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A review of canine parvoviral disease in Nigeria, with special focus on the multivalent DHLPP vaccine and vaccination

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Abstract

Dogs have been playing important roles in the lives of humans in various ways, especially as companions and guard animals, and the increasing demand for dog ownership in Nigeria account for the massive importation of numerous exotic dog breeds. Keeping these imported exotic breeds healthy is challenged by the high occurrence of canine parvovirus disease (CPD), which leads to losses either by death of the dogs or economic loss through financial expenses incurred during treatment by animal health practitioners. CPD is a very important viral disease of dogs, associated with high morbidity and mortality in both puppies and adults. The severe acute haemorrhagic enteritis and myocarditis that occur in the disease usually leaves dog owners and veterinary practitioners extremely disturbed. Currently, dogs are usually protected from CPD by vaccination with the multivalent five-way Distemper-Hepatitis-Leptospirosis-Parvovirus-Parainfluenza (DHLPP) vaccine. However, CPD is still being reported in DHLPP vaccinated dogs. In Nigeria, several concerns had been raised on the efficacy of different brands of DHLPP vaccines available, the effectiveness of the vaccination and the overall health of exotic breeds of dogs, in general. This review highlights the topical issues on CPD, vaccination of dogs with the DHLPP vaccine, vaccination protocols and possible factors militating against the effective use of available DHLPP vaccines for dogs in Nigeria. Furthermore, insights on the challenges encountered by veterinarians in the treatment, management, prevention and control of CPD are elucidated.

Keywords: Canine parvovirus disease; Dogs; DHLPP vaccine; Vaccination failure; Nigeria.

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Introduction

Canine parvovirus disease (CPD), also called canine parvoviral enteritis (CPE) is an acute, contagious and fatal disease of dogs, commonly associated with anorexia, emesis, sometimes bloody, severe haemorrhagic gastroenteritis resulting in loss of electrolytes and concomitant marked dehydration, lethargy, myocarditis, leucopaenia and in most cases death (Nandi and Kumar, 2010; Adejumobi *et al*., 2017; Odueko, 2020). It has been evidently well established that CPD is of great concern due to its high morbidity of about 100% and recurrent mortality up to 91% in puppies and 10% in adult dogs (Black *et al*., 1979; Mylonakis *et al*., 2016; Adejumobi *et al*., 2017). Higher death rates are recorded especially in unvaccinated puppies within the first few months of age as well as in puppies with history of unvaccinated bitches as their mothers (Pedroza-Roldán *et al*., 2022). Since the first reported occurrence of CPD in 1978, there has been continued global increase in the incidence of the disease, which has been attributed to the capability of the causative virus to undergo mutation, evolving into new, more virulent and resistant subspecies (Decaro *et al.,* 2006). Canine parvovirus disease has thus remained one of the most significant causes of gastroenteritis and death in dogs (Shima *et al*., 2020).

The causative agent of CPD is a small, non-enveloped, single-stranded DNA virus which requires specifically the cell nucleus of the host cell for viral replication, binding the host cell by the double-stranded ends of the genome (Goddard and Leisewitz, 2010). Canine parvovirus is reported to have been derived from the feline panleucopenia virus (FPV) as a host range variant emanating from a direct mutation from FPV, a mutation from a FPV vaccine virus and the adaptation to the new host dog via non-domestic carnivores, like mink and foxes (Nandi and Kumar, 2010). The virus has a high rate of adaptability to adverse environmental conditions enabling it to survive for long periods (Goddard and Leisewitz, 2010). In dogs, infection is from two distinct parvoviruses consisting of the minute virus of canine (MVC) equally known as CPV-1 and the highly pathogenic canine parvovirus (CPV-2) (Carmichael *et al*., 1994). Co-infection of CPV-1 with other viruses has been reported to produce symptoms of respiratory difficulty and severe diarrhoea with enteritis in dogs of 1 – 5 weeks of age (Mochizuki *et al*., 2002; Sun *et al*., 2009). On the other hand CPV-2 is a single-stranded DNA virus that belongs to the genus *Protoparvovirus*, and it is regarded as the most dreadful entero-pathogen in puppies and adult dogs worldwide (Cotmore *et al*., 2014). Canine Parvoviral Type-2 (CPV-2) is known to have three subtypes CPV-2a, CPV-2b and CPV-2c which occur worldwide in various proportions (Nandi *et al*., 2013). There is also a wild-type CPV but it is believed to no longer be in circulation (Nandi *et al*., 2013).

