Effects of intravenous, low-dose ketamine-diazepam sedation on the results of hematologic, plasma biochemical, and coagulation analyses in cats

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Objective—To evaluate the effects of an IV, low-dose ketamine-diazepam combination used for short-duration chemical restraint on the results of clinicopathologic testing in cats and to assess its practicality and tolerance.

Design—Prospective case series.

Animals—42 client-owned cats of various breeds, ages, and health status.

Procedures—Blood samples were obtained just prior to and just after IV injection of ketamine chlorhydrate (10 mg) and diazepam (0.5 mg). A CBC, plasma biochemistry panel, and coagulation profile were performed on each sample (ie, before and after chemical restraint). Practicality of the procedure was assessed, and cats were monitored for immediate and delayed effects.

Results—Significant changes were observed for most of the analytes tested. However, the magnitude of the observed changes was notably low and likely not of clinical relevance. The chemical-restraint procedure appeared effective, safe, and well tolerated.

Conclusions and Clinical Relevance—The IV, low-dose ketamine-diazepam combination used for short-duration chemical restraint in the present study may be suitable to assist physical restraint for blood sampling for assessment of hematologic, serum biochemical, and coagulation parameters in cats. (J Am Vet Med Assoc 2012;240:287–293)

Jugular venipuncture for blood sampling in cats was brought to the attention of the veterinary community more than 40 years ago. It has become established over time and has been considered as the reference method in this species for many years. However, numerous cats appear intolerant to jugular venipuncture and the associated physical restraint. As well as being an uncomfortable experience for the cat owner, consecutive struggle reactions can also lead to poor-quality samples, failed interventions, and injury to the veterinary staff or the animal. Moreover, studies have found that the stress inherent in this type of handling can have an impact on the cellular or chemical composition of the blood in cats. For all of these reasons, less invasive alternatives to jugular blood sampling have repeatedly been sought. However, the small blood volumes obtained by use of these methods permit only a relatively limited number of selected analyses. Thus, jugular venipuncture is still mandatory when a larger panel of hematologic or plasma biochemistry analyses, coagulation assays, or serum testing is required.

Attempts to use local anesthetic creams or facial pheromones to reduce feline struggle reactions during various clinical procedures have both shown limitations. Chemical restraint rather than force thus remains the humane and often safer way to deal with uncooperative animals. Use of CR is indeed elected by many veterinary practitioners to obtain jugular blood samples easily and safely from some of their feline patients. Cats can be reliably restrained with IV low doses of ketamine and diazepam. Intravenous administration allows immediate onset of action, use of lower drug doses, and faster recovery than IM or SC routes. Moreover, in our experience, it is well tolerated by most cats. However, to the best of our knowledge, the effects of IV administration of ketamine with diazepam on blood and plasma analytes have been documented only on cortisol secretion in cats; and only a few studies have been performed in other species. The primary objective of the study reported here was to investigate whether there are differences in the concentrations of the major blood analytes as measured on hematologic, serum biochemistry, and coagulation parameters, in unsedated cats,
and in the same animals following short-duration CR. A secondary objective was to document the practicality of a low-dose ketamine-diazepam combination administered IV in cats.

**Materials and Methods**

**Animals**—This study was performed between October 2007 and April 2008 at the National Veterinary School of Toulouse, France. It was reviewed and approved by the Ethics Committee in Animal Experiments for the Midi-Pyrénées Area, France. Cats owned by clients, students, and staff of the Small Animal Veterinary Teaching Hospital were used. Interview of owner and complete physical examination of each cat were performed by the same veterinarian in the 12 hours preceding blood sampling. Exclusion criteria were defined as body weight < 3.5 kg, suspected or confirmed severe anemia (pale mucous membranes or low Hct), suspected severe dehydration (persistent skin tent or dry mucous membranes), suspected or confirmed hypotension (weak pulse or measured systolic blood pressure below 90 mm Hg), suspected or confirmed coagulation disorder (bleeding tendency or abnormal coagulation panel), and previously observed adverse effect of one of the drugs used in the study. Breed, sex, age, body weight, and health status were fully recorded for each cat. Written consent was obtained from all owners of participating cats.

