Effects of Intravenous Lidocaine on Isoflurane Concentration, Physiological Parameters, Metabolic Parameters and Stress-related Hormones in Horses Undergoing Surgery

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With 2 figures and 3 tables

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Summary

Physiological parameters, metabolic parameters and stress-related hormones are evaluated in horses anaesthetized with isoflurane in oxygen combined with lidocaine intravenously. Two groups of horses anaesthetized with isoflurane (six horses in each group) were studied: a lidocaine group (IL), which received intravenous lidocaine and a control group (C), which received intravenous saline. Horses in both groups were premedicated with detomidine (IV), and anaesthesia was induced with midazolam-ketamine (IV). The lidocaine group received intravenous lidocaine as a loading dose of 2.5 mg kg⁻¹ at 15 min after induction of anaesthesia directly followed by a maintenance dosage of 50 μg kg⁻¹ min⁻¹, while the control group received saline (IV) following the same regime. End-tidal isoflurane and standard physiological parameters were measured. Blood was sampled for measurement of lidocaine, stress hormones and metabolic parameters. The end-tidal isoflurane concentration in the lidocaine group was 0.96 ± 0.06% versus 1.28 ± 0.06% (mean ± SD) in the control group, a significant ($P < 0.05$) reduction of 25%. No significant differences were found regarding stress-related hormones, metabolic and physiological parameters. This study suggests that the use of lidocaine to decrease the concentration of isoflurane to obtain a sufficient surgical anaesthesia has no subsequent effects on physiological and metabolic parameters or stress-related hormones.

Introduction

Lidocaine has traditionally been used as a local anaesthetic agent (Hall and Clarke 1991; Harkins et al., 1998) and for the treatment of premature ventricular contractions (Muir et al., 1995). Thereafter intravenously administered lidocaine may contribute to general anaesthesia and analgesia with minimal negative cardiovascular effects (Wood-Smith et al., 1975). Lidocaine is known to reduce the requirement for inhalation anaesthetics and analgesia with minimal negative cardiovascular effects (Wood-Smith et al., 1975). Lidocaine is known to reduce the requirement for inhalation anaesthetics and analgesia with minimal negative cardiovascular effects (Wood-Smith et al., 1975).

The anaesthetic effect of isoflurane is accompanied by a dose-related depression of the cardiovascular and respiratory function (Steffey and Howland, 1980; Thurmon et al., 1996) and little analgesic effect (Paddleford, 1991). By combining isoflurane with lidocaine, potentially less isoflurane will be needed, and therefore the negative effects of isoflurane on the cardiopulmonary system may be reduced.

Although no work has been reported on the effects of lidocaine on required isoflurane concentration in horses undergoing surgery, there is no evidence to suggest that the concentration of isoflurane would be effected differently by an infusion of lidocaine than halothane as was described by Doherty and Frazier (1998). The purpose of our study was to determine the effect of intravenous lidocaine infusion on required isoflurane concentration in horses (ASA class I or II) anaesthetized for elective surgery. Another objective was to determine plasma concentrations of cortisol, insulin, non-esterified fatty acids (NEFA) to assess stress response during isoflurane/lidocaine anaesthesia. Plasma lactate dehydrogenase (LDH), creatinine kinase (CK) and aspartate aminotransferase (ASAT) were measured to evaluate influence on procedure related muscle damage.

Materials and Methods

The study was approved by the Research Board and Clinical Committee of the Department of Equine Sciences of the Veterinary Faculty of Utrecht University.

Animals

The horses used for this study were randomly drawn from patients (ASA class I or II) referred to the Department of Equine Sciences of Utrecht University for elective surgery lasting at least 90 min. Six Dutch Warmblood geldings (group IL) aged 3–21 years (mean 8 years) and weighing 550–697 kg (mean 603 kg) were anaesthetized with the combination isoflurane/oxygen and lidocaine IV. Six Dutch Warmblood horses (three geldings and three mares) aged 2–13 years (mean 8 years) and weighing 550–697 kg (mean 605 kg) anaesthetized with isoflurane/oxygen were used as a control group (group C).