The distribution of the different variants of the canine parvovirus varies across the globe. Different parts of Asia have CPV-2a as the dominant strain (Zhou *et al*., 2017), while places like Laos and Thailand have more of the CPV-2c strain (Vannamahaxay *et al*., 2017; Charoenkul *et al*., 2019). Studies have shown that the three subtypes of CPV-2 are in circulation in Africa, including Nigeria, and the subtype CPV-2a is believed to be the predominant strain of the three (Shima *et al*., 2020). Recently, Maganga *et al*. (2023) characterised CPV-2a and CPV-2c variants from vaccinated dogs in Gabon. Earlier reports by Dogonyaro *et al*. (2013), in which dog faecal samples from Nigeria and South Africa were genetically analysed, showed that CPV-2a variant was found in Nigeria while CPV-2a and CPV-2b circulated in South Africa. Other reports of studies in Nigeria have shown several CPV-2 variants in circulation. Apaa *et al*. (2016) reported CPV-2a as the prevalent CPV-2 variant in faecal samples from 53 dogs presenting with acute gastroenteritis suspected to be and consistent with canine parvovirus disease. Both CPV-2c and CPV-2a had also been reported by Shima *et al*. (2020) from samples collected from seven states of Nigeria. Furthermore, CPV-2b variant had been reported following a molecular characterization of faecal samples from dogs in three south east states of Nigeria (Ukwueze *et al*., 2021). The three subtypes of CPV-2 were

established for the first time from the result of sequencing and phylogenetic analysis of 56 samples where 54 (96.4%) samples were positive and CPV-2a was identified as the prime subtype followed by CPV-2b and CPV-2c (Ukwueze *et al*., 2021). Interestingly, the co-existence of subtypes CPV-2a and CPV-2b; and CPV-2a and CPV-2c were reported in some dogs in Nigeria (Fagboghun and Omobowale, 2018).

Transmission of CPV to a susceptible animal is usually through direct or indirect contact with infected faeces (faeco-oral route) or contaminated surfaces (fomites) (Nandi and Kumar, 2010). The virus is often shed in the faeces of infected dogs within 4 – 5 days of exposure before clinical signs develop, and then throughout the period of illness, and also for 10 days after clinical recovery (Cynthia and Scott, 2010). Parvovirus is shed in the faeces by infected animals and this virus can remain stable in the environment for 7 months or longer as the viral particles can be transferred on the shoes, hands and clothes of people who then may expose an unprotected dog (Saknimit, 1998). It is very important to understand the ease of transmission and the fact that direct contact between the unprotected dog and the infected dog is not necessary for a pet to become exposed (Saknimit, 1998). The clinical signs of CPD usually appear within 3 – 7 days following an infection, first with non-specific clinical signs such as fatigue, fever, dehydration and anorexia. Depending on the severity of the disease, these clinical signs often progress to vomiting and haemorrhagic diarrhoea with a distinct foul odour (usually 24 – 48 hours following the onset of clinical signs), septic shock, decreased capillary refill time, tachycardia and hypothermia which can lead to death due to rapid dehydration (Aiello *et al*., 2010; Johnson, 2014).

Though there had been several reviews on CPD and CPV, there is none in available literature that focused on the Distemper-Hepatitis-Leptospirosis-Parvovirus-Parainfluenza (DHLPP) vaccine and vaccination in Nigeria. This present review explores existing documentation on the DHLPP vaccine, vaccination protocols, vaccination, vaccine failure and management approaches of CPD in Nigeria.

