Comparison of pentobarbital alone and pentobarbital in combination with lidocaine for euthanasia of dogs

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Summary: Pentobarbital alone, pentobarbital plus 1% lidocaine solution, pentobarbital plus 2% lidocaine solution, and pentobarbital plus 3% lidocaine solution were each used to euthanize 6 dogs. For each dog, time between the beginning of injection of the euthanasia solution and each of the following events was recorded: collapse, onset of apnea, flat-line electrocardiogram, flat-line electroencephalogram, loss of palpebral heartbeat, and loss of palpable pulse. Any signs of pain or discomfort were also recorded.

There were no significant differences among groups except for time to flat-line electrocardiogram. Dogs euthanatized with pentobarbital alone had significantly longer times than did dogs euthanatized with pentobarbital in combination with any of the lidocaine concentrations. We concluded that pentobarbital in combination with lidocaine was a reasonable alternative to pentobarbital alone when euthanatizing dogs.

Intravenous injection of a barbiturate acid derivative is the preferred method of euthanasia of dogs and cats, and pentobarbital sodium is commonly used for this purpose. Disadvantages of this technique include the need for special forms when ordering barbiturates and for sufficient skills to complete an iv injection, the appearance of signs of pain and irritation if a perivascular injection is accidentally performed, and the terminal gasps that can occur several seconds to minutes after the onset of apnea. In addition, after brain death, electrical potentials can be recorded from the heart for prolonged times even though there is no cardiac output.

A combination of pentobarbital and a 2% solution of lidocaine hydrochloride to be used for euthanasia was commercially available for a brief time in the mid 1980s and is currently undergoing testing for FDA approval. Lidocaine has anesthetic and sedative activities when administered in low doses and may cause temporary loss of consciousness when given to human beings. Lidocaine, administered prior to iv administration of thiopental sodium, reduces the amount of thiobarbiturate needed to produce anesthesia in dogs. The purposes of the study reported here were to determine whether lidocaine was synergistic with pentobarbital when used to euthanatize dogs and to compare the results of euthanasia using pentobarbital alone with the results of euthanasia using pentobarbital in combination with 1%, 2%, and 3% solutions of lidocaine.

Materials and Methods

The protocol for this study was approved by the Michigan State University All University Committee on Animal Use and Care. Twenty-four clinically normal dogs (11 female and 13 male) weighing between 7.3 and 23.6 kg were allotted into 4 groups of 6 dogs each. All dogs were euthanatized with pentobarbital or with pentobarbital in combination with lidocaine, given iv. Group A dogs were euthanatized with pentobarbital alone (86 mg/kg of body weight), group B dogs with a combination of pentobarbital (86 mg/kg) and a 1% solution of lidocaine (2.2 mg/kg), group C dogs with a combination of pentobarbital (86 mg/kg) and a 2% solution of lidocaine (4.4 mg/kg), and group D dogs with a combination of pentobarbital (86 mg/kg) and a 3% solution of lidocaine (6.7 mg/kg). Solutions were administered through a 20-gauge catheter placed in a cephalic vein to ensure intravascular administration. An observer, blinded to the treatment, administered each euthanasia solution at a rate of 1 ml/s; dogs were euthanatized in random order.

For each dog, the time between the onset of injection and the following 6 variables was measured: head drop (collapse); onset of apnea; appearance of a flat line on an electroencephalogram (EEG) recorded from electrodes placed subcutan-
ously over the left parietal, right parietal, and occipital regions of the cranium; appearance of a flat line or ventricular fibrillation on a lead II electrocardiogram\(^b\) (ECG); loss of a palpable heartbeat as determined by palpation of the ventral portion of the thorax; and loss of a palpable femoral pulse. The ECG was monitored only for the first 10 minutes after the onset of injection. Any signs of pain localized to the injection site or of systemic pain were recorded by the observer. The occurrence of terminal gasps, defined as exaggerated breathing attempts after the end of the last normal breath, was also recorded. Necropsies were completed on 4 of the dogs in group C. The Kruskal-Wallis rank test was used to test for differences among groups.\(^6\) The Mann-Whitney U test was used to compare the results of group A with the results of groups B, C, and D. A value of \(P < 0.05\) was considered significant.