**Obtaining blood samples**—The fur covering both jugular veins and 1 cephalic vein was clipped at the time of physical examination. For catheter placement and blood samplings, each cat was gently restrained in a sitting position by the same trained handler. One operator placed all catheters and performed all blood samplings. A catheter was first placed in 1 cephalic vein and secured. A stopper was attached to the catheter hub and immediately flushed with 0.5 mL of 25 U/mL heparinized saline (0.9% NaCl). The catheter and stopper were then covered with a light dressing. Difficulty in catheter placement was subjectively assessed by the operator and recorded. An anesthetic cream was then applied to the skin over both jugular veins. The cat was left in its transport carrier in a quiet room alone or with its owner. Blood sampling was delayed according to recommendations for use of the anesthetic cream in cats. A chronometer was started at the beginning of the first blood sample collection, and times were recorded at each following step, including analyses. Blood was obtained by direct venipuncture of a jugular vein with a 22-gauge needle successively into 3 tubes in the following order: 3.2% buffered Na3-citrate, EDTA-K3, and lithium heparin.

Immediately after complete filling of the third tube and removal of the needle, the catheter was flushed with 0.5 mL of saline solution. Ten milligrams of ketamine chlorhydrate and 0.5 mg of diazepam mixed in the same syringe were injected through the stopper followed by another 0.5-mL bolus of saline solution. Immediate (within < 10 seconds) CR was achieved, and the second blood sample was drawn immediately from the other jugular vein with exactly the same method. Difficulty in each of the 2 successive blood samplings was subjectively assessed by the operator and recorded. The cat was monitored until adequate recovery from CR and discharged from the hospital. Subsequent effects of the procedure were assessed by phone or direct contact with the owners 48 hours later.

**Preanalytic management of collected blood tubes**—Heparin and citrate tubes were centrifuged for 5 minutes at 4,000 rpm. Plasma was separated immediately after centrifugation and put into snap-cap microcentrifuge (Eppendorf) tubes. Ethylenediaminetetraacetic acid samples were homogenized on a rotating agitator for a minimum of 20 minutes.

**Analytic procedures**—All analyses were performed in the same batch for pre- and post-CR samples. A CBC (RBCs, hemoglobin concentration, Hct, mean corpuscular hemoglobin concentration, mean corpuscular volume, PLTs, and WBCs) was obtained from the EDTA specimen with a hematology analyzer. A blood smear was prepared and stained (May-Grunwald Giemsa) for 100-cell manual differential WBC count. A PCV was obtained by centrifugation of a microhematocrit tube and visual reading.

The concentrations of the following biochemical analytes were measured in heparinized plasma with a multilayer dry-slide–technology analyzer: sodium, potassium, chloride, total carbon dioxide, calcium, magnesium, inorganic phosphates, total proteins, albumin, urea, creatinine, cholesterol, triglycerides, glucose, and total bilirubin and the activities of ALT, AST, creatine kinase, alkaline phosphatase, amylase, lipase, and γ-glutamyl transferase were also measured. Prothrombin time, APTT, fibrinogen concentration, and antithrombin activity were measured in citrated plasma with an automatic analyzer.

All analyses were performed according to manufacturer’s recommendations and the laboratory’s procedures for quality control. Imprecision of the analyzers had been tested 2 weeks before the beginning of the experiment with the manufacturer’s recommended human control solutions, because specific feline controls were not available. This was performed according to internationally recognized published recommendations for laboratory standards by duplicating analyses in the morning and afternoon of 3 consecutive days. When different CVs were obtained at different concentrations, the mean was used for the interpretation of data. All imprecision of manual WBC differentials had been evaluated in another (unpublished) study by 2 experienced clinical pathologists who calculated the CV of 10 repeats of smear preparation and 100-cell counts.

**Statistical analyses**—Analysis of variance for paired data, correlation calculations, and regression analysis were used to compare the results obtained without or with CR. Statistical analyses were performed with a commercial software package. Two results for the same analyte in the same animal were considered analytically different if their difference was higher than could be expected from the repeatability (ie, > 2.77 × CV<sub>repeat</sub> × mean value).