Study design

All horses had food but not water which was withheld for 6 h before pre-medication. Pre-medication in both groups was with detomidine (Domosedan®; Orion Corporation, Espoo, Finland) (0.01 mg kg⁻¹) intravenously. Once sedation had developed an 8 cm 12-G polytetrafluoroethylene catheter...
(Intraflon 2®; Vygon Nederland BV, Veenendaal, The Netherlands) was placed percutaneously into the left jugular vein by which midazolam (Midazolam 5 mg ml⁻¹; Apotheek Diergeenekunde, University of Utrecht, the Netherlands) (0.06 mg kg⁻¹) and ketamine (Narketan® 100 mg ml⁻¹; Chassot AG, Belp, Berne, Switzerland) (2.2 mg kg⁻¹) were administered to induce anaesthesia. When recumbent, the horses were oro-tracheally intubated and anaesthesia was maintained with isoflurane (Isoflo®; Schering-Plough, Essex Tierarznei, Munchen, Germany) in oxygen (4 l min⁻¹). Isoflurane was delivered by an out-of-circuit isoflurane vaporizer (Isoflurane Vapour 19.3®; Dräger, Lübeck, Germany). Ringer’s solution (6 ml kg⁻¹ h⁻¹) was administered intravenously throughout the procedure. ECG and pulse-oximetry (Pulse oximeter, Nellcor; Hewlett Packard, Bad Homburg, Germany) were recorded continuously during anaesthesia. An arterial catheter was placed percutaneously into the facial artery or lateral metatarsal artery for measurement of arterial blood pressure and blood sampling. Systolic, diastolic and mean blood pressures were monitored continuously using a multichannel recorder (Multichannel recorder; Hewlett Packard). Inspiratory and expiratory concentrations of isoflurane, carbon dioxide and oxygen as well as respiratory frequency were measured continuously using a methane-insensitive infrared gas analyser (Infra-red anaesthetic gas analyser; Bruel & Kjaer, Naerum, Denmark). Ventilation was controlled to maintain PaCO₂ between 38 and 42 mmHg. As soon as a surgical level of anaesthesia was achieved a loading dose of lidocaine (Lidocaine HCL 2%; Eurovet, Bladel, the Netherlands) (2.5 mg kg⁻¹) to group IL and an equal volume of saline to group C was administered intravenously over 10 min. A maintenance dose of lidocaine 50 μg kg⁻¹ min⁻¹ (IL) or an equal volume of normal saline (C) was then administered during 75 min using an automatic infusion pump (Graseby 3400 Anaesthesia Pump; Graseby Medical Ltd, Watford Hertz, UK). The dosages of lidocaine were adopted from Doherty and Frazier (1998). Meanwhile, the end-tidal isoflurane concentration and plasma decreases between the means of group IL and group C with regards to end-tidal isoflurane concentration, HR, MAP, arterial blood pH, end-tidal CO₂ concentration, PaCO₂, PaO₂, NEFA levels, cortisol levels, insulin levels, muscle enzymes at different time points were analysed using the independent t-test with variances assumed unequal. A paired t-test was used to compare time point means for all the parameters to baseline means. Pearson’s correlation test was used to compare the decrease in required isoflurane concentration and plasma lidocaine levels. Data are presented as mean ± SD. Differences were considered to be significant when P < 0.05.

Blood samples collected for lidocaine analysis were stored at −80°C. The samples were centrifuged and the plasma was analysed by a fluorescence polarization immunoassay technique using a TDx/TDXFlx kit (TDx®/TDXFlx Lidocaine assay; Abbot Laboratories, Abbot Park, IL 60064, USA).

Table 1. Schedule for blood sampling for different parameters

<table>
<thead>
<tr>
<th>Time</th>
<th>Parameter Type of blood Anticoagulant</th>
<th>Lidocaine Venous Lithium/heparin</th>
<th>Cortisol/Insulin Venous EDTA/K₃</th>
<th>Muscle enzymes Venous Lithium/heparin</th>
<th>NEFA Venous NaF/EDTA/K₃</th>
<th>pH/blood Arterial Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
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<td>T₃₆₀₀</td>
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<td>T₆₆₀₀</td>
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<td>T₈₄₀₀</td>
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<td>T₉₃₀₀</td>
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</tbody>
</table>

