Effects of varying the progesterone content of CIDR intravaginal devices and multiple CIDR treatments on plasma hormone concentrations and residual hormone content

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ABSTRACT

Two trials were conducted to study factors which influenced the amount of progesterone (P4) remaining in a CIDR intravaginal device used for a treatment period of 15 days and the associated plasma P4 concentrations. In the first trial, the initial P4 content of these devices was varied from 0 to 2.67 g P4. In the second trial, animals were treated with either one or three devices which had been moulded to contain the same amount of P4 (1.9g/device).

Increasing the initial P4 content of a device increased plasma P4 concentrations, but at a diminishing rate so that devices containing 1.86 g P4 maintained similar levels of plasma P4 to devices containing 2.67 g P4 (2.48 vs 2.63 ng/ml). This was associated with a quadratic relationship in the residual P4 content in the used devices. Using three devices per animal trebled plasma P4 concentrations and did not alter residual P4 content.

These results indicated that P4 release is influenced more by device characteristics than by animal variation.

Keywords CIDR device; progesterone; plasma; intravaginal; cattle

INTRODUCTION

CIDR intravaginal devices (Carter Holt Harvey, Hamilton, New Zealand) are routinely moulded at a high temperature to contain progesterone (P4) which represents a concentration of 10% (w/w) in the silcon elastomer mattrix which covers a nylon spine. This short communication describes trials in which the P4 concentration was varied from 3.3% to 13.3%, or animals were treated with 3 CIDR's simultaneously. The measured responses were plasma P4 concentrations during or at the end of a 15-day treatment period, and the residual P4 content of the used device.

MATERIAL AND METHODS

Trial 1

Five forms of the CIDR device were moulded to contain 0, 0.63, 1.25, 1.9 or 2.53g P4/device representing P4 concentrations (w/w) of 0, 3.3, 6.6, 10 and 13.3% respectively. Twenty of each form of device were inserted into cycling American Holstein-Friesian heifers when 10 of the heifers were at cycle day 7 (oestrus = day 0) and 10 at cycle day 17. The 100 heifers were blood sampled before, during and after a 15-day treatment period, and the blood plasma assayed for P4 (ng/ml) by radioimmunoassay. After a CIDR had been withdrawn, it was washed in cold water, air dried and autoclaved before being returned to Ruakura. The elastomer skin from each of ten of the used CIDR's from each of the five forms was removed from the spine, diced and then immersed in ethanol in a soxhlet extraction unit. The amount of extracted P4 was measured by UV absorbance. This extraction procedure is routinely used for the quality assurance testing of freshly moulded devices.

Trial 2

Six non-lactating parous Friesian cows had either one or three CIDR's inserted into the vagina at mid-cycle for a treatment period of 15 days. A luteolytic dose of prostaglandin $F_{2\alpha}$ (5 ml Lutalyse; Upjohn NZ) was injected at CIDR insertion. Each CIDR was moulded to contain 1.9 g P4/device. The animals were blood

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sampled before and during treatment and the plasma assayed for P4 by radioimmunoassay. The residual P4 was extracted from each device.

RESULTS AND DISCUSSION

The placebo devices inserted into heifers in late dioestrus in Trial 1 did not prevent luteolysis, oestrus, ovulation and *corpus luteum* formation. This meant these heifers had normal dioestrous concentrations of plasma P4 at device removal (8.43 ng/ml; Table 1).

TABLE 1 Initial and residual progesterone content (g P4/device) of CIDR's and plasma P4 concentrations at device removal after a 15 day treatment (Trial 1).

CIDR Form	P4 content (g) Initial	Residual	Plasma P4 (ng/ml)
A	0	0	8.43
B	0.69	0.07	0.80
C	1.25	0.31	1.62
D	1.86	0.80	2.48
E	2.67	1.39	2.63

The quadratic relationship meant that devices containing 0.69 or 1.25 g P4/device maintained plasma P4 concentrations which were significantly less at device removal than devices containing 1.86 or 2.53 g P4 (0.80 and 1.62 vs 2.48 and 2.63 ng/ml). The latter two concentrations did not differ significantly, indicating a plateauing in the release or absorbance of P4 from devices containing at least 1.86 g P4.

The equation describing the relationship between the initial (IP) and residual (RP) content of the devices as g P4 per device was:

$$RP = -0.02 + 0.07\ IP + 0.18\ IP^2\ (R^2 = 0.95).$$

It showed that the amount of P4 lost from a device is described by a precise quadratic equation primarily influenced by initial P4 content.

In Trial 2, the insertion of three devices trebled average plasma P4 concentrations from treatment days 4 to 14 (8.4 vs 2.8 ng P4/ml; $P<0.01$, Table 2).

TABLE 2 Plasma progesterone concentrations (ng P4/ml) and residual P4 content of devices in cows treated with one or three CIDR devices for 15 days.

Treat. day	Plasma P4 (ng/ml) 3 dev./anim.	1 dev./anim.	Ratio 3 vs 1
4	13.2	4.1	3.2
8	7.9	2.8	2.8
11	6.2	2.3	2.7
14	6.4	1.9	3.4
4-14	8.4	2.8	3.0
Residual P4[a]	1.07	1.07	1.0

[a] g of P4 per used device

Since the average residual P4 content of the used CIDR's was not affected by how many devices were inserted into an individual animal (1.07 vs 1.07g P4; Table 2), it is apparent that the cows which were treated with three devices absorbed three times as much P4 as contemporaries treated with a single device.

The results of these two trials showed that the release of P4 from a CIDR device is a biophysical process which is controlled by P4 content and concentration in the silicon elastomer to a greater extent than possible variation between animals in their capacity to absorb the released P4.