**Results**

Forty-six screened cats met the inclusion criteria for this study. Blood samples could not be obtained...
from 4 of these cats because of failed attempts to place the catheter in 3 and unsuccessful first venipuncture in 1. All 6 tubes were obtained in all other cats, except the first heparinized specimen in 1 cat. All samples were obtained (ie, 42 paired hematologic or coagulation samples and 41 paired biochemistry samples were obtained, even when the mean differences between the 2 series were mostly low. The greatest difference between the duration of blood samplings performed without and with CR (paired Student t test; $P = 0.538$). The mean time between the beginning of the first sampling and the end of the second sampling run was $3.9 \pm 2.0$ minutes (range, 1.9 to 13.0 minutes). All analyses were completed within 36 to 70 minutes after the first venipuncture. The duration of CR (ie, time before the cat could remain in sternal position) ranged from 3.5 to 13.0 minutes (median, 7.4 minutes). Few adverse effects were reported by the owners in the 2 days following the procedure: 2 cats vomited once after their travel back home when they were released from their basket and showed agitated behavior, 3 cats were less active than usual for 24 hours, and 6 cats scratched their jugular zones for up to 48 hours.

The concentration of many analytes was significantly lower in the sedated series than in the unsedated series of samples, even when the mean differences between the 2 series were mostly low. The greatest differences observed for plasma biochemistry, coagulation, and blood cell counts were mean decreases of 8.7% and 3.4% for plasma triglycerides and albumin, respectively; mean increases of 7.5% and 0.9% for APTT and prothrombin time, respectively; and mean decreases of 6%, 13%, and 9% for RBC, WBC, and PLT, respectively.

The correlation between RBC decrease and WBC and PLT changes was weak or insignificant (Pearson $r = 0.39$ and 0.11, respectively), whereas it was higher for total protein ($r = 0.61$; Tables 1–3).

### Table 1—Effects of an IV, low-dose ketamine-diazepam combination* used for short-duration CR on the results of hematologic testing variables in cats ($n = 42$).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>RI</th>
<th>n</th>
<th>Before sedation</th>
<th>After sedation</th>
<th>$P$-value, after sedation vs before sedation</th>
<th>Difference (after sedation minus before sedation)</th>
<th>Analytic difference</th>
<th>Repeatability CV (%)</th>
<th>No. of cases &gt; An Dif</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RBC (10$^9$/L)</strong></td>
<td></td>
<td>42</td>
<td>8.58 (0.07–10.55)</td>
<td>8.09 (5.82–10.44)</td>
<td>$&lt; 0.0001$</td>
<td>$-0.52 (1.37–1.44)$</td>
<td>0.80</td>
<td>34t</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>80–150</td>
<td>42</td>
<td>126.5 (99–153)</td>
<td>119.5 (84–152)</td>
<td>$&lt; 0.0001$</td>
<td>$-7 (21–25)$</td>
<td>0.80</td>
<td>34t</td>
<td></td>
</tr>
<tr>
<td>PCV (L/L)</td>
<td>0.24–0.45</td>
<td>42</td>
<td>0.37 (0.26–0.45)</td>
<td>0.35 (0.24–0.44)</td>
<td>$&lt; 0.0001$</td>
<td>$-0.02 (0.05–0.06)$</td>
<td>$&lt; 0.10$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean corpuscular volume (fl)</td>
<td>310–350</td>
<td>42</td>
<td>340.1 (322.4–356.1)</td>
<td>339.7 (321.8–352.5)</td>
<td>0.1170</td>
<td>---</td>
<td>0.47</td>
<td>3t</td>
<td></td>
</tr>
<tr>
<td>Mean hemoglobin concentration (g/L)</td>
<td>39.0–55.0</td>
<td>42</td>
<td>40.5 (30.2–48.3)</td>
<td>40.6 (29.8–48.3)</td>
<td>0.0019</td>
<td>0.2 (1.2 to 0.9)</td>
<td>0.30</td>
<td>3t</td>
<td></td>
</tr>
<tr>
<td><strong>WBC (10$^9$/L)</strong></td>
<td>5.50–19.50</td>
<td>42</td>
<td>8.85 (2.00–16.30)</td>
<td>7.50 (1.50–15.30)</td>
<td>0.0005</td>
<td>$-1.15 (3.30 to 4.90)$</td>
<td>0.80</td>
<td>31t</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (10$^9$/L)</td>
<td>2.50–12.50</td>
<td>42</td>
<td>4.53 (0.52–11.81)</td>
<td>3.49 (0.47–11.78)</td>
<td>$&lt; 0.0001$</td>
<td>$-0.86 (2.59 to 2.62)$</td>
<td>15.5</td>
<td>34t</td>
<td></td>
</tr>
<tr>
<td>Basophils (10$^9$/L)</td>
<td>Rare</td>
<td>42</td>
<td>0.00 (0.00–0.57)</td>
<td>0.00 (0.00–0.30)</td>
<td>0.8582</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Eosinophils (10$^9$/L)</td>
<td>0.00–1.50</td>
<td>42</td>
<td>0.55 (0.00–4.56)</td>
<td>0.52 (0.00–4.00)</td>
<td>0.2631</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes (10$^9$/L)</td>
<td>1.50–7.00</td>
<td>42</td>
<td>3.20 (1.10–7.98)</td>
<td>2.77 (0.78–9.94)</td>
<td>0.4126</td>
<td>---</td>
<td>6.1</td>
<td>31t</td>
<td></td>
</tr>
<tr>
<td>Monocytes (10$^9$/L)</td>
<td>0.00–0.85</td>
<td>42</td>
<td>0.17 (0.00–0.76)</td>
<td>0.17 (0.00–0.56)</td>
<td>0.7286</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
</tbody>
</table>

