Immunological Responses after Vaccination Pre- and Post-Surgery in dogs

Tadashi MIYAMOTO*, Yasuho TAURA, Satoshi UNE, Makoto YOSHITAKE, Sanenori NAKAMA, and Seiji WATANABE[1)]

Department of Veterinary Surgery, Faculty of Agriculture, Yamaguchi University, Yamaguchi 753 and [1)]Kyoritsu Shoji Co., Ltd., Chiyoda-ku, Tokyo 102, Japan

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ABSTRACT. The effects of several commercially available vaccinations pre- and post-surgery on immune responses by monitoring the blastogenic responses of lymphocytes and humoral antibody responses in dogs were examined. Twenty clinical patients presented for surgery were studied. Canine parvovirus (CPV) serum antibody titers increased by twofold or more in 17 of 20 dogs and many dogs had an increase by day 7. In 3 of 4 dogs moderate hemagglutination inhibition (HI) titers (128 to 256) at the time of vaccination increased by twofold or more. Canine distemper virus serum antibody titers in 4 of 8 dogs with HI titers (< or = 32) at the time of vaccination had increased by twofold or more. In the blastogenic responses of lymphocytes to Concanavalin A and phytohemagglutinin, most dogs responded with a slight decrease following vaccination, but no significant change was noted. No adverse reaction caused by vaccination was noted and comparatively good production of serum antibody titers (CPV especially) was seen. Vaccination pre- and post-surgery neither induce severe immunosuppression, nor potentiate the severity of concurrent disease, and did not cause inapparent infection to become clinically apparent.—KEY WORDS: blastogenic responses of lymphocyte, canine, serum antibody titer, surgery, vaccination.

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Many dogs are often not vaccinated due to unawareness of the importance of vaccination among dog owners. To prevent nosocominal infections, it is very important to know whether the dog was vaccinated or to be vaccinated at admission or pre- or post-surgery. Under normal conditions, recommended vaccinations confer sufficient immune response to protect the patient. Nevertheless, underlying health factors, such as concurrent drug administration, stress, and age, often depress immune response to the administered antigens or exacerbate occult disease [9]. Various immunologic assays have confirmed the induction of immunosuppression by general anesthetics and surgery [4, 6, 12, 15]. With increased susceptibility to infections caused by the stress due to admission, anesthesia and surgery, nonvaccinated dogs may succumb to certain viral infectious diseases. To prevent such nosocominal infections, the efficiency of the vaccination pre- and post-surgery in nonvaccinated dogs remained to be investigated. On the other hand, several studies have emphasized the induction of immunosuppression by modified live virus (MLV) vaccines [7, 8, 11, 16] and vaccination may be immunosuppressive resulting in increase in the severity of concurrent disease or potentiate clinical signs of latent infections [16]. In contrast, vaccination with a mixture of inactivated canine parvovirus (CPV), MLV canine distemper virus (CDV) and MLV canine adenovirus (CAV) 1 vaccines may act in an immunomodulative rather than an immunosuppressive fashion [14].

The present study was conducted to clarify the effects of commercially available vaccination pre- and post-surgery on immune responses by monitoring blastogenic responses of lymphocytes and humoral antibody responses in dogs.

* PRESENT ADDRESS: MIYAMOTO, T., Department of Veterinary Medicine, College of Agriculture, University of Osaka Prefecture, Sakai, Osaka 593, Japan.

MATERIALS AND METHODS

Animals: Twenty clinical patients presented to the surgery were used (Table 1). The general condition of these dogs was not very severe pre- and post-surgery. The age ranged from 0.5 to 14 years, except one in which the age was not known. The breeds of these dogs varied. Anesthesia, surgery and drug administration were also varied. Dogs had not been vaccinated at least within a year. Six nonvaccinated beagles (dogs Nos. 21 to 26) aged from 1 to 5 years were used as controls (anesthesia, surgery, and drug administration were not done).