Baseline = before sedation, T₀ = time just after induction, T_end = end of anaesthesia, NEFA = non-esterified fatty acids, K₃ = Potassium, NaF = Sodium fluoride, *point at which blood sample was collected.
Results
The averaged end-tidal isoflurane concentration in group IL during lidocaine infusion was 0.96 ± 0.06 and 1.28 ± 0.06% (mean ± SD) during saline infusion in group C, accounting to a decrease of 25%. The difference between these two values is significant ($P < 0.05$). Plasma lidocaine concentration ranged from 0.03 to 4.23 μg ml$^{-1}$ (Fig. 2). There was a strong correlation ($P < 0.05$, $r = 0.766$) between the decrease in end-tidal concentration of isoflurane and plasma lidocaine concentration. No significant differences were observed between group IL and group C with regards to mean arterial pressure, end-tidal carbon dioxide, pH, PaO$_2$, PaCO$_2$, cortisol, NEFA, LDH, CK and ASAT. No significant differences were observed between group IL and group C with regard to insulin concentration, except at baseline reading, at 90 min of anaesthesia and at 30 min after end of anaesthesia. A detailed outline of the results is illustrated in Tables 2 and 3, Figs 1 and 2.

In group C, times to sternal recumbency and standing after termination of general anaesthesia were 11 ± 7 min and 15 ± 8 min, respectively. In group IL, times to sternal recumbency and standing after termination of general anaesthesia were 19 ± 9 and 27 ± 13 min, respectively. The difference in mean values of these times between the two groups was not statistically significant. Three of the horses in group C showed excitement during recovery from anaesthesia, while all the horses in group IL had incident-free recoveries.

The mean pre-operative temperature for both groups was 37°C, while the mean post-operative temperature for both groups was 36.7°C, and differences never exceeded 0.7°C.

Discussion
The significant reduction (25%) of required isoflurane concentration using 2.14–4.23 μg ml$^{-1}$ plasma lidocaine concentration compares well with results obtained on the effects of intravenous lidocaine on halothane requirements in ponies (Doherty and Frazier, 1998) in which halothane MAC was reduced by 20–70% in a lidocaine dose-dependent manner. Further studies are required to determine whether the dose-dependency observed in halothane studies also occurs with the lidocaine-isoflurane combination in horses. Studies in dogs have shown that intravenously administered lidocaine reduces halothane requirements by not more than 29% (Himes et al., 1977; Sasada and Smith 1997). It remains to be seen whether this ceiling effect also occurs with the lidocaine-isoflurane combination in horses.

There was a significant increase in heart rate over time compared with baseline values in group C and a steady heart rate in group IL. This suggests that intravenous lidocaine could have a stabilizing effect on heart rate. A significant increase in blood pressure from 45 min until end of anaesthesia compared with baseline values was observed in group IL only (Table 2). The increase in mean arterial blood pressure

