EFFECTS OF 1 α -OHD₃ INJECTION ON PLASMA CONCENTRATIONS OF 1,25-(OH)₂D, PTH AND CA IN HYPOCALCEMIC COWS

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Introduction

In the previous study, we carried out the injection of 1 α -hydroxyvitamin D₃(1 α -OHD₃) to compare its effects of on the plasma 1 α ,25-dihydroxyvitamin D(1,25-(OH)₂D) and calcium(Ca) concentrations in lactating cows, and suggested it to be appropriate for the prevention of the parturient hypocalcemia to inject 500 μ g of 1 α -OHD₃ intramuscularly within 2 to 5 days before parturition [6]. Bar et al. [1] injected 350 or 700 μ g of 1 α -OHD₃ to cows for 72 to 24 h before calving and reported that plasma 1,25-(OH)₂D concentration reached the peak at 24 to 48 h after injection and that plasma Ca concentration increased by 700 μ g 1 α -OHD₃ may be an effective prophylactic treatment against milk fever. However, it is difficult to predict exactly the time of parturition within 72 to 24 h before parturition. The purpose of the present study was, therefore, to investigate the effects of injection of 1 α -OHD₃ to cows within 24 h before parturition to make wide use of 1 α -OHD₃ injection for prophylactic treatment against milk fever.

Materials and Methods

Thirteen mature Jersey cows (4.2 average calvings) were divided into two groups, an untreated control (control group) consisting of 7 cows and a test group $(1 \alpha - OHD_3$ group) consisting of 6 cows. Each cow in the $1 \alpha - OHD_3$ group once received intramuscularly the injection of 500 μ g $1 \alpha - OHD_3$ (provided by Chugai Pharmaceutical, Co., Ltd.) at 28.5 to 11.5 h before parturition. Heparinized blood samples were obtained from the external jugular vein at 0800 h for 7 days before parturition and at 12, 24, 48, 72 h after parturition. Milk samples were taken from the mixture of a whole day milk every day for 4 days after parturition. The plasma concentration of $1,25-(OH)_2D$ was measured by a modified method of Lambert et al. [5]. The plasma PTH concentration was determined with a PTH radioimmunoassay kit (Commissarat L'enrgie Atomique). Plasma hydroxyproline(Hyp) was measured by the method of Jamall et al.

Results

The plasma 1,25-(OH)₂D concentration in the 1 α -OHD₃ group showed a tended to be higher than that in the control group at 12 h after parturition, but did not differ significantly from the latter (Fig.1). On the other hand, the plasma PTH concentration in the 1 α -OHD₃ group was significantly lower than that in the control group at 0, 24 and 48 h after parturition (Fig.2). The plasma Ca concentration in the 1 α -OHD₃ group was significantly higher than that in the control group at 0, 24 and 48 hrs after calving (Fig.3), while the plasma Pi concentration was significantly higher in the 1 α -OHD₃ group only at 48 h after calving (Fig.4). The plasma Hyp concentration (Fig.5) and the amounts of Ca and Pi in the milk did not differ significantly between both groups, respectively.



Fig. 1. Changes in plasma concentration of $1,25-(OH)_2D$ in control and 1 α -OHD₃ groups.





Fig. 2. Changes in plasma concentration of PTH in control and 1 α -OHD₃ groups.



Fig. 3. Changes in plasma concentration of Ca in control and 1 α -OHD₃ groups.



Fig. 4. Changes in plasma concentration of Pi in control and 1 α -OHD₃ groups.



Fig. 5. Changes in plasma concentration of Hyp in control and 1 α -OHD₃ groups.

Discussion

Bar et al. [1] injected 350 or 700 μ g of 1 α -OHD₃ intramuscularly to pregnant dry cows that had calved at 36 to 52 h before parturition, and reported that the plasma 1,25-(OH)₂D concentration of cows injected with 1 α -OHD₃ increased rapidly, and reached the peak at 24 to 48 h after parturition. In the present study, the plasma 1,25-(OH)₂D concentration in the 1 α -OHD₃ group showed the rapid increase at parturition(at 11.5 to 28.5 h after the injection), and reached the peak at 12 h after parturition. The pattern of increase of 1,25-(OH)₂D after 1 α -OHD₃ injection was almost similar to that reported by Bar et al., but the time of the peak after parturition was different between our and Bar's experiments [1]. This was thought to be caused by the difference in the injection time between 28.5 to 11.5 h before parturition in our experiment and 52 to 36 h before parturition in their experiment.

