Incidence and Clinical Relevance of Hyperglycemia in Critically Ill Dogs

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Background: Hyperglycemia associated with critical illness in nondiabetic human patients is a common occurrence in the intensive care unit (ICU), with a reported incidence as high as 71%.1 The consequences of hyperglycemia include altered fluid balance, predisposition to infections, increased morbidity after acute cardiovascular events, and increased risk for renal failure, polyneuropathy, and mortality after hospitalization in the ICU.2 Traditionally, the development of hyperglycemia has been thought simply to reflect illness severity. However, recent findings suggest that hyperglycemia itself may have deleterious effects, and treatment with insulin may ameliorate or decrease the risk of certain complications.

The term “stress hyperglycemia” is commonly used to describe an altered metabolic state induced by acute illness, characterized by transient increases in blood glucose concentration in individuals who lack a previous history of diabetes.3–5 Historically, acute increases in the blood glucose concentration of critically ill nondiabetic patients have been monitored until concentrations exceed 200 mg/dL, at which time insulin therapy is instituted to avoid adverse effects on fluid balance. However, this practice has been challenged in light of a recent report documenting that tight glycemic control by means of insulin therapy reduced morbidity and mortality in human patients admitted to a cardiac surgical ICU.6 Patients whose blood glucose concentrations were maintained between 80 and 110 mg/dL had marked reductions in mortality rate, bloodstream infections, acute renal failure, and critical illness-associated polyneuropathy compared with those patients whose blood glucose concentrations were not as closely regulated.6 This paper has changed the standard of care with respect to the development of hyperglycemia in nondiabetic critically ill human patients. Furthermore, later studies suggest that it is glycemic control rather than insulin administration that confers the beneficial effects.7–9

Although stress hyperglycemia also has been recognized in critically ill animals, the incidence and clinical relevance of hyperglycemia are unknown. Several recent studies in animals have raised the possibility that hyperglycemia may negatively impact outcome.10–13 Because insulin therapy in nondiabetic dogs is not without risk, a better understanding of hyperglycemia in nondiabetic dogs is warranted. The objectives of the present study were to report the incidence and clinical relevance of hyperglycemia in dogs hospitalized in the ICU and to assess whether the presence or degree of hyperglycemia affects morbidity or outcome.

Materials and Methods

All nondiabetic dogs admitted to the ICU of the Cummings School of Veterinary Medicine at Tufts University during the 8-week period between January 1, 2005 and February 28, 2005 were considered eligible for the study. Medical records of all dogs hospitalized in the ICU were examined daily, and all dogs with documented hyperglycemia were enrolled into the study. The blood glucose concentration was measured with either a blood gas
Table 1. Characteristics of hyperglycemic population compared with controls.  

<table>
<thead>
<tr>
<th></th>
<th>Hyperglycemic 38 Dogs</th>
<th>Cohort 76 Dogs</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>8.0 (range, 0.42–15)</td>
<td>6.0 (range, 0.17–16)</td>
<td>.075</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>23.9 (range, 2–57)</td>
<td>27.7 (range, 0.5–91)</td>
<td>.081</td>
</tr>
<tr>
<td>Length of hospitalization (days)</td>
<td>4 (range, 1–21)</td>
<td>3 (range, 1–18)</td>
<td>.137</td>
</tr>
</tbody>
</table>

*Age (years), weight (kg), and length of hospitalization (days) of dogs with hyperglycemia compared with a cohort population. Values listed are the median and range for each category. No significant difference between the 2 populations was noted (ie, the populations were similar in terms of age, weight, and length of hospitalization).  