*All cats received 10 mg of ketamine chlorhydrate* and 0.5 mg of diazepam in the same syringe injected via an IV catheter; 0.5 mL of saline (0.9% NaCl) solution was administered before and after injection. **Number of cats in which the value obtained after sedation exceeded the value obtained before sedation by the analytic difference or greater. †Number of cats in which the value obtained before sedation exceeded the value obtained after sedation by the analytic difference or greater. Results are median (range); comparisons of results before and after sedation were by use of the Wilcoxon test in the case of heterogeneity.

--- Difference was insignificant. An Dif = Analytic difference (2.77 × repeatability CV [%] × mean value). nr = Not relevant. RI = Reference interval.
Table 2—Effects of an IV, low-dose ketamine-diazepam combination* used for short-duration CR on the results of plasma biochemistry analysis in cats (n = 42).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>RI</th>
<th>n</th>
<th>Before sedation</th>
<th>After sedation</th>
<th>n</th>
<th>Before sedation</th>
<th>After sedation</th>
<th>P-value</th>
<th>Difference (after sedation minus before sedation)</th>
<th>Analytic difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/L)</td>
<td>153–161</td>
<td>41</td>
<td>154 (150–159)</td>
<td>155 (152–159)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>1 (1–4)</td>
<td>0.35</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.3–4.2</td>
<td>41</td>
<td>3.7 (3.2–4.6)</td>
<td>3.5 (3.2–4.5)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>0.1 (0.1–3)</td>
<td>0.75</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>304–360</td>
<td>41</td>
<td>324 (253–450)</td>
<td>382 (322–429)</td>
<td></td>
<td></td>
<td></td>
<td>0.0036</td>
<td>60 (44–76)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.20–1.80</td>
<td>41</td>
<td>0.50 (0.30–0.70)</td>
<td>0.46 (0.30–0.68)</td>
<td></td>
<td></td>
<td></td>
<td>0.0020</td>
<td>0.04 (0.02–0.08)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Magnesium (mmol/L)</td>
<td>0.86–1.05</td>
<td>41</td>
<td>0.86 (0.76–1.05)</td>
<td>0.86 (0.76–1.05)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>0.00 (0.00–0.06)</td>
<td>0.12</td>
</tr>
<tr>
<td>Phosphates (mmol/L)</td>
<td>1.10–2.10</td>
<td>41</td>
<td>1.48 (0.85–2.41)</td>
<td>1.47 (0.84–2.38)</td>
<td></td>
<td></td>
<td></td>
<td>0.0018</td>
<td>0.01 (0.01–0.14)</td>
<td>0.30</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>1.7–20.1</td>
<td>41</td>
<td>6.0 (5.0–7.0)</td>
<td>6.0 (5.0–7.0)</td>
<td></td>
<td></td>
<td></td>
<td>0.0333</td>
<td>0.75</td>
<td>0.0001</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>100–200</td>
<td>41</td>
<td>124 (75.1–186.2)</td>
<td>121 (74.2–186.2)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
<td>2.7 (0.8–1.10)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>15–60</td>
<td>41</td>
<td>28 (15–40)</td>
<td>28 (15–40)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>0.0 (0.0–0.0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Alanine (µmol/L)</td>
