlation between serum IGF-I levels and longitudinal tibial growth as well as tibial epiphyseal width. Plasma IGF-I in broiler chicks is minimized after 3 h of feed deprivation (Roberson, unpublished data). Edwards and Sorensen (1987) reported that feed deprivation periods of at least 4 h and not greater than 8 h are needed to decrease development of TD in broilers.

Ballard *et al.* (1990) reported levels of approximately 15 and 30 ng/ml of plasma IGF-I in two commercial strains of broiler chickens at 7 and 14 d of age, respectively. Hence, the data for plasma IGF-I in this study agrees with their observations. McMurtry *et al.* (1994) reported plasma IGF-I levels of about 10 and 20 ng/ml in 7 to 14 d-old broiler chicks regardless of whether a heterologous assay or a homologous assay for chicken IGF-I was used. However, there was a large (30-50%) difference in plasma IGF-I levels from 21 to 35 d of age between the two assays. Refeeding after a period of feed deprivation has previously been reported to result in plasma IGF-I levels equal to control levels 3 d after feed was returned to meat-type chickens (Kita *et al.*, 1996). Plasma IGF-I levels were restored by 2 h after refeeding leghorn chicks deprived of feed for 2 d (Kita *et al.*, 1998).

Local IGF-I in cartilage and bone may also be influencing the occurrence of TD through autocrine and paracrine effects (Nilsson *et al.*, 1986). Russell and Spencer (1985) demonstrated that administration of IGF-I into the tibial growth plate of hypophysectomized rats stimulated longitudinal bone growth. Cook and Leach (1991) demonstrated that IGF-I stimulates chondrocyte proliferation and chondroitin sulfate release in cultured broiler chick cartilage cells taken from the epiphyseal growth plate.

Short periods of feed deprivation with concomitant reduction of plasma IGF-I levels during the starter period appear to be an effective way to prevent TD in broiler chickens. A better management scheme may be needed to prevent a possible negative effect on feed efficiency. Plavnik *et al.* (1986) reported that broilers restricted to maintenance intake for 6 d beginning at 6 d of age weighed slightly more than control birds at 8 wk of

age. Hence, the small decrease in body weight at 3 wk of age due to feed deprivation may be eliminated by subsequent compensatory growth if sufficient time is allowed.

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