Vaccination: The vaccines used in this study were an inactivated CPV vaccine (DohyvacP®, Solvay Duphar, Weesp, Holland), a mixture of inactivated CPV, MLV CDV, and MLV CAV 1 vaccines (DohyvacDHP®, Solvay Duphar), a mixture of inactivated CPV, MLV CDV, MLV CAV 1, and two serovars of inactivated leptospira vaccines (DohyvacDHLP®, Solvay Duphar), and a mixture of MLV CPV, MLV CDV, MLV CAV 2, MLV canine parainfluenza, and two serovars of inactivated leptospira vaccines (Dohyvac7®, Solvay Duphar). All dogs received vaccines subcutaneously in a period from 10 days before to 3 days after surgery. The control dogs were subcutaneously administered with inactivated CPV, MLV CDV, and MLV CAV 1 vaccines (DohyvacDHP®).

Blood sampling: Blood samples were collected at 0, 3 to 7, and 14 to 28 days after the vaccination.

Serum antibody titers: CPV serum antibody titers were measured in all dogs on which operations were performed. The titers were assayed by the hemagglutination inhibition (HI) test [17]. The HI titer was recorded as the reciprocal of the highest dilution of serum showing complete

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Table 1. Summary of case histories of 20 dogs

Dog No.	Breed	Age (year)	Body weight(kg)	Surgery	Anesthesia[a)]	Day vaccinated from surgery	Vaccines[b)]
1	Mongrel	14	13.0	Repair of perineal hernia	K	1 day before	P
2	Shetland sheepdog	7	15.0	Tylectomy	K, L	the day	P
3	Mongrel	10	2.3	Repair of mandibular fractures	GOI	1 day after	DHP
4	Dachshund	6	10.5	Debridement	K	10 days before	DHP
5	Golden retriever	1	30.0	Arthrodesis	GOE	8 days before	DHP
6	Pomeranian	0.5	1.8	Repair of spinal fractures	GOI	the day	DHLP
7	Mongrel	0.5	4.6	Repair of spinal fractures	GOE	the day	DHLP
8	Shetland sheepdog	6	12.1	Ovariohysterectomy (pyometra)	GOI	the day	DHLP
9	Shetland sheepdog	3	9.5	Gastrotomy	GOE	the day	P
10	Borzoi	1	21.2	Repair of spinal fractures	GOE	the day	P
11	Mongrel	2	12.5	Cordectomy	GOI	10 days before	DHP
12	Beagle	6	18.7	Skin suture	GOE	6 days before	D7
13	Pomeranian	12	4.0	Tylectomy	L, K	the day	D7
14	Shetland sheepdog	4	15.0	Repair of spinal fractures	GOI	the day	DHP
15	German shepherd	5	27.0	Intestinal anastomosis	OE	2 days after	D7
16	Shetland sheepdog	8	11.0	Ovariohysterectomy (pyometra)	K	1 day before	DHP
17	Shiba	11	10.8	Repair of posterior cruciate ligament rupture	GOI	the day	DHP
18	Shetland sheepdog	1	8.0	Debridement	K	3 days after	P
19	Poodle	6	3.1	Repair of inguinal hernia	GOI	1 day after	DHLP
20	Mongrel	unknown	7.8	Ovariohysterectomy	GOI	the day	D7

a) Major anesthesia represented are: K, ketamine hydrochloride; G, laughing gas; O, oxygen; I, isoflurane; E, enflurane; L, lidocaine hydrochloride.
b) Kinds of vaccine.
P: DohyvacP, DHP: DohyvacDHP, DHLP: DohyvacDHLP, D7: Dohyvac 7.

inhibition of hemagglutination.

CDV serum antibody titers were measured in nine dogs on which operations were performed. The titers were assayed by microneutralization (SN) test [1]. SN tests were performed on Vero cells and the SN titer was calculated as the reciprocal of the highest serum dilution that neutralized viral infection and induced cytopathic effects in 2 of 3 replicate cultures.

