Effect of endotoxin administration in pregnant camels

A.M. AL-Dughaym a, A.M. Homeida b,*

a Department of Microbiology and Parasitology, College of Veterinary Medicine and Animal Resources, Saudi Arabia
b Camel Research Centre, King Faisal University, Al-Ahsa 31982, P.O. Box 1757, Saudi Arabia

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Abstract
Intravenous administration of Escherichia coli endotoxin at a dose of 0.05 μg/kg body-weight to pregnant camels resulted in abortion. The injection of endotoxin caused significant increases in the plasma concentration of 13,14-dihydro-15-prostaglandin F2α, the metabolite of prostaglandin F2α (PG F2α) and cortisol and a significant decrease in the concentration of progesterone. It is suggested that endotoxin caused abortion in camels was a consequence of endotoxin induced PG F2α secretion resulting in luteal regression and decreased progesterone concentration.

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1. Introduction
Endotoxin or lipopolysaccharide (LPS), the component of Gram-negative bacteria, is a complex glycolipid that remains associated with the outer wall in living bacteria and released upon cell lysis or death of micro-organisms (Morrison and Ryan, 1987; Raetz, 1993). Binding of LPS to target cells in the body of the host initiates a series of signal transduction events that culminate in the release of numerous biochemical mediators including cytokines, thromboxane, prostaglandins, leukotrienes and many others (Osln et al., 1995; AL-Dughaym and Homeida, 2008).

LPS has long been recognized as abortifacient agent (Zahl and Bjerknes, 1943; Giri et al., 1990). In the dromedary an abortion rate of up to 18% was reported (Agarwal et al., 1987; Enany et al., 1990). Suspected cause includes brucellosis and Bacillus cereus (AL-khalaf and El-Khaladi, 1989; Wernery, 1991). This study was conducted to investigate the possible effect of low dose of endotoxin administration in pregnant camels.

2. Materials and methods
Twenty camels comprising 10 early pregnant (1–2 months pregnancy), 5 mid-pregnant (7–8 months pregnancy) and 5 late pregnant female camels (10–11 months pregnancy) were used in this study. They were kept in an open pen in the vicinity of Camel Research Centre, at the College of Veterinary Medicine and Animal Resources, at King Faisal University in Al-Ahsa. Animals were fed on Rhodes grass hay while water was available ad libitum.

3. Endotoxin administration
Endotoxin lipopolysaccharide (Escherichia coli serotype 055:B5) was obtained from Sigma Chemicals, UK and
administered intravenously (AL-Dughaym, 2004). A dose of
0.1 g/kg bodyweight was considered lethal to the camel
(AL-Dughaym, 2004); therefore, a bolus of 0.05 g/kg body
weight was given to animals.

Animals were divided into 4 groups. Group 1 (1–2 months
pregnant) animals were injected I.V. with saline. Group 2 (1–
2 months pregnant), Group 3 (7–8 months pregnant) and
Group 4 (10–11 months pregnant) were injected with LPS.

4. Collection of blood samples

Blood samples were collected immediately after injection in
EDTA tubes. Plasma was then separated and at frequent inter-
vals stored at −30 °C until analyzed for hormones.

5. Analysis of hormones

The concentration of progesterone and prostaglandin F2α
metabolite, 13,14-dihydro-15-keto prostaglandin F2α (PGFM)
in the plasma were estimated by radioimmunoassay (RIA) as
previously described (Homeida and Klalafalla, 1987). The in-
tra- and inter-assay coefficients of variation were 4.5% (n = 10)
and 10.2% (n = 10), respectively for progesterone and
8.2% (n = 11) and 11.3% (n = 10), respectively for PGFM.
Assay sensitivity was 75 pg/ml for progesterone and 45 pg/ml
for PGFM. Plasma cortisol was determined with commercial
solid phase RIA kit (Coat A count, Diagnostic Product, Los
Angeles, USA) The intra- and inter-assay coefficients of varia-
tion were 8% (n = 9) and 9.6% (n = 10), respectively and as-
say sensitivity was 3 pg/ml (AL-Dughaym, 2004).

6. Statistical analysis

Data were expressed as means ± SD. Analysis of variance
(Anova) for repeated measures using general linear model
(GLM) procedure of the statistical analysis system (SAS)
was used to test the effect of endotoxin. Comparison of means
in different groups was made by Duncan’s multiple-range test.
P < 0.05 was accepted as statistically significant.

7. Results

All animals in Group 2 aborted within 3 days of LPS injection.
Animals in Groups 3 and 4 aborted on days 4 and 5 of LPS
injection. None of the animals in Group 1 (controls) aborted.