The hypocalcemia at parturition probably induced the secretion of PTH [4]. The high plasma PTH after parturition, together with the decrease in the plasma Ca, appear to account for the increased kidney production of $1,25-(OH)_2D$ and for its accumulation in the plasma. The present results indicate that a injection of 500 μ g 1 α -OHD₃ prevented the decrease of plasma Ca and increase of plasma PTH at parturition. The mechanism of the prevention of hypocalcemia associated with the high $1,25-(OH)_2D$ concentration may have resulted from increased intestinal Ca absorption, reduced Ca excretion by the kidney, and increased bone resorption [3]. Increased plasma Hyp is believed to be associated with bone resorption [2]. Injection of 1 α -OHD₃ did not cause significant changes in plasma Hyp and suggested that 1 α -OHD₃ increased plasma Ca and Pi through a mechanism other than increased bone resorption.

These findings suggest it to be appropriate for the prevention of the parturient hypocalcemia to inject 500 μ g of 1 α -OHD₃ intramuscularly at foreknowable time (for 0.5 to 1 day) of parturition before calving.

Summary

Thirteen mature cows (4.2 average calvings) were divided into two groups, a control group consisting of 7 cows and a 1 α -OHD₃ group consisting of 7 cows. Each cow in the 1 α -OHD₃ group once received intramuscularly the injection of 500 μ g 1 α -OHD₃ (provided by Chugai Pharmaceutical, Co., Ltd.) at 28.5 to 11.5 h before parturition. The plasma 1,25-(OH)₂D concentration in the 1 α -OHD₃ group tended to be higher than that in the control group. On the other hand, the plasma PTH concentration in the 1 α -OHD₃ group was significantly lower than that in the control group at 0, 24 and 48 h after injection. The plasma Ca concentration in the 1 α -OHD₃ group was significantly higher than that in the control group at 0, 24 and 48 h after calving, while the plasma Pi concentration was higher in the 1 α -OHD₃ group only at 48 h after calving. These findings suggest it to be appropriate for the prevention of the parturient hypocalcemia to inject 500 μ g of 1 α -OHD₃ intramuscularly at foreknowable time(for 0.5 to 1 day) of parturition before calving.

References

1. Bar, A., Perlman, R., Observation on the Use of 1 α -Hydroxyvitamin D₃ in the Prevention of Bovine Parturient Paresis. J Dairy Sci 68:1952-1958. 1985.

2. Black, H.E., Capen, G.G., Urinary and Plasma Hydroxyproline during Pregnancy, Parturition and Lactation in Cows with Parturient Hypocalcemia. Metabolism 20:337-344. 1971.

3. Goff, J.P., Reinhardt, T.A., Horst, R.L., Enzymes and Factors Controlling Vitamin D Metabolism and Action in Normal and Milk Fever Cows. J Dairy Sci. 74:4022-4032. 1991.

4. Hollis, B.W., Draper, H.H., Burton, J.H., Etches, R.J., A Hormonal Assessment of Bovine Parturient Paresis: Evidence for a Role of Oestrogen. J. Endocrinol. 88:161-171. 1981.

5. Lambert, P.W., Toft, D.O., Hodgson, S.F., Lindmark, E.A., Witrak, B.J., Roos, B.A., An Improved Method for the Measurement of $1,25-(OH)_2D_3$ in Human Plasma. Endocirne Res. Commun. 5:293-310. 1978.

6. Naito, Y., Sato, A., Sato, R., Taniguchi, K., Murakami, D., Effects of 1 α -Hydroxyvitamin D₃ Injection on Plasma 1 α ,25-Dihydroxyvitamin D Concentration in Lactating Cows. Jpn. J. Vet. Sci. 49:477-483. 1987.