Pharmacokinetical Study of Enrofloxacin in Sheep

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SUMMARY

Enrofloxacin was injected subcutaneously to five
sheep as a single dose of 5mg/kg b.w. Blood samples were
collected periodically over 24 hours period and analysed
by a microbiological method.

Results indicated that the peak plasma concentration
of 1.30 ± 0.09 ug/ml was achieved two hours after the
drug administration. The average biological elimination
half-life from plasma was 2.42 ± 0.27 hour, the apparent
volume of distribution was 2.00 ± 0.18 l/kg and clearance
of the drug was 9.80 ± 0.61 ml/kg/min.

INTRODUCTION

Enrofloxacin (Baytril)™ is a new antimicrobial agent
of the quinolone carboxylic acid derivative (4). Members
of this group has been known to act by impairing the
bacterial gyrase, an enzyme which play a role in the
replication of DNA (2).

Enrofloxacin was developed exclusively for use in
veterinary medicine for the treatment of infections
cased by gram(-) and gram (+) bacteria as well as
mycoplasma in various animal species (6). The drug can be
administered by parenteral and oral route. Tissue and
serum concentrations of enrofloxacin was determined in
different animal species after administration of the drug
orally and parenterally (7).

In our clinics this drug has been introduced
recently for the treatment of bacterial infections in
animals and poultry. Few studies in this department have
proved its clinical value in poultry (5). resistance to
enrofloxacin was clear specifically in vitro (1), therefore in the present study the levels of the drug and its attainable level duration in plasma was estimated in order to find the relation between the attainable level and the duration of activity of the drug against pathogenic bacteria.

MATERIALS AND METHODS

Five sheep clinically healthy of awasi breed aged 6-7 months weighing from 20 to 30 kg were used in this experiment. They were housed in concrete stalls, water, green and concentrate food were available ad libitum.

The sheep were injected enrofloxacin (Baytril® 2.5%, injection, Bayer, Leverkhausen) subcutaneously into the side of the neck at a single dose of 5 mg/kg body weight. Blood samples were withdrawn from a jugular vein by heparinized syringes before administration of the drug and after 0.5, 1, 2, 4, 6, 8, 12 and 24 hours of administration. Plasma was obtained by centrifugation of the samples and kept at -20°C until analysed by the method described by the Agricultural analytical Chemistry, Lilly Research Laboratories based on the microbiological method (3).

The concentration of the drug was calculated from semi-log plot and the pharmacokinetic parameters were calculated according to (8).

RESULTS

The concentrations of enrofloxacin in sheep plasma after S.C administration are presented in Table 1. Figure 1 shows the disappearance curve of the drug which is presented as means and standard errors of the mean.

The peak plasma concentration of enrofloxacin was achieved after 1-2 hours of its administration and ranged from 1.11-1.30 ug/ml, thereafter the concentrations were dropped. No antibacterial activity was detected in the samples after 24 hours of the drug administration.
Table 1: Plasma concentrations (μg/ml), biological half-life (t 1/2, h), apparent volume of distribution (Vd, 1/kg) and clearance (cl, ml/kg/min) of enrofloxacin in sheep following a single S.C. injection of 5 mg/kg b.w.