Table 2. Data and independent t-test statistical analysis $P$-values of the parameters measured during period of anaesthesia in the control group and group IL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time</th>
<th>Baseline</th>
<th>0 min</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>75 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET ISO (vol %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td></td>
<td>1.3 ± 0.2</td>
<td>1.3 ± 0.1</td>
<td>1.3 ± 0.1</td>
<td>1.2 ± 0.1</td>
<td>1.3 ± 0.1</td>
<td>1.3 ± 0.1</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>NS</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td></td>
<td>1.3 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>1.0 ± 0.1*</td>
<td>0.9 ± 0.1*</td>
<td>0.9 ± 0.1*</td>
<td>0.9 ± 0.1*</td>
<td>0.9 ± 0.1*</td>
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<tr>
<td>Heart rate (bpm)</td>
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<tr>
<td>Control group</td>
<td></td>
<td>29 ± 3</td>
<td>32 ± 5</td>
<td>33 ± 3</td>
<td>35 ± 4*</td>
<td>36 ± 4*</td>
<td>36 ± 5</td>
<td>40 ± 3</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.022</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td></td>
<td>32 ± 5</td>
<td>31 ± 4</td>
<td>32 ± 4</td>
<td>31 ± 5</td>
<td>31 ± 5</td>
<td>29 ± 6</td>
<td>31 ± 5</td>
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<tr>
<td>MAP (mmHg)</td>
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<td></td>
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<tr>
<td>Control group</td>
<td></td>
<td>64 ± 16</td>
<td>69 ± 12</td>
<td>72 ± 9</td>
<td>72 ± 11</td>
<td>79 ± 14</td>
<td>86 ± 20</td>
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<tr>
<td>P-value</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.022</td>
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<tr>
<td>Lidocaine group</td>
<td></td>
<td>75 ± 9</td>
<td>70 ± 13</td>
<td>77 ± 16</td>
<td>87 ± 20*</td>
<td>94 ± 19*</td>
<td>99 ± 20*</td>
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<tr>
<td>ET CO$_2$ (% vol)</td>
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<td></td>
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<tr>
<td>Control group</td>
<td></td>
<td>5.5 ± 0.9</td>
<td>4.9 ± 0.3</td>
<td>5.4 ± 0.3</td>
<td>5.0 ± 0.3</td>
<td>5.1 ± 0.3</td>
<td>4.7 ± 0.5</td>
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<tr>
<td>P-value</td>
<td></td>
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<td>NS</td>
<td>NS</td>
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<td>NS</td>
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<tr>
<td>Lidocaine group</td>
<td></td>
<td>5.7 ± 1.1</td>
<td>5.6 ± 1.1</td>
<td>5.2 ± 0.9</td>
<td>5.5 ± 1.1</td>
<td>5.4 ± 0.9</td>
<td>5.3 ± 0.8</td>
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<tr>
<td>pCO$_2$ (mmHg)</td>
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<tr>
<td>Control group</td>
<td></td>
<td>45 ± 5.5</td>
<td>49 ± 2.3</td>
<td>47 ± 5.2</td>
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<tr>
<td>P-value</td>
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<td>NS</td>
<td>NS</td>
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<tr>
<td>Lidocaine group</td>
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<td>51 ± 7.3</td>
<td>51 ± 8.5</td>
<td>49 ± 7.4</td>
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</tr>
<tr>
<td>Control group</td>
<td></td>
<td>7.4 ± 0.03</td>
<td>7.4 ± 0.02</td>
<td>7.4 ± 0.02</td>
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<tr>
<td>P-value</td>
<td></td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Lidocaine group</td>
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<td>7.4 ± 0.05</td>
<td>7.4 ± 0.05</td>
<td>7.4 ± 0.04</td>
<td></td>
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</tr>
</tbody>
</table>