<td>1.7–10.0</td>
<td>41</td>
<td>4.6 (3.0–6.0)</td>
<td>4.6 (3.0–6.0)</td>
<td></td>
<td></td>
<td></td>
<td>0.75</td>
<td>1.0 (0.4–0.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>100–700</td>
<td>41</td>
<td>102 (85–115)</td>
<td>102 (85–115)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
<td>0.1 (0.0–0.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CPK (µmol/L)</td>
<td>100–700</td>
<td>41</td>
<td>102 (85–115)</td>
<td>102 (85–115)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
<td>0.1 (0.0–0.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>3.5–6.5</td>
<td>41</td>
<td>5.1 (3.5–6.5)</td>
<td>5.1 (3.5–6.5)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>0.0 (0.0–0.0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Lipase (µmol/L)</td>
<td>0.10–0.5</td>
<td>41</td>
<td>0.20 (0.10–0.3)</td>
<td>0.20 (0.10–0.3)</td>
<td></td>
<td></td>
<td></td>
<td>0.0099</td>
<td>0.0 (0.0–0.0)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>27.0–39.0</td>
<td>41</td>
<td>32.5 (28.5–39.5)</td>
<td>31.7 (27.6–38.0)</td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
<td>0.1 (0.1–1.7)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*No. of cases

Table 3—Effects of an IV, low-dose ketamine-diazepam combination* used for short-duration CR on the results of coagulation testing in cats (n = 42).

<table>
<thead>
<tr>
<th>Analyte</th>
<th>RI</th>
<th>n</th>
<th>Before sedation</th>
<th>After sedation</th>
<th>P-value</th>
<th>Difference (after sedation minus before sedation)</th>
<th>Analytic difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin time (s)</td>
<td>9.8–12.4</td>
<td>42</td>
<td>10.7 (9.8–12.4)</td>
<td>10.8 (9.5–12.7)</td>
<td></td>
<td>0.0036</td>
<td>1 (0.4–0.6)</td>
</tr>
<tr>
<td>APTT (s)</td>
<td>12.8–20.3</td>
<td>39*</td>
<td>15.7 (10.5–21.6)</td>
<td>16.5 (13.5–23.2)</td>
<td></td>
<td>&lt; 0.0001</td>
<td>1.2 (1.7–5.8)</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>0.90–2.00</td>
<td>42</td>
<td>1.42 (0.99–2.36)</td>
<td>1.42 (0.96–2.95)</td>
<td></td>
<td>0.6383</td>
<td>—</td>
</tr>
<tr>
<td>Antithrombin (%)</td>
<td>100.0–156.0</td>
<td>42</td>
<td>135.1 (97.0–173.0)</td>
<td>132.0 (98.0–181.0)</td>
<td></td>
<td>0.5673</td>
<td>—</td>
</tr>
</tbody>
</table>

*No. of cases

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*See Table 1 for remainder of key.
Discussion

The IV, low-dose ketamine-diazepam combination used for short-duration CR in the present study may be suitable to assist physical restraint for blood sampling for assessment of hematologic, serum biochemical, and coagulation parameters in cats. The primary objective of this study was to determine whether the results of routine clinical pathology tests and their clinical interpretation could be changed by IV, low-dose KDCR in cats. Two issues needed to be addressed: first, to determine what a clinically relevant change was, and second, to compare our results with those in the literature.

