Comparative electrocardiographic studies, and differing effects of pentazocine on ECG, heart and respiratory rates in young sheep and goats

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Abstract

The effects of pentazocine on electrocardiogram (ECG) heart and respiratory rates were studied in young sheep and goats as a prelude to its clinical use as an opioid analgesic in the two species. The ECG was monitored by standard bipolar leads that provided discernible electrocardiographic features only in Lead I. Electrocardiograms of lambs differ significantly from those of kids with respect to QRS complex, P–R interval and T wave. Higher basal heart rate in lambs is apparently due to shorter P–R interval and shorter interval between successive cardiac cycles (p < 0.05). Pentazocine, 3 mg kg\(^{-1}\) i.m., appears safer for lambs than kids as it significantly decreased P–R interval, Q–T interval, cardiac cycle duration, interval between successive cardiac cycles, respiration rate, and increased heart rate in kids but not in lambs (p < 0.05). © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Electrocardiogram; Pentazocine; Sheep; Goat

1. Introduction

Electrocardiographic studies are infrequently reported (Unshelm et al., 1974; Smith, 1978; Razakhani and Ejtehadi, 1980; Nazki, 1984; Montoya and Ponce, 1986; Tovar et al., 1986a, b; 1987a, b). Report that compare ECG parameters in adult sheep and goats are rare (Lumb and Jones, 1984). The effects of pentazocine, a potent opioid analgesic with established pre-anæsthetic potential in veterinary practice (Lumb and Jones, 1984; Booth, 1988), on ECG parameters and respiratory and heart rates have not been reported in these species. Opiate receptor activity is known to regulate central neural control on cardiovascular functioning (Booth, 1988) and increased (sigma receptor mediated) or decreased (\(\mu\)-, \(\kappa\)- and \(\delta\)-receptor mediated) respiratory functioning (Tripathi, 1999). Pentazocine has partial agonistic activity on \(\mu\)- and \(\delta\)-opiate receptors and full agonistic activity on \(\kappa\) and \(\Sigma\)-opiate receptors (Ghosh, 1984; Tripathi, 1999) and has reportedly varying effects on cardio-pulmonary function in domestic animals and in humans (Kamerling et al., 1986; Booth, 1988; Tripathi, 1999). Pentazocine has overall many favourable
features for its clinical utility as a potent analgesic; easy availability in Indian market, higher analgesic potency than pethidine, lack of profound sedation in animals, minimal side-effects at analgesic dose rate and toxic effects appearing only at very high doses (Davis and Sturm, 1970; Lumb and Jones, 1984). Pentazocine is a valuable analgesic in domestic animals (Barragry, 1994). Accordingly, the present investigations aimed to compare ECG parameters, heart and respiration rates of lambs and kids in the presence and absence of pentazocine treatment.

2. Materials and methods

Apparently healthy Corriedale crossbred lambs and Alpine crossbred kids of either sex, 2–5 months old and 7–21 kg body weight were utilized. Each group contained six animals equally balanced with respect to sex and age group. The animals were maintained at Sheep Breeding Farm, Shuhama, Srinagar (J&K), situated at an altitude of 1586 m.

The ECG pattern was monitored with standard bipolar leads using the Einthoven’s triangle in the ventral plane with conscious standing animal. The leads were placed subcutaneously through hypodermic needles to provide the best electrical contact (Hecker, 1983), and were connected on to EKG coupler (Bio-Devices Physiograph, Ambala, India). Respiration rates were monitored either manually or by using a Respiration coupler (RT-411, Bio-Devices Physiograph, Ambala). Pentazocine lactate (Ranbaxy Laboratories, New Delhi, India) was reconstituted in normal saline and given at the dose rate of 3 mg salt per kg body weight intramuscularly. The drug shows rapid absorption from the site with peak plasma concentrations achieved at 15 min and has a \( t_{1/2} \) of 51 min in goats at the test dose rate (Davis and Sturm, 1970). Plasma drug concentrations within the half-life period of a drug are sufficient to maintain its pharmacodynamic profile. Therefore, the observations were made before (as control), and 20–30 min after pentazocine treatment. Intramuscular route is as good as intravenous one for use of pentazocine at equivalent dose range (0.4–2.0 mg per kg) to provide effective analgesia for 1–6 h in domestic animals (Gerring, 1983; Barragry, 1994).

The results obtained were analyzed statistically using Student’s \( t \)-test; unpaired \( t \)-test between control means of the two species, and paired \( t \)-test between means obtained before and following treatment within each species (Snedecor and Cochran, 1967).