*Significantly different from time$_{0\text{min}}$ (immediately after induction) value or baseline (before pre-medication) for heart rate, NS = non-significant difference between control group and lidocaine group, ET ISO = end-tidal isoflurane concentration, MAP = mean arterial pressure, ET CO$_2$ = end-tidal carbon dioxide concentration, pO$_2$ = arterial blood oxygen partial pressure, pCO$_2$ = arterial carbon dioxide partial pressure. Values are expressed as mean ± SD.
Table 3. Data and independent t-test statistical analysis P-values of stress indicators in the group C and group IL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>0 min</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
<th>End</th>
<th>End + 30 min</th>
<th>End + 60 min</th>
<th>End + 3 h</th>
<th>End + 24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin (IU ml⁻¹)</strong></td>
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</tr>
<tr>
<td>Control group</td>
<td>9.4 ± 3</td>
<td>4.2 ± 3*</td>
<td>3.5 ± 1*</td>
<td>5.0 ± 3*</td>
<td>2.2 ± 0*</td>
<td>5.5 ± 5</td>
<td>11.8 ± 7</td>
<td>26.9 ± 23*</td>
<td>27.1 ± 16*</td>
<td>29.9 ± 22*</td>
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<tr>
<td>Lidocaine group</td>
<td>5.7 ± 3</td>
<td>2.8 ± 1</td>
<td>2.5 ± 1*</td>
<td>2.2 ± 0*</td>
<td>1.6 ± 0*</td>
<td>2.3 ± 1*</td>
<td>4.0 ± 2.6</td>
<td>8.1 ± 6</td>
<td>17.5 ± 8*</td>
<td>19.9 ± 1*</td>
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<td>P-value</td>
<td>0.049</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.049</td>
<td>NS</td>
<td>0.038</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td><strong>Cortisol (nmol ml⁻¹)</strong></td>
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</tr>
<tr>
<td>Control group</td>
<td>112 ± 43</td>
<td>114 ± 57</td>
<td>113 ± 55</td>
<td>122 ± 93</td>
<td>237 ± 29</td>
<td>188 ± 112</td>
<td>216 ± 94*</td>
<td>245 ± 68</td>
<td>203 ± 62</td>
<td>172 ± 67</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td>140 ± 38</td>
<td>144 ± 73</td>
<td>91 ± 33*</td>
<td>138 ± 74</td>
<td>307 ± 40*</td>
<td>228 ± 140</td>
<td>255 ± 90*</td>
<td>250 ± 80*</td>
<td>207 ± 73</td>
<td>161 ± 34</td>
</tr>
<tr>
<td>P-value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>NS</td>
<td>NS</td>
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<tr>
<td><strong>NEFA (mmol l⁻¹)</strong></td>
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<tr>
<td>Control group</td>
<td>0.3 ± 0.07</td>
<td>0.3 ± 0.1</td>
<td>0.4 ± 0.08</td>
<td>0.4 ± 0.17</td>
<td>0.2 ± 0.07</td>
<td>0.4 ± 0.25</td>
<td>0.2 ± 0.11</td>
<td>0.1 ± 0.14</td>
<td>0.2 ± 0.08</td>
<td>0.2 ± 0.11</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td>0.3 ± 0.2</td>
<td>0.3 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>0.2 ± 0.2</td>
<td>0.3 ± 0.21</td>
<td>0.22 ± 0.10</td>
<td>0.1 ± 0.05</td>
<td>NS</td>
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<tr>
<td>P-value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>NS</td>
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<tr>
<td><strong>LDH (U l⁻¹)</strong></td>
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<tr>
<td>Control group</td>
<td>512 ± 183</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>631 ± 225</td>
<td>651 ± 233*</td>
<td>527 ± 119</td>
<td>535 ± 158</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td>503 ± 128</td>
<td>NS</td>
<td>NS</td>
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<td>P-value</td>
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<td><strong>CK (IU l⁻¹)</strong></td>
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<tr>
<td>Control group</td>
<td>81 ± 27</td>
<td>113 ± 33</td>
<td>NS</td>
<td>351 ± 226*</td>
<td>214 ± 139*</td>
<td>250 ± 164</td>
<td>261 ± 142</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Lidocaine group</td>
<td>159 ± 38</td>
<td>186 ± 79</td>
<td>NS</td>
<td>178 ± 54</td>
<td>201 ± 70</td>
<td>184 ± 89</td>
<td>236 ± 99</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>P-value</td>
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*Significantly different from baseline (before pre-medication) value, NS = non-significant difference between control group and lidocaine group, End = termination of anaesthesia, NEFA = non-esterified fatty acids, LDH = lactate dehydrogenase, CK = creatinine kinase, ASAT = aspartate amino-transferase. Values are expressed as mean ± SD.
observed in lidocaine-treated horses could be due to an increase in systemic resistance caused by lidocaine (Sasada et al., 1997).

Toxic concentrations of lidocaine may result in paleness, restlessness, convulsions, respiratory failure and severe cardiovascular depression (Sasada et al., 1997). To prevent these effects, Doherty and Frazier (1998) suggested that the lidocaine loading dose for purposes of supplementing inhalation anaesthesia should be given over a period of about 15 min and the end-tidal anaesthetic concentration be reduced appropriately prior to lidocaine administration. In our study, the loading dose of lidocaine was administered over 10 min. No negative effects on the cardiovascular system, respiratory system or nervous system were observed during the period of anaesthesia or period of recovery from anaesthesia in lidocaine-treated horses in this study.

