CLINICAL PHARMACOLOGY OF A NEW PGF2α ANALOG (ALFAPROSTOL) IN PIGS AS COMPARED WITH CATTLE

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The prostaglandins most widely used in animal husbandry and veterinary medicine are unquestionably the F2α . These have clear luteolytic action in some animals of interest to breeders (Cooper and Furr 1974, McCraken et al.1981). In swine, these compounds are mainly used to induce and synchronize parturition (Dhiel et al., 1974) and the practice is linked to some preventive effect on MMA (Einarsson et al., 1975).

During tests of induction of parturition in sows using a new PGF2α analogue (alfaprostol), we noted a certain sedative effect in addition to the specific inducive action.

The PGF2α compounds are known, besides their luteolytic action, to have other effects on various organs and systems (Wolfe & Coceani 1979, Strandberg 1981) such as the respiratory and circulatory systems, and antagonist effects depending on the type of prostaglandins.

We therefore deemed it worth investigating further the possibility of this new analogue having other activities and focussed on the cardio-respiratory system and basal temperature, keeping records of any other objective clinical signs.

A group of 35 young sows (80-100 kg) (L X LW) was used, and the finding were compared with those in 20 non-pregnant Italian Friesian cows (500-600 kg). These animals were given high i.m. doses of alfaprostol bearing in mind that optimal luteolytic doses are 1.5 mg/100 kg live weight for cows and 2 mg/animal for swine.The concentration of alfaprostol is 1 mg/1 ml of Prop. glyc.). The sows were divided into 7 groups of 5,and given 6, 12 or 21 mg i.m. of alfaprostol, 6, 12 or 21 ml i.m., of propylene glycol alone, or 12 mg of alfaprostol to a group pretreated with 4 mg/100 kg b.w. of atropine. The cows were divided into 4 groups of 5 and injected with 16 and 45 mg/animal i.m. of alfaprostol, or 16 and 45 ml/ animal i.m. of propylene glycol.

The animals were checked for clinical good health, caged individually, and the following records were kept: a) heart examination using a Cardioline electrocardiograph; b) respiratory pattern; c) rectal temperature profile.

RESULTS

After doses from 3-10 times the therapeutic level, the treated sows' heart rate was reduced, as shown by the ECG tracings; these values returned to normal by 120 min. after treatment, with no further alterations to the ECG record. Propylene glycol alone -- as reported by Gross et al. (1979) -- also induced a mild reduction in heart rate, but much less than the drug-induced bradycardia.

When 12 mg/animal was given to atropine pretreated sows no bradycardia was observed; this suggest the vagal nerve is involved in the slowing of the heart rate observed in the other groups.

The bradycardiac action of this new analogue can thus be compared with that in the dog, described by Dusting and Vane (1980), as regards the properties of PGI2 in inducing bradycardia through a vagal reflex. Triulzi et al. (1981) also reported that PGI2 had a vagal effect in swine.

In the cows we found no changes in the morphology of the ECG tracing, even though doses equivalent to 6 times the luteolytic level were given to these animals.

Only very large doses of alfaprostol raised the number of respirations in both species as already reported by Kadowitz et al. (1974) and Clement et al. (1979) for other types of PGF2α. There was, however, a difference in the onset of response, the pigs responding earlier than the cows.

Rectal temperature recorded immediately after drug administration and after propylene glycol remained constant in the pigs; at larger doses there was a slight rise in temperature starting around 30 min. in the cattle.

After administration of alfaprostol, especially at the high doses, the sows but not the cows showed a state of sedation lasting about an hour.

CONCLUSIONS

It is interesting that the compound causes bradycardia in sows but not in cattle. We found no signs of excitation (biting the cage bars, urination and defecation) such as those reported by Maffeo et al. (1977) using natural PGF2α, and Ash and Heap (1973) with analogues.

Selected references: Ash R.W. and Heap R.B., J. Agric. Sci. Comb. (1973) 81:365; Clement M.G., Maffeo G., Sacchi C., Aguggini G., Prostaglandin and Medicine (1979) 3:367; Cooper M.J. and Furr B.J., Vet. Rec. (1974) 94: 161; Diehl J.R., Godke R.A., Killian D.B., Day B.N., J. Animal Sci. (1974) 38 (6) : 1229; Dusting G.J. and Vane J.R., Supp. I Circ. Res. (1980) 46 (6) : 183; Einarsson J., Gustafsson B., Larsson R., Nord. Vet. Med. (1975) 27:429; Gross D.R., Kuzman J.V., Adams H.R., Am. J. Vet. Res. (1979) 40 (6) : 783; Kadowitz P.J., Joiner P.D., Hyman A. L., Proceedings of the Society for Exp. Biol. and Med. (1974) 145:53; Maffeo G., Socci A., Redaelli G., Casiraghi F., La Clinica Veterinaria (1977), 100, 780; McCraken J.A., Schzamm W., Barcikowski B., Wilson L. Jr., Acta Vet. Scand. (1981) suppl. 77:71; Strandberg K., Acta Vet. Scand. (1981) suppl. 77:39; Triulzi M.O., Clement M.G., Celsi A., Aguggini G., Prostaglandin and Medicine (1981) 7:281; Wolfe L.S. and Coceani F., Ann. Rev. Physiol. (1979) 41:669.