Fructose and its Effect on Turkey Plasma Uric Acid Levels and Productive Performance

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ABSTRACT

Previous studies have shown that addition of fructose to the diet of broilers raises plasma uric acid (PUA) concentration and improves productive performance. The purpose of this experiment was to establish the effect of feeding fructose on turkey PUA concentration and productive performance. Turkey poult (n = 64) were weighed and randomly assigned to diets containing 0 (control), 5, 10, and 15% fructose with four replicates of four pouls each per treatment. All diets were isocaloric and isonitrogenous. Feed and water were offered ad libitum for 14 wk. Body weights were measured biweekly throughout the study, and blood samples were drawn from wk 8 to 10 for determination of PUA concentration, leukocyte oxidative activity (LOA), and differential leukocyte counts. Relative liver size (g/kg BW) was also determined. The heaviest body weights were recorded from turkeys fed 10% fructose diet ($P < 0.05$). Supplementation of fructose had no effect on the feed to gain ratio, relative liver size, or PUA concentrations. LOA increased in pouls fed the 15% fructose diet. Turkeys fed 10 and 15% fructose diets had higher monocyte and lower polymorphonuclear lymphocyte counts ($P < 0.05$) compared to those fed control and 5% fructose diets. Feeding fructose to turkeys at 10% of the diet improved productive performance. However, dietary fructose had no effect on PUA or, consequently, LOA.

(Key words: fructose, plasma uric acid, polymorphonuclear lymphocyte, monocyte, turkey performance)

INTRODUCTION

There has been abundant research involving supplementary dietary fructose in mammals owing to the increasing use of fructose in human foods. Comparably, there are a number of studies with broilers although none have been performed with turkeys. Dietary fructose is known to elevate plasma uric acid (PUA) concentrations (Maenpaa et al., 1968; Simkin, 1969; Miles et al., 1987), which has been suggested to confer increased resistance to disease by reducing oxidative stress (Simoyi et al., 2002). For this reason we hypothesized that dietary fructose will increase PUA in turkeys, lower oxidative stress and consequently improve productive performance.

Oral or intravenous administration of fructose to children results in dramatic increases in both uric and lactic acid concentrations in serum and an increase in urinary uric acid excretion (Perheentupa and Ravio, 1967). These increases are suggested to be caused by rapid nucleic acid degradation due to the increased intracellular lactic acidosis in the liver. Lactate also reduces renal excretion of urate (Yu et al., 1967) and so the relative importance of hepatic or renal factors in the resultant hyperuricemia is not immediately apparent. Studies of Cebus monkeys have demonstrated hyperuricemia and increases in urinary uric acid excretion after infusions of high concentrations of hexoses, with fructose having the greatest effect (Simkin, 1969).

Because adenosine triphosphate (ATP) is used in the phosphorylation of fructose to fructose-1-phosphate, adenosine monophosphate (AMP) accumulates (Figure 1; Woods et al., 1970). AMP is then dephosphorylated to adenosine or deaminated to inosine monophosphate, both of which are intermediates in purine catabolic pathways that produce uric acid. Furthermore, depletion of ATP removes the inhibitory effect that ATP normally exerts upon the degradation of AMP, thereby exacerbating its breakdown. Maenpaa et al. (1968) reported an increase in PUA and its degradation product, allantoin, in rats after intravenous administration of fructose. This was accompanied by a rapid depletion of liver ATP and inorganic phosphate ($P$).

Many diseases and degenerative processes have been linked in some way to the action of free radicals. Free
radicals are not necessarily the only cause for these conditions but make the body more susceptible to other disease-initiating factors, enhance the progression of diseases, and may inhibit the body’s own defenses and repair processes (Cross et al., 1987). Overall health depends to a large extent on the body’s ability to control free radicals and thus reduce oxidative damage to tissues, cells, and DNA. Therefore, antioxidants play an essential role in disease prevention, longevity, and overall well-being (Cross et al., 1987). Whether dietary fructose contributes to the antioxidant profile in turkeys as well as its effect on turkey performance, PUA concentration and oxidative stress were thus the objectives for this investigation.