Appraisal of a significant change in any clinical pathology result can, however, be difficult. In clinical settings, a relevant change would be one that would affect medical decision making. Unfortunately, such changes are largely assessed subjectively and their relevance may depend on the individual patient.

Thus, the first criterion used in the present study was statistical significance, which may have nothing to do with clinical relevance. Another arbitrary criterion is the analytic relevance of the differences observed; if the differences observed may result from the variability of the method, then they cannot be interpreted from a clinical point of view. As the analyses of all paired samples were performed in the same run, we used the 
\[(2.77 \times CV_{\text{repeat}} \times \text{mean})\]
limit for all analytes, according to the CVs determined previously, in accordance with published recommendations. Even this criterion is highly questionable, as the imprecision of methods involving modern analyzers and the corresponding analytic differences are very low. This meant that a large number of statistically significant differences and discrepancies between the measurements taken before and after sedation were found even though their amplitude was in fact very slight and in our opinion had no clinical relevance.

Use of the critical difference (ie, taking into account both analytic and intraindividual variability) would likely have been more adequate. However, to the best of our knowledge, critical differences have not been determined in cats, and when they have been determined in other animal species, the time between repeated sampling in the same animals ranged mostly from 1 day to 1 week. \(^{31-33}\) It can be estimated that the concentrations of most routine analytes are not expected to change notably over a very short period of time, such as with the few minutes’ delay in the present study. Even owing to pathological conditions, it is unlikely that results for any blood or plasma analyte value will change so abruptly. It is therefore also very unlikely that the inclusion of diseased subjects could have biased the results of this study. Moreover, assessment of effects of KDCR could be achieved only if observed over a wide range of values, justifying inclusion of diseased animals.

It has also been proposed that the relevance of the difference between 2 test results could be graded by comparison of the median value of the difference with the corresponding reference interval. Indeed, comparison of the median of the differences between the 2 samples for each variable with the measured values obtained in the present study indicated that the differences observed would not be likely to lead to misdiagnosis (Tables 1–3). Moreover, the median values of the differences and the maximal differences observed for RBC counts, PCV, and hemoglobin concentration in this study were equal to or lower than those observed and concluded to be of minor practical importance in a previous study \(^{28}\) in which 2 distinct sites for blood sampling in cats were compared.

Moreover, it cannot be established from the present study that the observed differences could be attributed to KDCR effects. For such a purpose, the order of the blood sampling runs should have been randomized, which was impossible. It may be that some of the effects observed in this study were the result of the first sampling process in the unsedated cats rather than those of KDCR alone.

One possible confounding factor was a stress-induced modification of some of the analytes measured. \(^{7,5}\) Indeed, it would have been interesting to clarify whether the cats in our study were stressed during the first blood sample procedure, as they were client-owned and mostly unfamiliar with blood sampling. However, stress cannot be easily assessed in cats, as it could be suspected both in individuals that are overtly aggressive and struggle during restraint and venipuncture as well as in those that are easily removed from the cage and do not resist the sampling process. \(^{29}\) We speculate, however, that stress was likely very limited, as hyperglycemia and lymphocytosis were observed in only 1 of 41 and 2 of 42 cats, respectively, following the first series of samples, and stress-induced hyperglycemia and lymphocytosis have both been reported in cats. \(^{30}\) Plasma glucose concentration and blood lymphocyte count were in fact 2 of the few analytes that showed no significant variation between the 2 series of samples.