Blastogenic responses of lymphocytes: The blastogenic responses of lymphocytes were measured in nine dogs on which operations were performed. The procedure for determining the blastogenic responses of lymphocytes was a modification of previously described ethidium bromide fluorescence assays [5, 14]. Concanavalin A (ConA, Wako Pure Chemical Industries Ltd., Japan) and phytohemagglutinin-P (PHA, Difco Laboratories, Michigan, U.S.A.) were used as mitogens. The blastogenic responses of lymphocytes were expressed as a stimulation index (SI), which was defined as the ratio of experimental to control intensity. The following formula was used: % response of prevaccination = (SI value of after vaccination/SI value of prevaccination)× 100.

RESULTS

Clinical findings: No adverse reaction after vaccination, such as abnormal reaction on the site of administration, fever, depression, or anorexia was noted in any of the dogs.

Serum antibody titer assay after vaccination: The

Table 2. Changes in serum titers of antibody (HI titers) to canine parvovirus

Dog	Vaccination		
No.	Pre.	3 to 7 days	14 to 28 days
1	<8	8	8
2	<8	<8	512
3	<8	64	256
4	<8	32	256
5	8	16	512
6	<8	32	NT[a)]
7	<8	128	256
8	16	16	16
9	16	64	128
10	16	32	256
11	16	NT	2048
12	16	128	NT
13	16	256	128
14	32	128	128
15	32	32	128
16	64	NT	512
17	128	256	128
18	256	1024	8192
19	256	NT	2048
20	256	256	1024
21	<8	512	1024
22	<8	1024	4096
23	<8	64	256
24	8	1024	2048
25	16	16	128
26	16	4096	4096

a) NT: Not tested.

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Table 3. Changes in canine distemper serum antibody titers (SN titers)

Dog	Vaccination		
No.	Pre.	3 to 7 days	14 to 28 days
16	2	NT[a)]	4
20	<2	<2	<2
3	<2	<2	32
6	<2	32	NT
7	<2	<2	4096
8	16	8	8
13	16	64	32
17	32	32	32
11	1024	NT	2048
14	2048	4096	2048
21	<2	4	512
22	<2	<2	512
23	<2	<2	256
24	<2	8	512
25	<2	64	1024
26	<2	16	256

a) NT: Not tested.

Table 4. Changes in blastogenic responses of lymphocytes to Concanavalin A

Dog	Vaccination		
No.	Pre.	3 to 7 days	14 to 28 days
2	100.0[a)]	88.9	94.4
7	100.0	56.5	58.1
8	100.0	92.3	92.3
11	100.0	NT[b)]	80.0
13	100.0	NT	100.0
14	100.0	90.0	86.7
17	100.0	90.9	104.6
19	100.0	NT	123.1
20	100.0	140.9	130.3
21	100.0	87.6	85.3
22	100.0	119.6	103.6
23	100.0	60.6	86.3
24	100.0	133.6	112.1
25	100.0	110.7	100.0
26	100.0	45.7	82.3

a) SI values at the time of vaccination are represented as 100.0.
b) NT: Not tested.

changes in CPV serum antibody titers are shown in Table 2. CPV serum antibody titers increased by twofold or more in 17 of 20 dogs. Only 3 dogs (Nos. 1, 8 and 17) were not immunized; dog No. 17 had moderate HI titers (128) at the time of vaccination and dog No. 1 was 14 years old. HI titer increased by twofold or more in 9 of 14 dogs in 7 days. In three dogs (Nos. 18, 19 and 20) with moderate HI titers (128 to 256) at the time of vaccination there was a twofold or greater increase. The control dogs developed high titers of humoral antibody, and the HI titer increased by twofold or more in 5 of 6 dogs in 7 days.

The changes in CDV serum antibody titers are shown in Table 3. HI titers in 4 of 8 dogs (< or = 32) at the time of vaccination increased twofold or more. Two dogs (Nos. 11 and 14) with high HI titers, 1024 and 2048, respectively, at the time of vaccination responded with slightly increased titers. The control dogs developed high titers of humoral antibody, and half the dogs had a twofold or greater increase in 7 days.