FIGURE 1. A schematic representation of fructose metabolism in the liver depicting its interrelationship with glucose formation, lipid biosynthesis, and purine catabolism leading to the formation of uric acid.
TABLE 1. Diet composition

<table>
<thead>
<tr>
<th>Item</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn</td>
<td>38.64</td>
</tr>
<tr>
<td>Soybean meal</td>
<td>39.36</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>1.02</td>
</tr>
<tr>
<td>Dicalcium phosphate</td>
<td>2.47</td>
</tr>
<tr>
<td>Limestone</td>
<td>0.30</td>
</tr>
<tr>
<td>Salt</td>
<td>0.30</td>
</tr>
<tr>
<td>Turkey vitamin premix</td>
<td>1.02</td>
</tr>
<tr>
<td>DL-Methionine</td>
<td>0.10</td>
</tr>
<tr>
<td>Coban 68</td>
<td>0.24</td>
</tr>
<tr>
<td>Trace mineral salt</td>
<td>0.10</td>
</tr>
<tr>
<td>Alfalfa meal</td>
<td>1.79</td>
</tr>
<tr>
<td>Fructose or cornstarch</td>
<td>15.0</td>
</tr>
</tbody>
</table>

1Manganese (3.40%), selenium (120 ppm), zinc (3.40%), vitamin A (900,000 IU/kg), vitamin D3 (360,000 ICU/kg), and vitamin E (1,350 IU/kg).

2Zinc (3,500 ppm), manganese (2,800 ppm), iron (1,750 ppm), copper (350–450 ppm), iodine (70 ppm), and cobalt (70 ppm).

MATERIALS AND METHODS

Sixty-four 1-d-old turkey poults were tagged, weighed, and randomly assigned to four diets containing 0 (control), 5, 10, and 15% fructose with four replicates of four poults each per treatment. All diets were isocaloric and isonitrogenous. Cornstarch was used as filler for diets containing less than 15% fructose (Table 1). Feed and water were offered ad libitum for 14 wk. Blood samples were drawn into heparinized tubes at wk 8 and 10 for PUA and glucose determination and measurement of oxidative stress. Differential leukocyte counts were measured during wk 10. Body weights were taken biweekly until termination of project. Turkeys were killed at 14 wk of age, and liver weights were recorded.

Uric Acid and Glucose Determination

The PUA was determined using a commercially available diagnostic kit. Plasma glucose (PG) was measured using the YSI 2700 Select biochemistry analyzer.

Differential Leukocyte Counts and Oxidative Activity

Chemiluminescence techniques are functional assays to quantify the release of oxidants from cells or tissues (Van Dyke, 1987; Radi et al., 1993). Luminol-based chemiluminescence was used to estimate leukocyte oxidative activity (LOA) as described by Iqbal et al. (1999). Leukocytes were separated out by centrifugation of whole blood on monopoly resolving medium (Ficoll hy-paque). The final reaction mix comprised luminol, phosphate-buffered saline, leukocytes, and phorbol myristic acid. A Berthold luminometer was used for this procedure, and results were reported as integrated light units. A Coulter Multisizer II electronic cell counter was used to enumerate polymorphonuclear lymphocytes (PMN) and monocytes. Leukocytes (5 μL) were suspended in 20 mL of an electrolyte solution, and 500 μL was sampled for the counts. PMN were grouped in the 4.0-to-6.5-μm diameter range, whereas monocytes were grouped in the 6.5-to-10.0-μm range.

Experimental Design

Sixteen pens were assigned diets containing four levels of fructose with four replicates of four poults each per treatment in a split plot design. The smallest unit to which treatment was assigned, the pen with four turkeys, was the experimental unit. The main plot of treatments was the level of fructose in the diet. The randomization procedure for the main plot was done as a completely randomized design in which pens were assigned randomly to diets. The subplot of treatments constituted the length of time turkeys consumed diets.

Statistics

Statistical analyses were performed with SAS software (SAS Institute, 1995) using the general linear models procedure to perform analysis of variance. Multiple comparisons were performed between treatment means using Fisher’s least significant difference procedure. Differences were considered significant at ($P < 0.05$).