Another effect that might have been expected in the present study was RBC loss and plasma volume disturbances from the repeated blood sampling. A total volume of 8 mL of blood was taken in the first series of samples. In a review of body fluids in cats and dogs, mean feline blood volumes ranged from 56.3 to 66.7 mL/kg. \(^{30}\) In the smallest of the cats, which weighed 3.5 kg, and using a mean value of 60 mL/kg, the total blood volume was approximately 200 mL, suggesting that < 5% of the total blood volume was taken or < 2 mL/kg. Parallel increase or decrease or stability of plasma albumin concentration and Hct was observed in cats after a 4 mL/kg blood withdrawal. \(^{31}\) This is in agreement with the results of the present study, in which total protein concentration, RBC, Hct, and hemoglobin concentration also showed parallel changes but mostly decreased in the second set of samples.

The vast majority of the results obtained in the control series of samples were within the feline reference intervals of the analytes measured. \(^{32,33}\) This could be expected, as most cats were clinically healthy. Moreover, when an animal has a disease, only some of the results among the large panel of analyses performed in this study would be altered by this disease. Therefore, although unlikely, a larger difference between the results obtained without or with KDCR in more severely diseased animals cannot be fully excluded.
In the few prior studies of cats, after SC injection of ketamine (15 mg/kg [6.8 mg/lb]) alone, a significant decrease in leukocyte count (mainly neutrophils) was observed within 15 minutes, whereas the Hct and protein concentration were not affected. After IM injection of ketamine (33 mg/kg [15 mg/lb]), the leukocyte count, Hct, RBC count, and hemoglobin concentration decreased significantly, whereas AST and ALT activities increased significantly during deep sedation. The rationale for these changes remained conjectural. Our results are in partial agreement with these 2 studies as WBCs and RBCs decreased after KDCR, even though the observed differences were not clinically relevant, but no effect was observed on ALT and AST activities. The origin of this discrepancy remains unknown, but higher drug concentrations and delayed analyses in the previous studies could account for these differences.

A secondary objective of the present study was to assess some practical aspects of the CR procedure elected. Ketamine-diazepam CR appeared very satisfactory; however, IV catheter placement could not be achieved in only 3 of 46 cats. Thus, it can be expected that some other CR strategy will need to be used in a few feline patients. In these cases, IM or SC administration of higher doses of ketamine could be considered with expected effects on blood analytes, plasma analytes, or both.

Other CR protocols can also be chosen, but unless they have been fully evaluated, it is impossible to foretell their influence on clinical pathology results. Duration of KDCR was confirmed to be short, lasting only a few minutes. Such rapid recovery is clearly a benefit, as it allows the veterinarian to return the cat home after only a brief period of monitoring. Some owners reported, however, that their cats appeared less active for up to 24 hours after KDCR. Although, it cannot be ascertained whether this was a consequence of KDCR alone or induced by other parts of the procedure. However, such a consequence should be anticipated in at least some individual patients and should be explained to cat owners when KDCR is planned. Very few other adverse effects were reported. Itching of the skin over the jugular veins was thought to be a consequence of clipping, of venipuncture, or, although not previously reported, of the anesthetic cream rather than KDCR. However, although exclusion criteria were defined only to specifically avoid blood volume depletion or risks associated with venipuncture, most cats included in the present study were healthy. Therefore, the good tolerance observed in our population cannot be extrapolated to disease conditions other than those we encountered.

The cats included in this study were selected to be representative of the feline population seen at the National Veterinary School of Toulouse Small Animal Veterinary Teaching Hospital. In particular, behavioral characteristics were not taken into account for the inclusion process. Nevertheless, when attempted, blood sampling without CR was successful in 42 of 43 cats. Moreover, no significant difference was observed in the duration of this blood sampling and the one performed on the same cats after KDCR. However, it should not be concluded from these data that CR is rarely required when blood sampling is to be performed in cats. Indeed, the dedicated and time-consuming conditions of the present study were specifically implemented to obtain as many blood samples from as many unsedated cats as possible for comparison. Although the extra measures provided for that purpose proved to be effective, it is the authors’ strong opinion that the conditions of our study were by far more propitious to feline blood sampling than those of everyday practice. Furthermore, it was clearly apparent that KDCR made this clinical procedure easier, as 0 of 42 blood samplings under KDCR versus 9 of 42 performed without KDCR were subjectively considered difficult by the operator.

References