Concentrations of hormones are shown in Table 1. Rapid de-
crease in progesterone concentration was observed 4 h post-
injection (P < 0.05). Levels were <1 ng/ml 24 h post-injection
in Groups 2, 3 and 4.

The concentration of PGFM started to increase 30 min
post-injection (P < 0.05), rising to >1 ng/ml and remaining
high for 4 h, in Groups 2, 3 and 4.

Plasma cortisol concentrations began to increase 15 min
post-injection (P < 0.05). The level was significantly
(P < 0.05) higher for 2 h post-injection compared to controls.
Concentrations of hormones were not affected by injection of
saline in the control group.

8. Discussion

All animals aborted following endotoxin injection. Endotoxin
was previously shown to induce abortions in cows (Giri et al.,
1990; Foley et al., 1993), goats (Edqvist et al., 1984) and horses
(Duels et al., 1987). The dose of endotoxin used was 0.05 μg/
kg, far <0.5 μg Salmonella typhimurium LPS/kg used to in-
duce abortion in cows (Foley et al., 1993).

The significant rapid decrease in progesterone concentra-
tion would suggest luteal regression induced by endotoxin
prior to abortion. This is further substantiated by endotoxin
increasing the release of PGFM the metabolite of PGF2α, the

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Duration of pregnancy</th>
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<tbody>
<tr>
<td>Progesterone (ng/ml)</td>
<td>Group 1 (1–2 month control)</td>
</tr>
<tr>
<td>15 min (Post-injection)</td>
<td>4.2 ± 0.6</td>
</tr>
<tr>
<td>30 min (Post-injection)</td>
<td>4.3 ± 0.6</td>
</tr>
<tr>
<td>1 h (Post-injection)</td>
<td>4.1 ± 0.5</td>
</tr>
<tr>
<td>2 h (Post-injection)</td>
<td>4.2 ± 0.5</td>
</tr>
<tr>
<td>4 h (Post-injection)</td>
<td>4.0 ± 0.6</td>
</tr>
<tr>
<td>24 h (Post-injection)</td>
<td>4.3 ± 0.6</td>
</tr>
<tr>
<td>PGFM (pg/ml)</td>
<td></td>
</tr>
<tr>
<td>15 min (Post-injection)</td>
<td>120 ± 12</td>
</tr>
<tr>
<td>30 min (Post-injection)</td>
<td>105 ± 11</td>
</tr>
<tr>
<td>1 h (Post-injection)</td>
<td>110 ± 12</td>
</tr>
<tr>
<td>2 h (Post-injection)</td>
<td>95 ± 14</td>
</tr>
<tr>
<td>4 h (Post-injection)</td>
<td>115 ± 12</td>
</tr>
<tr>
<td>24 h (Post-injection)</td>
<td>122 ± 11</td>
</tr>
<tr>
<td>Cortisol (pg/ml)</td>
<td></td>
</tr>
<tr>
<td>15 min (Post-injection)</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>30 min (Post-injection)</td>
<td>12 ± 2</td>
</tr>
<tr>
<td>1 h (Post-injection)</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>2 h (Post-injection)</td>
<td>6 ± 2</td>
</tr>
<tr>
<td>24 h (Post-injection)</td>
<td>9 ± 2</td>
</tr>
</tbody>
</table>

PGFM = 13,14 dihydro-15-keto-prostaglandin F2α.

*P < 0.05, significantly different from controls.
uterine luteolysin (Horton and Poyser, 1976). Induction of abortion in female camelids is possible at any stage of pregnancy using PGF$_{2a}$ analogues (Jonson, 1989). Furthermore, endotoxin induced abortions in cows, goats and horses have been associated primarily with increased PGF$_{2a}$ production and luteolysis (Edqvist et al., 1984; Daels et al., 1987; Giri et al., 1990). However, luteal function does not appear to be adversely affected by endotoxaemia in rodents (Baines and Gendron, 1990).

Endotoxin may produce direct effects on the foetus. Placental haemorrhage and teratogenicity have been associated with endotoxin induced abortion in laboratory animals. However, in mammals like human endotoxin failed to cross chorioamnionic membranes (Romero et al., 1987).

The sudden rise in plasma cortisol as a response to endotoxin injection is similar to that observed in previous reports (AL-Dughaym, 2004; AL-Dughaym and Homeida, 2008). The stress of endotoxaemia in camels is responsible for the observed increases (AL-Dughaym, 2004). Increased secretion of cortisol has been associated with parturition in the camel.

In conclusion, it seems likely that endotoxin induced abortion in camels is via PGF$_{2a}$ causing luteal regression.

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References