RESULTS

Growth Response

Differences in weight gain became noticeable from the tenth week. The least weight gain was recorded from turkeys consuming the 15% fructose diet during the last 4 wk of the study ($P < 0.05$). Turkeys consuming the 10% fructose diet had the highest weight gain during the same period ($P < 0.05$) as shown in Figure 2.

Feed Intake and Efficiency

Feed intake did not differ between treatments. A feed gain ratio below two was recorded only from turkeys fed the diet supplemented with 10% fructose (Table 2). Overall, differences in feed to gain ratio were not significant.

Relative Liver Size and Weight Gain

Relative liver sizes of turkeys consuming fructose-supplemented diets did not differ from the relative liver sizes of turkeys consuming the control diet ($P > 0.05$) (Table 2). The weight gains of turkeys fed diets con-
FIGURE 2. The rate of growth of turkeys consuming control (Cont.), 5 (F5), 10 (F10) or 15% (F15) fructose diet for 14 wk. Growth rates among treatments differ significantly \((P < 0.05)\) from wk 10 onward. Pooled standard error = 0.32.

taining 10% fructose were greater \((P < 0.05)\) than those of turkeys fed diets containing 0 (control), 5, or 15% fructose. The lowest weight gains were recorded from turkeys fed the 15% fructose diet.

Differential Leukocyte Counts

As the dietary fructose level increased, PMN counts decreased \((P < 0.01)\). Turkeys consuming diets supplemented with 15% fructose had higher monocyte counts than other treatments \((P < 0.05)\) as shown in Table 3.

PUA and LOA

The PUA concentrations for turkeys consuming the control, 5, or 10% fructose diet were significantly higher at wk 10 than those recorded at wk 8 \((P < 0.05)\). There were no dose-response trends among dietary fructose levels and PUA concentrations (Figure 3).

The LOA of turkeys consuming the control, 5, or 10% fructose diet did not differ \((P > 0.05)\). The LOA of turkeys consuming diets supplemented with 15% fructose was significantly higher \((P < 0.05)\) than the LOA of other treatments. There was an increase in LOA of turkeys consuming diets supplemented with 15% fructose from wk 8 to 10 \((P < 0.05)\). In all other treatments, LOA did not differ among weeks \((P > 0.05)\) as shown in Figure 4.

PG

The PG concentration increased as dietary fructose increased \((P < 0.001)\). PG concentrations between turkeys consuming 5 and 10% fructose diets did not differ \((P > 0.05)\). Week 8 and 10 PG concentrations did not differ \((P > 0.05)\) for all treatments (Figure 5).

DISCUSSION

This experiment was primarily designed to determine if dietary fructose elevated PUA concentration and lowered oxidative stress in turkeys. Contrary to the findings of Miles et al. (1987) who reported increased PUA concentration associated with dietary fructose in chickens, we did not measure a change in turkey PUA concentration. The difference in the effect of dietary fructose on PUA concentration in chickens and turkeys could be explained by differences in the activity of enzymes involved in fructose metabolism. The mechanism by which dietary fructose affects uric acid level is via the phosphorylation of fructose to fructose-1-phosphate resulting in an increase in adenosine diphosphate, which then leads to nucleotide degradation that ultimately re-

**TABLE 2.** Feed intake and efficiency, relative liver size (RLS), and final BW of turkeys fed fructose-supplemented diets for 14 wk

<table>
<thead>
<tr>
<th>Fructose (%)</th>
<th>Feed intake (kg/bird)</th>
<th>Feed efficiency (kg feed/kg gain)</th>
<th>RLS (g/kg BW)</th>
<th>Final BW (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>17.4</td>
<td>2.41</td>
<td>11.6</td>
<td>7.3(^a)</td>
</tr>
<tr>
<td>5</td>
<td>18.1</td>
<td>2.39</td>
<td>12.2</td>
<td>7.6(^b)</td>
</tr>
<tr>
<td>10</td>
<td>16.1</td>
<td>1.93</td>
<td>12.3</td>
<td>8.3(^c)</td>
</tr>
<tr>
<td>15</td>
<td>15.1</td>
<td>2.35</td>
<td>12.0</td>
<td>6.6(^d)</td>
</tr>
<tr>
<td>PSE(^2)</td>
<td>3.4</td>
<td>0.49</td>
<td>1.0</td>
<td>0.8</td>
</tr>
</tbody>
</table>

\(^a–b\)Means with different superscript within column differ significantly \((P < 0.05)\).