**Results**

All dogs died after a single dose of each solution; none of the dogs developed ventricular fibrillation. Each dog in group A had electrocardiographic activity longer than 10 minutes after the onset of pentobarbital administration. During the study, 12 of the 24 dogs had activity longer than 10 minutes, and the probability that all 6 dogs in one or more treatment groups would have activity longer than 10 minutes was 0.02746. Therefore, we concluded that pentobarbital alone tended to induce electrocardiographic activity after death of longer duration than did any of the pentobarbital-lidocaine combinations. Times to collapse, apnea, flat-line EEG, loss of palpable heartbeat, and loss of palpable femoral pulse were not significantly different among groups (Table 1).

None of the dogs had signs of pain localized to the injection site. Three dogs (1 group-A dog and 2 group-D dogs) had signs of minor systemic pain. The proportion of dogs that had signs of pain was not significantly different among groups.

Responses that were not considered to be signs of pain or discomfort were recorded from a few dogs. Among group-A dogs (pentobarbital only), one had a deep sigh 10 seconds after the onset of injection, a second had leg movement (extension) until the onset of apnea and terminal gasps, and a third had a return of palpable heartbeat for approximately 1 minute. Among group-B dogs (pentobarbital plus 1% lidocaine solution), one had terminal gasps 91 and 108 seconds after the onset of injection. The dog was breathing rapidly after it collapsed, and a palpebral reflex could be elicited until breathing stopped (53 seconds). Electrical activity restarted in a second group-B dog 90 seconds after the onset of injection and continued another 25 minutes. Neither a femoral pulse nor a heartbeat could be palpated during this time, and the EEG was flat. Among group-C dogs (pentobarbital plus 2% lidocaine solution), one had a deep sigh 8 seconds after the onset of injection. Electrical activity of this dog's heart stopped and started 3 times before it stopped permanently. Neither a femoral pulse nor a heartbeat could be palpated during this time. Among group-D dogs (pentobarbital plus 3% lidocaine solution), one continued to breathe for 27 seconds after the heartbeat could no longer be palpated; a palpebral reflex could be elicited during this time. A second dog took a step backward on the table as the euthanasia solution took effect, and the dog passed a small amount of feces 7 minutes after the injection. A third dog had abdominal muscle fasciculations 108 seconds after the beginning of injection.

Postmortem examination of 4 dogs from group C revealed lesions consistent with hypoxia. Other gross or histologic lesions were not seen.

**Discussion**

A humane method of euthanasia would result in cortical depression (loss of consciousness) followed by apnea or cardiac arrest.\(^1\) All 4 methods used in this study satisfied this criterion. Dogs collapsed approximately 13 seconds after the beginning of injection. This roughly corresponds to the normal circulation time from the cephalic vein to the brain.\(^7\) Mean time to loss of brain function, as

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Pentobarbital alone</th>
<th>Pentobarbital plus 1% lidocaine solution</th>
<th>Pentobarbital plus 2% lidocaine solution</th>
<th>Pentobarbital plus 3% lidocaine solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to collapse</td>
<td>14 (2)</td>
<td>14 (4)</td>
<td>13 (2)</td>
<td>16 (2)</td>
</tr>
<tr>
<td>Apnea</td>
<td>25 (29)</td>
<td>18 (17)</td>
<td>13 (2)</td>
<td>21 (11)</td>
</tr>
<tr>
<td>Flat-line EEG</td>
<td>30 (4)</td>
<td>32 (11)</td>
<td>28 (13)</td>
<td>27 (4)</td>
</tr>
<tr>
<td>Flat-line ECG</td>
<td>600 (61)</td>
<td>409 (237)</td>
<td>540 (72)</td>
<td>302 (148)</td>
</tr>
<tr>
<td>Heartbeat</td>
<td>42 (59)</td>
<td>62 (52)</td>
<td>24 (13)</td>
<td>18 (3)</td>
</tr>
<tr>
<td>Pulse</td>
<td>24 (18)</td>
<td>28 (14)</td>
<td>17 (2)</td>
<td>16 (1)</td>
</tr>
</tbody>
</table>