3. Results and discussion

It is generally believed that the standard lead positions for humans are not applicable to sheep as the orientation of the sheep’s heart is different to that of man, and a number of modifications in placement of electrodes have been reported (Hecker, 1983). Present investigations employed human technique of Einthoven’s triangle in ventral plane quite successfully in both sheep and goats in their standing positions. It was observed that various components of an ideal electrocardiogram were quite discernible in Lead I compared to Leads II and III. Therefore, comparisons were based on Lead I electrocardiograms (Fig. 1, Table 1). Einthoven’s triangle in frontal plane has been successfully used to monitor ECG events in goats (Montoya and Ponce, 1986).

Electrocardiographic events in sheep are known to show age-related alterations (Tovar and Santisteban, 1987a, b). This information guided the use of similar age groups in the study to evaluate species-related alterations.

A comparative evaluation of various observed parameters in lambs and kids (Table 1 and Fig. 1) revealed a prominent T wave in kids with significantly higher amplitude (0.206 ± 0.03 mV, \( p < 0.01 \)) by 255% and longer duration (120 ± 5 ms) by 20% in comparison to corresponding values of amplitude (0.058 ± 0.012 mV) and duration (100 ± 7 ms) observed in lambs (\( p < 0.05 \)). The amplitude of QRS complex, 0.517 ± 0.086 mV, was higher by 93% (\( p < 0.01 \)) and its duration, 93 ± 7 ms, shorter by 15% (\( p < 0.05 \)) in kids compared to those of lambs. The P–R interval, 153 ± 4 ms as well as the interval between successive cardiac cycles, 280 ± 52 ms, were significantly longer in kids by 18 and 96%, respectively, compared to lambs (\( p < 0.05 \)). Other ECG events did not differ significantly in the two species. T wave prominence in kids signifies rapid and greater contraction of the basal part of ventricles and subsequently repolarization phenomena of the ventricles, as

The results obtained were analyzed statistically using Student’s \( t \)-test; unpaired \( t \)-test between control means of the two species, and paired \( t \)-test between means obtained before and following treatment within each species (Snedecor and Cochran, 1967).
Fig. 1. Electrocardiograms, Lead I, of a lamb (L) and a kid (K) before (C) and after pentazocine treatment, 3 mg kg\(^{-1}\) body weight i.m. (T) using Bio-Devices Physiograph, Ambala, India. Sensitivity 500 \(\mu\)V per 2 cm, and chart speed, 2.5 cm per second.

Table 1

A comparative EGG pattern in young sheep and goats, and effects of pentazocine lactate, 3 mg kg\(^{-1}\) i.m.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Lambs(^a)</th>
<th>Control</th>
<th>Treatment</th>
<th>Kids(^a)</th>
<th>Control</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P wave</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voltage (mV)</td>
<td>0.05 ± 0.007</td>
<td>0.045 ± 0.005</td>
<td>0.039 ± 0.005</td>
<td>0.036 ± 0.005</td>
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<tr>
<td>Duration (ms)</td>
<td>62 ± 7</td>
<td>60 ± 7</td>
<td>65 ± 3</td>
<td>58 ± 10</td>
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<td></td>
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<tr>
<td><strong>QRS complex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voltage (mV)</td>
<td>0.268 ± 0.090</td>
<td>0.385 ± 0.096</td>
<td>0.517** ± 0.086</td>
<td>0.717 ± 0.109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration (ms)</td>
<td>110 ± 3</td>
<td>107 ± 12</td>
<td>93** ± 7</td>
<td>78 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>T wave</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Voltage (mV)</td>
<td>0.058 ± 0.012</td>
<td>0.066 ± 0.012</td>
<td>0.206** ± 0.03</td>
<td>0.020 ± 0.023</td>
<td></td>
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</tr>
<tr>
<td>Duration (ms)</td>
<td>100 ± 7</td>
<td>83 ± 14</td>
<td>120** ± 5</td>
<td>107 ± 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-R interval (ms)</td>
<td>130 ± 8</td>
<td>143 ± 20</td>
<td>154** ± 4</td>
<td>130** ± 32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-T interval (ms)</td>
<td>197 ± 21</td>
<td>160 ± 31</td>
<td>220 ± 12</td>
<td>208 ± 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q-T interval (ms)</td>
<td>307 ± 14</td>
<td>267 ± 32</td>
<td>313 ± 13</td>
<td>287b* ± 18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac cycle durations (ms)</td>
<td>437 ± 18</td>
<td>410 ± 20</td>
<td>467 ± 12</td>
<td>417b* ± 18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval between cardiac cycles (ms)</td>
<td>143 ± 13</td>
<td>146 ± 19</td>
<td>280b* ± 52</td>
<td>198b* ± 44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (min(^{-1}))</td>
<td>105 ± 5</td>
<td>110 ± 6</td>
<td>83** ± 6</td>
<td>101b* ± 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiration rate (min(^{-1}))</td>
<td>57 ± 5</td>
<td>63 ± 7</td>
<td>45*** ± 4</td>
<td>31b* ± 2</td>
<td></td>
<td></td>
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</tbody>
</table>

\(^a\) Values are expressed as mean ± SE of six observations; 6 animals per group. Values followed by superscript letters 'a' and 'b' are significantly different from corresponding control values in lambs and corresponding pre-treatment value in kids, respectively.