\(^1\)There were four pen replicates per treatment.

\(^2\)PSE = pooled standard error.
results in the formation of uric acid (Hallfrisch, 1990). In a previous study, we observed that turkeys consuming inosine-supplemented diets had higher plasma hypoxanthine and xanthine concentrations compared to chickens consuming similar diets that had higher PUA concentration (unpublished data, 2002). This finding signified that xanthine oxidase, the enzyme responsible for the oxidation of hypoxanthine to xanthine and finally to uric acid, has greater affinity for substrate or is more abundant in the chicken. Based on the finding that the effect of dietary fructose on uric acid is through purine catabolism in which xanthine oxidase catalyzes the last two steps leading to the formation of uric acid, turkeys would show marginal increases in PUA concentration when fructose is included in their diets.

The phosphorylation of fructose requires P
i. This increased use of P
i may result in a reduction of P
excretion in turkey excreta. There is a significant amount of P that is excreted annually in poultry manure (Li et al., 2001). d-Fructose has been shown to reduce the hepatic concentration of P
i in perfused rat livers and healthy humans by trapping P
i through its phosphorylation to fructose-1-phosphate (Masson et al., 1994). Hepatic depletion of P
i may result in increased degradation of purine nucleotides since P
i is an important AMP deaminase inhibitor, an enzyme that catalyzes a rate-limiting step in AMP decomposition (Fox, 1981).

When fructose is administered to humans, a transient depression in blood glucose level is observed, which is pronounced in patients with hereditary intolerance to fructose (Froesch et al., 1963), in newborn infants (Schwartz et al., 1964), and with larger doses in normal adults (Felber et al., 1959). These results suggest that the subjects could not metabolize fructose or that their systems were overloaded before this depression occurred. In the present study, we report increased PG concentration as dietary fructose increased. This finding may be due to the differences in fructose metabolism in humans and turkeys since after the initial phosphorylation, fructose-1-phosphate enters and affects a variety of pathways, i.e., carbohydrate, protein, lipid, and nucleic acid metabolism either directly or indirectly. In turkeys, dietary fructose may impact carbohydrate metabolism (as depicted in Figure 1) more than nucleic acid metabolism (i.e., uric acid production), and the reverse could be true for humans. Maenpaa et al. (1968) reported increased uric acid and allantoin production and marked depression in protein synthesis concomitantly with low levels of ATP in humans.

The effect of fructose metabolism in turkeys is ameliorated in some respects because of certain inherent characteristics of turkeys. For instance, dietary fructose did not significantly elevate PUA levels due to differences in the way fructose impacts purine metabolism in turkeys.
Dietary fructose did elevate PG concentration, which might have suppressed the feed intake of turkeys consuming diets supplemented with 15% fructose, the diet that resulted in the highest PG concentration. Turkeys consuming diets supplemented with 10% fructose had the highest weight gains and the fastest growth rate from wk 10. Overall, turkeys consuming the 10% fructose diet exhibited the best performance.

A noteworthy observation was the effect of dietary fructose on differential leukocyte counts. The PMN counts decreased with increasing dietary fructose, whereas the reverse was true for monocytes. Monocyte counts were markedly increased in turkeys consuming the 15% fructose diet, suggesting stimulation of the immune system. Fructose feeding has been reported to cause a reduction in the activity of the selenoenzyme glutathione peroxidase in rodents (Fields et al., 1984), a scavenger of oxidants. However, if fructose feeding in turkeys had resulted in a concomitant increase in uric acid, another potent scavenger of oxidants, the immune system might not have been similarly stimulated. These observations demonstrate that dietary fructose improved performance when included up to 10% of the diet but had no effect on PUA and consequently LOA. We thus recommend including fructose in turkey rations as not more than 10% of the diet.

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