Table 5. Changes in blastogenic responses of lymphocytes to phytohemagglutinin

Dog	Vaccination		
No.	Pre.	3 to 7 days	14 to 28 days
2	100.0[a)]	72.2	83.3
7	100.0	102.0	80.0
8	100.0	100.0	91.7
11	100.0	NT[b)]	86.1
13	100.0	NT	86.7
14	100.0	76.3	78.9
17	100.0	99.3	96.5
19	100.0	NT	86.7
20	100.0	116.7	108.3
21	100.0	78.1	90.3
22	100.0	134.6	118.1
23	100.0	81.6	94.8
24	100.0	120.2	120.2
25	100.0	138.6	122.3
26	100.0	46.2	77.7

a) SI values at the time of vaccination are represented as 100.0.
b) NT: Not tested.

Blastogenic responses of lymphocytes after vaccination: Changes in the blastogenic responses of lymphocytes to ConA and PHA are shown in Tables 4 and 5. Reductions in the responses to ConA were seen in 5 of 6 dogs tested on 3 to 7 days. Although a 50% reduction was seen in dog No. 7, the other 4 dogs responded with a slight decrease. Dog No. 20 responded with an increase of about 40%. The control dogs responded with an increase or decrease of up to about 40% in 28 days. Significant changes were not seen in two groups.

In the responses to PHA, 8 dogs except No. 20, responded with a decrease in 14 to 28 days but the rate of decrease was low. The control dogs responded with an increase or decrease of up to about 50% in 28 days. No significant change was seen in either group.

DISCUSSION

Several studies have emphasized the induction of immunosuppression by virulent and/or vaccine strains of CPV on the basis of the following assumptions: CPV was a common cause of lymphopenia [3, 10, 13] and a depletion of lymphocytes from the lymph nodes and thymus of dogs infected with virulent CPV [2, 13]. A modified live CPV vaccine suppressed lymphocyte response to mitogen even in canine parvovirus immune dogs [11], but little is known about cell mediated immunity after CPV vaccination.

There are few reports on the effects of surgery in dogs on response to concomitant vaccination [6]. Kelly [6]

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reported that there is nothing to suggest that in dogs antibody response to distemper vaccine is adversely affected by concomitant surgery. That in the present study 13 of 15 dogs (86.7%) with HI titers (< or = 64) at the time of vaccination responded with an increase in CPV serum antibody titers suggested that the response to CPV vaccine pre- and post- surgery was satisfactory. Furthermore, many dogs responded with an increase in CPV serum antibody titers in 7 days. This indicates that CPV antibody titers were usually at protective levels within 7 days after vaccination. It is therefore suggested that non-emergency surgery should be conducted at least 7 days after vaccination, and if it is impossible, then careful isolation from pathogens, especially by day 7 after vaccination is to be done. Three of 4 dogs with moderate HI titers responded with increased titers after vaccination. It seems, therefore, that vaccination of the dogs with moderate HI titers is effective. In CDV serum antibody assay 4 of 8 dogs (50%) with SN titers (< or = 32) at the time of vaccination responded with an increase in the titers, but the dogs that became positive were few compared with CPV titers. This indicates that careful attention should be paid to CDV infection even if the CDV vaccine is administered.

Phillips *et al.* [16] reported that polyvalent commercially available canine vaccines caused significant suppression of lymphocyte response to mitogen and that vaccine induced immunosuppression might potentiate the severity of concurrent disease or allow inapparent infection to become clinically apparent [16]. In this study, most dogs responded with a slight decrease in blastogenic responses to ConA and PHA and no significant change was seen compared with control dogs. It is suggested, therefore, that vaccination pre- and post-surgery neither induce severe immunosuppression, nor potentiate the severity of concurrent disease and does not cause inapparent infection to become clinically apparent. Although we did not have sufficient data due to clinical cases, it is considered that vaccination pre- and post-surgery is effective.

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