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Brief Communication

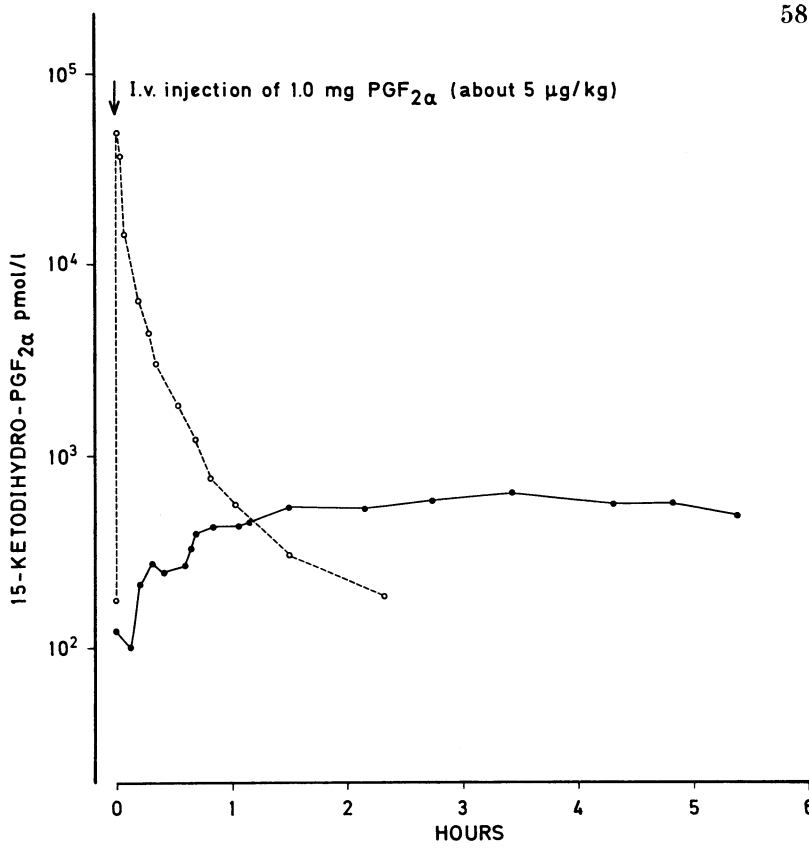
A TISSUE CAGE MODEL FOR THE STUDY OF PROSTAGLANDIN KINETICS IN CATTLE

Tissue cages have been used to study the composition of interstitial fluid in various species (*Guyton* 1963), *Bengtsson et al.* 1984). The analysis of tissue cage fluid (TCF) is an approach to study the pharmacokinetics of various drugs in interstial fluid. The cage has also been used for the study of local inflammatory reactions including analyses of primary prostaglandins (*Higgins & Lees* 1984). The metabolism of prostaglandins released in the whole body circulation is very rapid and to study this release suitable parameters and optimal sample frequencies have to be found (*Granström & Kindahl* 1982a). The aim of this investigation was to study the appearance and disappearance of 15-keto-dihydro-$PGF_{2\alpha}$, the main initial metabolite in blood of $PGF_{2\alpha}$, in the TCF.

The tissue cages were made of silastic rubber tubing sealed at both ends with silicone rubber plugs. The length of the tube was about 100 mm and with an inner diameter of 15 mm. About 80 holes were punched out in each end of the tube leaving 40 mm in the middle of the cage unperforated. The cages were surgically implanted subcutaneously in the neck and flank areas in two calves of the Swedish Red and White breed. The animals had been used in earlier pharmacokinetical experiments and at the time of this study the cages have been inserted for about 30 weeks. The weight of the animals were about 200 kg. A full description of the cages was given by *Bengtsson et al.* (1984).

Prostaglandin $F_{2\alpha}$, 1.0 mg, was dissolved in physiological saline solutions and injected intravenously (animal A) or intramuscularly (animal B) at time zero. Repeated TCF samples were collected frequently from 1 neck and 1 flank cage (see Fig. 1).

Figure 1. Concentrations of 15-ketodihydro-$PGF_{2\alpha}$ in tissue cage fluid (TCF) (●——●) and jugular vein (O---O) after 1.0 mg $PGF_{2\alpha}$. The upper panel shows the results after intravenous injection of $PGF_{2\alpha}$ (animal A) and the lower panel after intramuscular injection (animal B). Note the logarithmic scale on the Y-axis.