*Collapse = time to collapse (head drop) of the dog; apnea = time to last normal breath; flat-line EEG = time to flat line on electroencephalogram; flat-line ECG = time to flat line on electrocardiogram or maximal recording time of 600 seconds; heartbeat = time to loss of palpable heartbeat as determined by palpation of ventral portion of thorax; and pulse = time to loss of palpable femoral pulse. \(^*\)Significantly different from other groups. For each group, \(n = 6\) dogs.

Values in parentheses are ns.
evidenced by a flat-line EEG, was between 27 and 32 seconds. This is similar to the results of euthanasia studies that measured time to flat-line EEG. Electrical activity could be recorded electrocardiographically long after the onset of apnea and a flat-line EEG; however, mechanical activity could not be palpated (electrical-mechanical dissociation). The addition of lidocaine to pentobarbital enhanced the depressant effects of pentobarbital on electrical activity in cardiac tissue. This synergism between lidocaine and pentobarbital has been reported elsewhere.\(^{10-13}\) Although pentobarbital plus 3% lidocaine solution tended to stop cardiac electrical activity fastest, this high a concentration of lidocaine may induce muscle fasciculations that could be disconcerting to observers.\(^{12}\) The muscle fasciculations seen in 1 group-D dog could have been a result of lidocaine toxicity. The dosages of lidocaine used in this study were less than the dosage (10 mg/kg) that has been reported to produce convulsions in awake dogs.\(^{14}\)

One of the undesirable results of euthanasia with pentobarbital alone is the occurrence of terminal gasps several seconds to minutes after the onset of apnea. This reflex, which is apparently a result of a disparity between the sensitivity of medullary respiratory centers to hypoxia and the sensitivity of the cerebral cortex, is upsetting to observers and pet owners attending the euthanasia. None of the dogs euthanatized with pentobarbital plus 2% lidocaine solution or with pentobarbital plus 3% lidocaine solution had terminal gasps. The terminal gasps observed in 1 dog euthanatized with pentobarbital alone and in 1 dog euthanatized with pentobarbital plus 1% lidocaine solution may indicate that low concentrations of lidocaine will not prevent terminal gasps. We believe that a lower percentage of dogs euthanatized with pentobarbital plus 2% lidocaine, compared with dogs euthanatized with pentobarbital alone, would have terminal gasps. In our (ATE, JM, JS) experience with 2,041 dogs euthanatized with pentobarbital plus 2% lidocaine, 6.7% had terminal gasps.

The lack of signs of pain localized to the injection site was not unexpected, because all euthanasia solutions were injected through an IV catheter, eliminating the possibility of perivascular injection. Signs of pain associated with IV and accidental subcutaneous injection of euthanasia solutions have been reported.\(^{15}\) Combining lidocaine with pentobarbital may decrease the irritation associated with perivascular injection of pentobarbital alone. This could be important in animal shelters where euthanasia is performed with needle puncture of veins, and the risk of perivascular injection would be greater than in this study. Another advantage of adding lidocaine to pentobarbital is that pentobarbital alone is a DEA class-II substance, but pentobarbital plus lidocaine is a class-III substance. Class-III substances are easier to obtain and require less documentation than do class-II substances. On the basis of the results of this study, there was no difference between the various lidocaine concentrations. However, 2% lidocaine solution has been studied extensively, is familiar to veterinarians as a local anesthetic, and has been proven to be clinically effective. In this study, 2% lidocaine solution appeared to be concentrated enough to enhance the effects of pentobarbital and reduce the prevalence of terminal gasps but dilute enough that it did not induce the adverse effects sometimes seen with higher concentrations.

**References**