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Weight (Kg)</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>12</th>
<th>24</th>
<th>t1/2</th>
<th>Vd</th>
<th>cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>0.87</td>
<td>1.58</td>
<td>1.26</td>
<td>0.36</td>
<td>0.08</td>
<td>0.08</td>
<td>0.07</td>
<td>0.00</td>
<td>2.24</td>
<td>2.19</td>
<td>11.34</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>0.43</td>
<td>0.67</td>
<td>1.46</td>
<td>1.11</td>
<td>0.71</td>
<td>0.08</td>
<td>0.08</td>
<td>0.00</td>
<td>2.04</td>
<td>1.74</td>
<td>9.83</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>0.07</td>
<td>1.07</td>
<td>0.95</td>
<td>0.75</td>
<td>0.51</td>
<td>0.24</td>
<td>0.08</td>
<td>0.00</td>
<td>2.89</td>
<td>2.60</td>
<td>10.42</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>0.07</td>
<td>1.34</td>
<td>1.26</td>
<td>1.11</td>
<td>1.11</td>
<td>1.11</td>
<td>0.99</td>
<td>0.00</td>
<td>1.61</td>
<td>1.42</td>
<td>10.18</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>0.07</td>
<td>0.87</td>
<td>1.54</td>
<td>1.46</td>
<td>1.11</td>
<td>1.11</td>
<td>0.18</td>
<td>0.00</td>
<td>3.30</td>
<td>2.07</td>
<td>7.23</td>
</tr>
</tbody>
</table>

- **X**

  | 0.30 | 1.11 | 1.30 | 0.96 | 0.70 | 0.52 | 0.28 | 0.00 | 2.42 | 2.00 | 9.80 |

- **SE**

  | 0.14 | 0.14 | 0.09 | 0.16 | 0.17 | 0.21 | 0.15 | 0.00 | 0.27 | 0.18 | 0.61 |
Fig. 1. Blood disappearance curve of enrofloxacin (mean ± SE) in sheep following a single S.C injection of 5 mg/kg.
The calculated biological half-lives of elimination from plasma and the apparent volume of distribution and clearance of the drug are presented in Table 1.

**DISCUSSION**

The present study reveals that enrofloxacin is quickly absorbed when given subcutaneously. The maximum plasma concentration was reached 2 hours after the drug administration. These results are comparable to those observed in calves when the drug was administered at a rate of 2.5–5 mg/kg body weight (7) which also suggests a good absorption of the drug in this species.

The mean concentration attained after 12 hours of the drug administration (0.28±0.15 μg/ml) is higher than the minimum inhibitory concentration (MIC) for most clinically important infectious agents such as E.coli, Salmonella, Pasteurella, Klebsiella and Haemophilus that have MIC values ranged from 0.008–0.06 μg/ml (6). This mean that the drug offers an antibacterial activity for a period of at least 12 hours when given in such a dose.

The higher value of Vd in the present study indicates that enrofloxacin is distributed well to the infective tissues and control the infection. This result is in agreement with the finding of (7) who found that the concentration of enrofloxacin in the tissues of different animal species was higher than those in the serum.

The mean biological elimination half-life of the drug was (2.42±0.27 hours) which is relatively shorter than those in other domestic animals (7). This could be explained on the base of differences in the rate of metabolic degradation, however the value of t 1/2 of enrofloxacin in poultry was recorded to be in the range of 2–6 hours (7).

In conclusion, the dose of enrofloxacin used in the present study offer therapeutic concentration to most of
the sensitive micro-organism for at least 12 hours after its administration.

References


دراسة دوائية لعقار الأتروفلوكساسين في الاغنام

نجل عبد القادر محمد علي، ضياء جعفر خماس، علي عزيز الخياط،
فرع الإدوية والسموم، فرع التوليد والإمراض التناسلية،
كلية الطب البيطري، جامعة بغداد

الخلاصة

اعطي الأتروفلوكساسين حقناً تحت الجلد لخمسة اغنام كجرعة
منفردة وكمعدل جرعة قدرها 0.002 مل/كم² من وزن الجسم. قمت
بجمع نماذج دم بأوقات متساوية خلال 24 ساعة وتم تحليلها بطريقة
مايوكروميا بولوجيا.

اشتهر النتائج أن معدل تركيز العقار وقع 0.342+0.90، مايكروغرام/مل بلغ ذروته بعد ساعتين من الإعطاء.
وقد بلغ معدل عمر النصف ل اختفاء العقار في البلازما 47+27 ساعة وحجم الانتشار الظاهري بلغ 18+22، لتر/كم² وتلفية
العقار بلغ 0.89+11.80، مل/كم²/دقيقة.

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