\(^* p < 0.05; \quad ** p < 0.01; \quad *** p < 0.10.\)
compared to lambs. Ventricular depolarization in kids also appears to be greater in strength as evident from higher amplitude of ORS complex. In kids lower basal heart rate (83 ± 6 cycles per minute) as compared to that of lambs (105 ± 5 cycles per minute) is apparently due to increased P–R interval and increased interval between successive cardiac cycles in kids (Table 1). Heart rates of kids and lambs fall within the reported range of 60–135 cycles per minute in sheep and goats with younger animals having higher rates (Fraser, 1991). Respiration rates in lambs (57 ± 5 per minute) and kids (45 ± 4 per minute) in the present study are higher than the adult range of 12–25 per minute reported for sheep and goats (Hemingway and Hemingway, 1966; Miller and West, 1972). This is consistent with the fact that younger animals owing to higher surface area (or BMR) have higher respiration rates. Heart and respiration rates were significantly lower \( (p < 0.05 \text{ and } p < 0.10, \text{ respectively}) \) in kids as compared to those of lambs.

Effects of pentazocine on ECG, heart and respiration rates were evaluated as a prelude for its clinical utility in the test species. The drug is a potent analgesic with reported minimal cardiovascular and mild respiratory depressant actions in domestic animals (Lumb and Jones, 1984). It has been recommended as an effective analgesic for relief of severe pain in domestic animals (Gerring, 1983; Barragry, 1994). The intramuscular route is as effective as the intravenous route, and provides analgesia for at least 1 h. Besides practical convenience, intramuscularly administered pentazocine is rapidly absorbed in man (Resine and Pasternak, 1996) and some domestic species including goats (Davis and Sturm, 1970) with peak values achieved at 15 min. Pharmacokinetic data of pentazocine in sheep are not available. Therefore, data available with goats served as a guide for sheep. Its possible use in pre-anaesthetic medication entailed its evaluation of effects on ECG, heart and respiratory rates in the test species. The drug is known to affect respiration and heart rates in animals and humans varyingly (Ahlgren and Stephen, 1966; Perez and Matus, 1986; Resine and Pasternak, 1996).

Effects of pentazocine on observed parameters were marked in kids but not in lambs. The drug did not significantly alter any of the test parameters in lambs (Table 1). However, in kids pentazocine caused significant decrease in respiration rate by 31% and increase in heart rate by 22% \( (p < 0.05) \). There was significant decrease in P–R interval by 15%, Q–T interval by 8%, cardiac cycle duration by 11%, and interval between successive cardiac cycles by 29% \( (p < 0.05) \). Other ECG parameters in kids were not significantly affected by pentazocine. The drug-induced tachycardia in kids is apparently due to decrease in cardiac cycle duration and decreased interval between successive cardiac cycles; and decreased cardiac cycle duration is apparently mainly due to decreased P–R and Q–T intervals (Table 1). It appears conduction time for cardiac impulse is shortened both in auricles (P–R interval) as well as in ventricles (Q–T interval), and the heart more rapidly re-starts the cardiac cycle (shortened interval between cardiac cycles) under pentazocine treatment in kids than in lambs. This may reflect increased adrenergic activity on the heart under central opiate activity affected by pentazocine selectively in kids relative to lambs. Further studies are needed to evaluate the reasons. Pentazocine 5 mg kg\(^{-1}\) in dogs has depressed respiration rate (Ahlgren and Stephen, 1966) without affecting heart rate (Parez and Matus, 1986) while its analog ethyl ketazocine in horses at lower dose rate has failed to affect respiration or cardiac rates (Kamling et al., 1986). The effects of pentazocine in kids on heart and respiration rates in the present study are comparable to similar effects reported in humans (Resine and Pasternak, 1996; Tripathi, 1999).

The results indicate that the electrocardiograms of lambs and kids are comparable. Pentazocine may be a useful pre-anaesthetic analgesic in lambs but not in kids when electrocardiographic events are under considerations. Effects of the drug on respiration and heart rate also favour its use in lambs but not in kids.

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**References**