Seventy per cent of administered lidocaine is metabolized in the liver by N-dealkylation and hydrolysis (Wood-Smith et al., 1975). The metabolites of lidocaine metabolism in the horse include 3-hydroxyliodocaine, dimethylaniline, 4-hydroxydimethylaniline, monoethylglycinexylidine, 3-hydroxymonoethylglycinexylidine and glycinexylidine (Harksins et al., 1998). Some of these metabolites have been shown to share some of the pharmacological effects of lidocaine in guinea-pigs (Burney et al., 1974), dogs (Smith and Duce, 1971) and in rats (Blumer et al., 1973). The contribution of some of these metabolites to the reduction in isoflurane requirement is not known. Plasma concentrations of these metabolites in the horse could not be measured at the time of our study because no reliable technique was available. It is therefore impossible to draw any conclusions about the contribution of these metabolites to an analgesic effect, if any. In this study, plasma lidocaine concentration had almost returned to baseline levels within 3 h of termination of intravenous lidocaine infusion (Fig. 2). This observation agrees with an earlier observation (Doherty and Frazier, 1998) in which an elimination half-life of lidocaine of 120 min was observed. In the current study, two plasma lidocaine concentration peaks were observed (Fig. 2). The first plasma lidocaine concentration peak observed after 30 min of anaesthesia was from the bolus injection, while the second peak was observed at 90 min of anaesthesia. The pharmacokinetics and pharmacodynamics of lidocaine cannot be determined properly in this study, as a steady state of plasma lidocaine concentration was not achieved within the time the horses were in anaesthesia. Suggestions have been made to maintain the intravenous lidocaine for periods longer than the half-life of lidocaine (Doherty and Frazier, 1998) and to collect samples more frequently in order to be able to obtain quantitative information on the pharmacokinetics and pharmacodynamics of lidocaine in horses.

Stress response is non-specific, consisting of activation of the sympathoadrenal and corticomedullary systems. These responses include secretion of catecholamines (epinephrine and norepinephrine), adrenocorticotropic hormone (ACTH), cortisol, glucagon, cAMP, vasopressin, growth hormone, renin and a non-concomitant decrease in insulin (Benson et al., 2000). The results obtained for the levels of cortisol, NEFA and muscle enzymes in this study show no significance difference between the mean values of group C and group IL. This suggests that there is no difference with regard to stress levels between the two groups. There are two factors that could have influenced plasma insulin concentration in this study. First detomidine, which is known to decrease plasma insulin concentration (Brown et al., 1985) and secondly, stress response, which is characterized by production of catabolic hormones, such as cortisol, which have an anti-insulin effect. In our study, first there was a decrease in plasma insulin levels in both groups, and then there was an increase in plasma insulin concentration from the end of anaesthesia up to 24 h post-operatively. The decrease in plasma insulin concentration first noticed in both groups could have been due to the detomidine effect, while the increase later noticed after end of anaesthesia could be due to the reduced stress response post-surgery and the reduced detomidine effect. NEFA have become increasingly popular in evaluating stress response (Carrol et al., 1997). Low concentrations during anaesthesia have been documented in horses and are believed to be associated with less sympathetic tone and perhaps decreased fear and apprehension (Carrol et al., 1997). In the current study, no significant differences in NEFA concentration were found between group C and group IL. Horses may have increased ASAT and LDH values as a result of surgical trauma, hepatic injury or post-anaesthetic myopathy (Stockham, 1995). CK has a high specificity for muscle damage. The fact that no differences were found between the control group and the lidocaine group suggests that intravenous lidocaine has no significant impact with regards to muscle enzyme concentration. When compared with baseline values, a significant increase in LDH after 24 h from end of anaesthesia was observed in group C. A significant increase in CK after 3 and
of the metabolites of lidocaine.

The results of this study have shown that intravenously administered lidocaine at dosages already indicated reduces the amount of isoflurane used by 25%. Use of less isoflurane will reduce the occurrence of unwanted side-effects. Long-term exposure to volatile anaesthetics poses a significant health risk to personnel (Joubert, 1999). With use of less isoflurane, there is less exposure, and therefore reduced health risk to personnel. Volatile anaesthetics destroy the ozone layer and are classified as greenhouse gases. (Joubert, 1999).

We therefore conclude that, intravenous administration of lidocaine at 2.5 mg kg$^{-1}$ and 50 µg kg$^{-1}$ min$^{-1}$, loading and maintenance dosages, respectively, results to a 25% reduction in isoflurane requirement, without negative effects on the cardiovascular system. Further studies are required to determine the effects of intravenous lidocaine administration in endotoxemic horses and to determine the pharmacokinetics of the metabolites of lidocaine.

Acknowledgements

We would like to thank all staff members of the Department of Equine Sciences, Faculty of Veterinary Medicine, Utrecht University for their support, Dr Cas Kruitwagen of the Centre for Biostatistics, Utrecht University for statistical analysis of data and Prof. Dr J. Fink-Gremmels for analysing lidocaine data.

References