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INFORMATION

Hokkaido University conferred the degree of Doctor of Philosophy (Ph.D) in Veterinary Medicine on December 25, 2006 to 2 recipients.

The titles of theses and other information are as follows :

Studies on the prevention of calf diarrhea

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Calf diarrhea is a complex disease involving several factors : infectious agents, immune status of the calf, and environmental stress. Despite improvements in the identification of the infectious agents, management practice, and treatment and prevention strategies, diarrhea remains the most common disease in calves, especially in Japanese Black. In this study, immunological feature of Japanese Black calves and dams, effects of passive immunity against bovine rotavirus (BRV) infection, and effects of bovine interferon- τ (boIFN- τ), for the control of calf diarrhea and in immunomodulation in calves were examined.

At first, the correlation between the concentrations of serum immunoglobulin (Ig) G1 derived from colostrum of dams of 90 Japanese Black calves at day 2 and the mortalities from diarrhea was examined. The percentages of calves with failure passive Ig transfer (FPT ; serum IgG1 concentration < 10.0 mg/ml) and mortalities from diarrhea were 15.6% and 28.6%, respectively. In Japanese Black calves, number of peripheral blood lymphocytes was not significantly increased within 4 weeks after birth, and number of lymphocytes and $\gamma\delta$ T cells of peripheral blood were significantly lower than in Holstein calves.

Effects of quality, quantity and timing of colostrum feeding on IgG1 transfer to Japanese Black calves were examined. The average yield of colostrum obtained from Japanese Black cows was less than that of Holstein cows, however, the concentration of IgG1 in the colostrum of Japanese Black cows was higher than that of Holstein cows. The average volume of colostrum which Japanese Black calves could suckle was 9.7% of the body weight, and the concentration of IgG1 in calf serum and absorption of IgG1 did not depend on the time of the first colostrum feeding during the first 6 hours after birth.

Next, the effects of maternal vaccine against newborn calf diarrhea in the field condition were evaluated to address the occurrence of calf diarrhea while calves received adequate colostrum. The commercial combined vaccine induced high titers of antibodies in the colostrum and sera of the vaccinated cows against BRV, bovine coronavirus, and K99 *Escherichia coli*, and enhanced the levels of passive immunity in calves. However, no differences were seen in the morbidity of diarrhea and BRV-associated diarrhea in the calves of the vaccinated and control cows.

In addition, the correlation between maternal antibodies in the sera of calves at 2

days old and protection against diarrhea caused by natural BRV infection was examined. Titers of BRV neutralizing antibodies in the sera of calves that developed diarrhea were significantly lower than those from calves that had no diarrhea. In the BRV-associated diarrheic calves, a positive correlation was found between the titers of BRV neutralizing antibodies and age on the onset of diarrhea. Negative correlations were shown between the titers of BRV neutralizing antibodies and, duration of the diarrhea, cumulative fecal scores and, duration of virus shedding. These results suggested that the titers of BRV neutralizing antibodies in serum could be an indicator of the protection from and the severity of the disease in a newborn calf.

Finally, the antiviral activities of boIFN- τ in-vitro and the effects of boIFN- τ for the immunomodulation in calves and the control of calf diarrhea were examined. In the in-vitro experiments, viral titers of BRV, bovine viral

diarrhea virus and bovine leukemia virus were decreased in boIFN- τ treated cells. Although a high dose of boIFN- τ (10^5 U/kg) was administered subcutaneously three times every 3 days, no adverse effects were observed and lymphocyte subsets did not change after stimulation with the vaccine. Moreover, newborn calves were given with a low dose of boIFN- τ (200 U/head) orally for 4 weeks, whereas diarrheic calves were given for 5 days. However, there was no effect seen on the duration of the diarrhea or in the daily weight gain. These results suggested that boIFN- τ may not be effective for the immunomodulation in calves or for the prevention of diarrhea.

Present experiments showed the effects of colostrum feeding, passive immunity and the possible effects of boIFN- τ for the protection of diarrhea in Japanese Black calves.

Original papers for this thesis appeared in part in *J. Vet. Med. Sci.*, 59 : 1023-1025 (1997), *J. Vet. Med. Sci.*, 62 : 219-221 (2000), *J. Vet. Med. Sci.*, 66 : 1161-1164 (2004) and *J. Vet. Med. Sci.*, 69 : 15-19 (2007)

Studies on the mechanism of Ca²⁺ signaling in rat and pig olfactory receptor neurons :
Effect of intensity of stimulation and involvement of T-type Ca²⁺ channels

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