Results  

During the study period, 245 dogs were evaluated, of which 38 (16%) were hyperglycemic. Seventy-four percent (28/38) of dogs in this population were hyperglycemic at presentation, whereas 26% (10/38) developed hyperglycemia during hospitalization. The hyperglycemic group consisted of 18 females (17 spayed females and 1 intact female) and 20 males (13 castrated males and 7 intact males) and did not differ significantly from the cohort population of 76 dogs, which consisted of 30 females (22 spayed females and 8 intact females) and 46 males (35 castrated males and 11 intact males). There was no statistical difference between the dogs in the hyperglycemic group and the cohort group in terms of age, body weight, and LOH (Table 1). Of the 38 hyperglycemic dogs, all but 4 were pure breeds with the Labrador Retriever most commonly represented (n = 7; 18%). Labrador Retrievers and Golden Retrievers also were the most common pure breeds in the cohort group. The median blood glucose concentration was statistically different between the hyperglycemic population (146 mg/dL; range, 120–310 mg/dL) and the cohort population (102 mg/dL; range, 58–119 mg/dL; P < .01). Eleven percent (4/38) of the hyperglycemic population was hypothermic. Nine percent (7/76) of the cohort population was hypothermic. The median body temperatures were not statistically significant between the hyperglycemic and cohort populations (100.9°F; range, 97–105.6°F versus 100.3°F; range, 98–104.3°F; P < .19). The hyperglycemic population of dogs consisted of dogs with trauma (n = 6), sepsis (n = 5), heart disease (n = 4), neoplasia (n = 4), intervertebral disc disease (n = 4), seizures (n = 4), metabolic disease (n = 4), immune-mediated disease (n = 3), toxin exposure (n = 2), and 1 each of respiratory disease and lower motor neuron disease. The cohort population of dogs consisted of dogs with gastrointestinal disease (n = 14), neoplasia (n = 11), trauma (n = 10), neurologic disease (n = 8), heart disease (n = 7), immune-mediated disease (n = 6), intervertebral disc disease (n = 6), metabolic disease (n = 6), respiratory disease (n = 3), sepsis (n = 2), toxin exposure (n = 2), and nonhealing ulcers (n = 1).

Seventy-one percent (27/38) of the hyperglycemic dogs were managed for medical diseases whereas 29% (11/38) required surgical intervention. This case type distribution was not statistically different from the
cohort population in which 71% (54/76) of dogs were medical cases, whereas 29% (22/76) were surgical cases ($P = .89$). Sixty-three percent (24/38) of the hyperglycemic dogs were receiving medications known to influence glucose metabolism. In this population, 29% (7/24) were receiving nonsteroidal anti-inflammatory drugs alone; 12.5% (3/24) were receiving furosemide alone; 8% (2/24) were receiving thyroid supplementation alone; 8% (2/24) were receiving catecholamine therapy, furosemide, and nonsteroidal anti-inflammatory drugs; 8% (2/24) were receiving steroid therapy alone; 8% (2/24) were receiving dextrose supplementation; 1 dog was receiving steroid therapy, catecholamine therapy, total parenteral nutrition, and insulin therapy; 1 dog was receiving furosemide and dextrose supplementation; 1 dog was receiving catecholamine therapy and furosemide; 1 dog was receiving total parenteral nutrition and insulin therapy; 1 dog was receiving steroid therapy, catecholamine therapy, total parenteral nutrition, insulin therapy, furosemide, and dextrose supplementation; and 1 dog was receiving steroid therapy, total parenteral nutrition, insulin therapy, and dextrose supplementation. None of the dogs in this population was treated solely with insulin. Forty-nine percent (37/76) of the cohort were receiving medications known to influence glucose metabolism. Of this population, 35% (13/37) were receiving steroid therapy alone; 16% (6/37) were receiving nonsteroidal anti-inflammatory drugs alone; 16% (6/37) were receiving dextrose supplementation alone; 8% (3/37) were receiving furosemide alone; 8% (3/37) were receiving steroid therapy and dextrose supplementation; 1 dog was receiving thyroid supplementation alone; 1 dog was receiving catecholamine supplementation and dextrose supplementation; 1 dog was receiving steroid therapy and furosemide; 1 dog was receiving steroid therapy, furosemide, and dextrose supplementation; 1 dog was receiving total parenteral nutrition and dextrose supplementation; and 1 dog was receiving catecholamines, total parenteral nutrition, and dextrose supplementation. None of the cohort dogs were receiving insulin therapy. The administration of medications was not significantly different between the 2 populations ($P = .144$). There was no significant difference between the hyperglycemic population and the cohort population in terms of LOH (4 days; range, 1–21 days versus 3 days; range, 1–11 days; $P = .176$). The LOH of dogs that developed hyperglycemia during hospitalization was significantly shorter than that of dogs that presented with hyperglycemia. Dogs that developed hyperglycemia during hospitalization had a median length of hospitalization of 2.5 days (range, 1–10 days; $P < .01$).

