Xylitol Toxicosis in a Miniature Australian Shepherd Crossbreed

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The owner of Piper, a 4-year-old, 23.8-lb (10.8-kg) spayed miniature Australian shepherd crossbreed, reported to an animal poison control center that, one hour earlier, the dog had ingested 225 to 240 fast-dissolve 5-mg melatonin tablets (strawberry flavored).

Presentation

Piper was lethargic and had spontaneously vomited unspecified material that matched the color of the pills. Large, acute overdoses of melatonin in dogs are typically well tolerated, although transient vomiting and lethargy may be noted. However, on examination of the product label, xylitol was found at the top of the "other ingredients" list, causing greater concern.

Each fast-dissolve tablet contained 0.25 g (250 mg) of xylitol, resulting in a dose of 5.2-5.5 g/kg body weight.[1] In dogs, doses exceeding 0.1 g/kg may result in hypoglycemia, with doses greater than 0.5 g/kg carrying the added risk for hepatic necrosis. Because of the massive dose of xylitol consumed and the dog's clinical state, immediate referral to an emergency hospital was made.

Physical Examination Findings

Piper was presented to a 24-hour care facility 1.5 hours after ingesting the pills. On presentation, the dog had improved and appeared bright, alert, and responsive with normal vital signs. There were no abnormal findings noted on examination nor any apparent lethargy. This is an atypical presentation, as most dogs that have ingested xylitol doses of this magnitude are presented with lethargy or weakness due to hypoglycemia.

Diagnosis

Initial laboratory values revealed normal CBC, moderately elevated alanine aminotransferase (ALT; 312 U/L), mild hypokalemia (3.6 mEq/L), mild hyponatremia (134 mEq/L), and severe hypophosphatemia (0.8 mg/dL), with the remainder of the chemistry profile and coagulation parameters within normal limits (***Table***).

Hypokalemia and hypophosphatemia are anticipated findings in cases of xylitol toxicosis and are thought to be secondary to increased serum insulin concentrations that cause intracellular shifts. Piper's blood glucose was likely checked immediately on presentation using a glucometer, but this value was not recorded.

Serum chemistry profiles obtained 17 hours postingestion revealed a significant increase in ALT at 1289 U/L coupled with a mild increase in activated partial thromboplastin time (aPTT; 114.2 seconds) consistent with hepatocellular injury. Aspartate aminotransferase (AST) was not measured. At 24 hours postingestion, ALT became too high to read (>2 000 U/L) until 60 hours after ingestion, at which point the level began a slow, progressive decrease (***Table***). ALT was not diluted.

TREATMENT AT A GLANCE

- Blood glucose concentration should be checked immediately on presentation and before inducing emesis because of the potential for rapid onset hypoglycemia. Hypoglycemia should be corrected with IV dextrose before emesis is induced.
- Rarely, the onset of hypoglycemia is delayed 6 to 12 hours postingestion. This delay is thought to result from formulation of the product (eg, fast-dissolve tablet vs intact gum).[3,6-10]
- Activated charcoal is not indicated, as it does not bind well to xylitol.[11]
- Clinicians should monitor for hypoglycemia, hypokalemia, and hypophosphatemia secondary to intracellular shifts, as well as liver enzyme elevation (ie, AST and/or ALT) and thrombocytopenia. Hypoglycemia and electrolyte imbalances should be corrected as necessary.
- In cases of hepatic damage, coagulation parameters should be monitored closely and blood products provided if prothrombin time (PT) and/or aPTT exceed 1.5 times normal values. Treat with hepatoprotectants such as acetylcysteine, SAMe, and silymarin as needed.[12-13]

Treatment & Long-Term Management

On presentation, additional vomiting was induced using apomorphine. The dog produced at least 4 bouts of vomitus that contained visible tablets, both whole and partially dissolved. Based on the condition of the tablets, it was not possible to accurately quantify the amount of product produced.

Because of the risk for severe hypoglycemia and hepatic necrosis, the following therapies were immediately instituted:

- Plasmalyte (IV) with 2.5% dextrose (15-30 mL/hr). Dextrose administration, even in states of euglycemia, may be helpful if hepatotoxic doses of xylitol were ingested.
- Acetylcysteine (140 mg/kg IV loading dose, followed by 70 mg/kg IV q6h at 7 doses) can help restore or maintain glutathione concentrations in the liver.
- Denosyl (225 mg PO q24h; denosyl.com) contains SAMe (*S*-Adenosylmethionine), which, along with helping to restore glutathione concentrations in the liver, provides support for transmethylation, transsulfation, and aminopropylation pathways.
- Marin Plus Chew for Dogs (1 chew PO q24h; marinplusliver.com) contains silymarin, Vitamin E, and other ingredients that aid in hepatoprotection. Silymarin is thought to act as an antioxidant and free radical scavenger by inhibiting lipid peroxidase and β-glucuronidase.