I.v. injection of 1.0 mg PGF2α (about 5 µg/kg)
15-KETODIHYDRO-PGF2α pmol/l
10⁵
10⁴
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10²
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3
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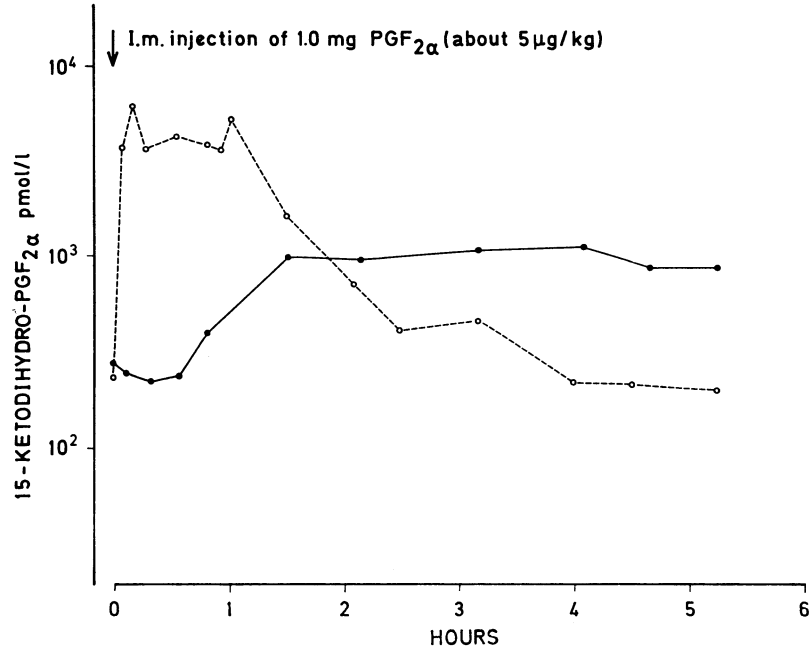
HOURS


I.m. injection of 1.0 mg PGF2α (about 5µg/kg)
15-KETODIHYDRO-PGF2α pmol/l
10⁴
10³
10²
0
1
2
3
4
5
6
HOURS

At each occasion 0.5 ml sample was collected. Frequent blood samples were collected from the jugular vein in heparinized Vacutainer tubes. Plasma was immediately isolated after centrifugation and plasma or TCF were kept frozen until analysis. The samples were analyzed for the content of 15-ketodihydro-$PGF_{2\alpha}$ with a radioimmunoassay technique according to the method of *Granström & Kindahl* (1982b).

The appearance of the prostaglandin metabolite in blood was very rapid after intravenous injection. About 50 nmol/l was recorded 1 min after injection. The concentration decreased rapidly to pretreatment values about 2 h after injection. A less dramatic rise was found after intramuscular injection with a plateau about 4 nmol/l during the first hour after injection and then a slow return to pretreatment values at about 3—4 h after injection.

In both animals the content of the prostaglandin metabolite in TCF before injection was of the same order as in the plasma. After injection, however, the appearance of the metabolite was rather slow. In the case of intravenous injection an increased concentration was seen about 10 min after the injection. After intramuscular injection the first increase was seen at about 40 min. In both animals the prostaglandin metabolite concentration increased to a plateau at about 1½ h and was maintained until the end of the experiment 6 h after injection. The plateau values were 600 pmol/l and 1000 pmol/l, respectively, in the 2 animals. A comparison between the plateau and pretreatment values in TCF shows a 4—5 fold increase after injection of 1.0 mg $PGF_{2\alpha}$. No difference was seen in the prostaglandin metabolite concentrations between neck and flank cages and the data presented in Fig. 1 for TCF values are a combination of all samples.

In studies of prostaglandin release in domestic animals, e.g. luteolysis or parturition several approaches can be done. The most accurate picture is obtained by analyzing 15-ketodihydro-$PGF_{2\alpha}$ in blood with very frequent sampling. For long-term studies alternative approaches are to follow changes in 11-keto-tetranor PGF metabolites in blood or urine (*Granström & Kindahl* 1982a, *Harvey et al.* 1984). These metabolites are more long-lived in the circulation than the initial 15-ketodihydro-$PGF_{2\alpha}$. Further studies are needed to evaluate the endogenous variation of prostaglandin release as reflected in the TCF.

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