No significant difference was found in complication rate between the hyperglycemic and cohort population ($P = .28$). The overall complication rate for hyperglycemic dogs was 47% (18/38) with sepsis accounting for 13% (5/38) of the complications. The overall complication rate for the cohort population was 37% (28/76) with sepsis accounting for 2.6% (2/76) of the complications. The occurrence of sepsis as a complication was significantly higher in the hyperglycemic group than in the cohort group ($P = .01$).

Seventy-one percent (27/38) of the hyperglycemic dogs were discharged from the hospital, whereas the remaining 29% (11/38) died or were euthanized. Seventy-five percent (57/76) of dogs in the cohort group were discharged from the hospital, whereas the remaining 25% (19/76) died or were euthanized. No significant difference was found between the 2 populations with respect to outcome ($P = .766$). Hyperglycemic dogs then were categorized into 3 groups reflecting the severity of their hyperglycemia. Patients in group 1 had blood glucose concentrations ranging from 120 to 160 mg/dL and consisted of 25 of the 38 (65%) patients. Four of the 25 patients (16%) in this group did not survive. Group 2 consisted of patients with blood glucose concentrations between 160 and 200 mg/dL. Nine of the 38 (24%) patients were included in this group. Three of these 9 patients (33%) did not survive to discharge. Finally, the 3rd group consisted of patients with blood glucose concentrations $>200$ mg/dL. Four of the 38 (11%) patients were included in this group. All 4 (100%) of these patients did not survive to discharge. When comparing outcome, those patients that did not survive to discharge had a significantly higher median glucose concentration (median, 176 mg/dL; range, 122–310 mg/dL) compared with those that were discharged from the hospital (median, 139 mg/dL; range, 121–191 mg/dL; $P = .021$; Table 2).

**Table 2.** Survival analysis of hyperglycemic dogs based on severity of hyperglycemia.

<table>
<thead>
<tr>
<th>Blood Glucose Concentration</th>
<th>120–160 mg/dL</th>
<th>160–200 mg/dL</th>
<th>&gt;200 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient number</td>
<td>25/38 (65%)</td>
<td>9/38 (24%)</td>
<td>4/38 (11%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>4/25 (16%)</td>
<td>3/9 (33%)</td>
<td>4/4 (100%)</td>
</tr>
</tbody>
</table>

Discussion

In this study, the incidence of hyperglycemia in dogs hospitalized in a veterinary teaching hospital ICU was 16%. To the authors’ knowledge, the incidence of hyperglycemia in critically ill dogs has not been previously reported. Patients that developed hyperglycemia during hospitalization had a longer LOH compared with dogs that presented with hyperglycemia, and dogs with hyperglycemia had a higher incidence of septic complications compared with the cohort population. Nonsurvivors had higher glucose concentrations compared with survivors, and the degree of hyperglycemia may negatively affect mortality.
Previous studies of veterinary patients have suggested a negative association between the presence of hyperglycemia and a variety of diseases. In 1 study, dogs with congestive heart failure that were hyponatremic and hyperglycemic had a higher morbidity than those patients that lacked these biochemical abnormalities. In dogs and cats with head trauma, hyperglycemia was shown to correlate with the severity of the head trauma. More recently, the development of hyperglycemia associated with the administration of total parenteral nutrition to cats was shown to negatively affect survival. Given the current finding of a 16% incidence of hyperglycemia and the possibility that increased blood glucose concentrations may have detrimental effects in critically ill veterinary patients, the relationship between blood glucose concentration and patient morbidity and mortality warrants further investigation. Issues that need to be resolved include whether development of hyperglycemia simply serves as a marker of illness severity or directly contributes to adverse outcome. In people, hyperglycemia is known to increase oxidative stress, increase susceptibility to infection, and increase the release of pro-inflammatory mediators. If these findings are confirmed in dogs and cats, insulin therapy may have a role in the management of hyperglycemia in critically ill hospitalized animals.