Daily glucose curves checked glucose every 2 to 4 hours, and the dextrose dose was increased to 5% PRN to maintain euglycemia. Because of the dog's significant increase in ALT and concurrent increase in aPTT on the second day of hospitalization, the following treatments were initiated:

- Vitamin K_1 (5 mg/kg SC q24h)
- Pantoprazole (1.6 mg/kg IV q24h)

TABLE

LABORATORY FINDINGS

Parameter	Reference Range	Time Since Ingestion (Approximate)						
		2 h	**17 h**	**24 h**	**36 h**	**60 h**	**72 h**	**84 h**
Albumin	2.5-4.4 g/dL	2.5	2.8	3.2	3.6	2.8	3.2	2.9
Total protein	5.4-8.2 g/dL	6	5.4	5.9	6.6	6.3	6.8	6.3
ALP	20-150 U/L	25	15	37	56	59	52	49
ALT	10-118 U/L	312	1289	>2000	>2000	1732	1606	1263
Total bilirubin	0.1-0.65 mg/dL	0.3	0.3	0.3	0.3	0.3	0.3	0.3
BUN	7-25 mg/dL	12	12	9	9	9	6	7
Glucose*	60-110 mg/dL	87	99	104	92	96	92	91
Creatinine	0.3-1.4 mg/dL	1.2	0.9	0.8	0.9	0.8	0.6	1
Calcium	8.6-11.8 mg/dL	9.9	9.9	10.4	10.4	10.4	10.8	10.5
Phosphorus	2.9-6.6 mg/dL	0.8	2.5	2.8	3.7	3.9	4.1	3.6
Sodium	138-160 mEq/L	134	139	140	140	139	140	141
Potassium	3.7-5.8 mEq/L	3.6	3.1	3.5	4.3	4.4	4.6	3.9
PT	14-19 seconds	16.7	18.2	17.6	17.6**	16.5**	16.3**	15.5**
aPTT	75-105 seconds	88.8	114.2	112.9	107.4**	105.5**	N/A	99.2**
Hematocrit	37.3%-61.7%	47.9	41.9	51.9	40.1	37.3	42.1	35.5
WBC	5.05-16.76 × 10^3/μL	7.39	10.97	14.12	10.74	10.5	10.55	10.7

*Blood glucose concentrations while receiving 2.5%-5% dextrose supplementation
**After fresh frozen plasma transfusions
N/A = not available

ALP = alkaline phosphatase
ALT = alanine aminotransferase
aPTT = activated partial thromboplastin time
PT = prothrombin time

TAKE-HOME MESSAGES

- Xylitol is among the top 10 canine toxins reported to animal poison control.[5]
- Atypical sources of xylitol should be noted—including sweetened medications, sugar-free foods, and nonfood sources (eg, deodorant, skin care products).[2,3,5]
- Xylitol doses exceeding 0.1 g/kg can result in hypoglycemia; doses greater than 0.5 g/kg may result in hepatic necrosis.[2,4,6-9]
- Vomiting, lethargy, diarrhea, and ataxia are the most common clinical signs of xylitol toxicosis.[3]
- Because the xylitol dose is key for guiding treatment and prognosis, clinicians should consult with an animal poison control or the product manufacturer if the amount ingested is not readily apparent.
- Increase in liver enzymes (ie, AST or ALT) occurs 12 to 48 hours postingestion.[2,4,6-9]
- Although hypophosphatemia is common and likely caused by an intracellular shift, hyperphosphatemia can occur and has been associated with a poor prognosis.[7]

ALP = alkaline phosphatase
ALT = alanine aminotransferase
aPTT = activated partial thromboplastin time
PT = prothrombin time

- Two fresh frozen plasma transfusions (125 mL/kg over 3 and 4 hours, respectively)
  - Plasma transfusions are typically reserved for cases in which the PT/aPTT exceeds 1.5 times normal values and/or clinical evidence of a coagulopathy is present. In the author's opinion, they were not yet indicated in this case.

Overall, Piper tolerated hospitalization well with bright response and good appetite. Except for one episode of liquid diarrhea with frank blood (ie, hematochezia) on the third day of hospitalization, no major physical abnormalities were appreciated.

Piper was discharged 4 days' postingestion with Vitamin K_1 (25 mg PO q24h for 10 days), Denosyl (225 mg PO q24h for 60 days), Marin Plus Chews (1 chew [based on body weight dosing] PO q24h for 60 days), and omeprazole (20 mg PO q24h for 14 days).

Prognosis & Outcome

After discharge, Piper continued to do well at home. She was presented to the same hospital 6 months later with a perforated intestinal foreign body that was successfully corrected via surgery. Pre-anesthetic blood work, including a CBC and serum chemistry profile, revealed no abnormalities. In general, the prognosis following xylitol toxicosis is good to excellent if appropriate medical care is received.[2-4]

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