In the present study, hyperglycemic dogs had a higher incidence of septic complications. In human surgical patients, there is strong evidence that hyperglycemia also is associated with increased risk for wound infections and incision-line sepsis. Studies have suggested that metabolic abnormalities resulting from hyperglycemia impair macrophage and neutrophil function including leukocyte chemotaxis, opsonization, and phagocytosis as well as cell-mediated immune responses including intracellular killing, leukocyte adherence, and superoxide activity. The overall effects of hyperglycemia on the microvasculature lead to decreased tissue perfusion and predispose to aerobic and anaerobic infections.

Additional studies are needed to specifically investigate the relationship between hyperglycemia and septic complications of critical illness in dogs. Furthermore, dogs that developed hyperglycemia during hospitalization had a longer LOH compared with those that presented with hyperglycemia. The importance of this finding currently is unknown, but possible confounding factors such as drug therapy on the risk of developing hyperglycemia must be further evaluated. Treatment modalities such as catecholamine infusions, glucocorticoids, glucose-containing fluids, and parenteral nutrition are known to cause hyperglycemia and therefore may warrant vigilant monitoring. Although no significant difference was found between the hyperglycemic and cohort populations in terms of medications that are known to influence glucose metabolism, this result could be due to the small sample size of this study. In addition, body temperature has been shown to affect glucose metabolism. However, in the present study no correlation between body temperature and persistent hyperglycemia or hyperglycemia was observed. A possible explanation for the lack of statistical significance in terms of body temperature between the hyperglycemic and cohort populations could be the small sample size.

One limitation of this study was that determination of blood glucose concentration was performed by with more than 1 method. Three of the 38 hyperglycemic dogs (8%) had their blood glucose concentrations measured with a glucometer rather than a blood gas analyzer. Although several studies in people have evaluated the accuracy of the glucometer used in this study to measure blood glucose concentrations, no such studies have been reported in the veterinary literature. However, in 1 study performed to evaluate the use of other types of glucometers, it was concluded that all of the meters tested were highly accurate in determining blood glucose concentrations in dogs.

In this study, increased mortality rates were noted with increasing severity of hyperglycemia. Such analysis must be interpreted with caution, and a study with the primary endpoint of evaluating this possibility would need to be performed in order to confirm this finding. In addition, severity of illness scoring might have been useful in determining if the sickest animals were those with the highest blood glucose concentrations.

In conclusion, the results of this study suggest that hyperglycemia may be an important feature of critical illness in dogs. Studies evaluating hormones related to glucose regulation in critically ill dogs are ongoing and may help explain some of the changes observed in the present study. Future studies are warranted to confirm and better define the detrimental effects of hyperglycemia on patient morbidity and mortality and to investigate a possible role for insulin therapy in the glycemic control of nondiabetic dogs.

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**Footnotes**

a NOVA Biomedical Stat Profile Critical Care Express, NOVA Biomedical, Waltham, MA

b Ascensia Elite XL Glucometer, Bayer Corporation, Mishawaka, IN

c SPSS 12.0 for Microsoft Windows, SPSS Inc, Chicago, IL

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**Acknowledgments**

This study was performed in the Foster Hospital for Small Animals at the Cummings School of Veterinary Medicine at Tufts University, North Grafton, MA.

**References**