Prevalence of CPD in Nigeria vis a vis DHLPP vaccination

Canine parvoviral enteritis is known to be endemic in Nigeria, with clinical cases occurring even in dogs vaccinated with the DHLPP vaccine. The highest incidence of the disease in Nigeria has been reported to occur in dogs aged 0 – 5 months (Tion *et al*., 2018). In a retrospective study on dogs in Markurdi, Benue State Nigeria, it was reported that 28.1% of the vaccinated study population had CPE (Tion *et al*., 2018). A study in Effurun/Warri metropolis of Delta State reported an overall prevalence of 13.4%, with a specific prevalence of 27.9% in vaccinated dogs and 52.9% in unvaccinated ones (Shima *et al*., 2015). In Ilorin and its surrounding towns, an overall prevalence of 6.4% was reported in a 10-year retrospective study, with 8.6% occurrence in vaccinated dogs and 81.9% prevalence in unvaccinated ones (Daodu and Ajiboye, 2018). A CPE prevalence of 7.97% was reported in a study in Yola metropolis, Adamawa State, Nigeria, with unvaccinated dogs (8.73%) having a higher prevalence than vaccinated dogs (6.99%) (Francis *et al*., 2019). In another retrospective study carried out in Ibadan, a prevalence of 61% was obtained for gastroenteritis in dogs presented at the Veterinary Teaching Hospital Ibadan, caused majorly by parvoviral infection (Adejumobi *et al*., 2017). One common factor with these studies reported is, that a higher prevalence of CPE was found in dogs that had not been vaccinated, but a lower percentage of dogs already vaccinated still came down with the disease. Studies show that unvaccinated dogs are more prone to the infection due to the absence of humoral and cell mediated immunity against the CPV infection (Willard, 2005).

Canine parvovirus enteritis cases recorded in vaccinated dogs could be due to vaccine failure. Studies also show that the common cause of vaccine failure in puppies is as a result of inadequate protective immunity from vaccination due to interference from maternally-

derived antibodies. Another possibility is that the first and second shots of DHLPP vaccination administered mop up the antibodies already developed following the first field challenge of CPV (Daodu and Ajiboye, 2018). Some other suggested causes of vaccine failure were immune system incompetence as a result of delay in the maturation of the immune system or a poorly developed immune system, incapability to genetically respond to certain vaccine antigens, the use of geographically incompatible CPV variant as seed in the development of the vaccine, inconsistent vaccine quality, ineffective vaccine load and inability to maintain an appropriate cold chain due to improper vaccine storage (Willard, 2005, Schultz, 2000; Tizzard and Yawei, 1998). Human error could also be another important factor for the reason CPE occurs in vaccinated dogs. This could be due to the administration of the DHLPP vaccine at an inappropriate dose, inadequate record keeping of the vaccines already administered and non-compliance of dog owners to follow the strict vaccination schedule. Some of the studies reviewed indicated that some of the dogs in the study populations received only the first dose of the CPV vaccine and did not complete the ideal three primary serial vaccinations from 6 weeks of life, 3 – 4 weeks apart which could be the reason for the incidence of cases seen in vaccinated dogs, as such dogs that were not completely vaccinated had inadequate protection (Willard, 2005; Tizzard and Yawei, 1998).

Management and Treatment of Canine Parvovirus Enteritis

Cases of canine parvovirus enteritis have a survival rate of 85 – 90% under conditions of intensive care and treatment, and recovery generally occurs in 3 – 7 days (Ettiger and Feldman, 1995). Mortality rates increase substantially in dogs that are not placed under intensive care and are given appropriate treatment, and death is usually due to sepsis and/or dehydration (Macintire, 2004). Correcting dehydration and electrolyte imbalances and reducing further fluid loss is critical to successfully managing CPV infection and most times hospitalization, administration of intravenous (IV) fluids, IV antibiotics, antiemetics, and GI protectants are the mainstay of treatment (Mylonakis *et al*., 2016). In dehydrated patients, synthetic colloids such as Hetastarch (20 ml/kg/day CRI) is beneficial in replacing intravascular volume, maintaining hydration and managing shock (Decaro and Buonavoglia 2012). Once the infected animal has been hydrated, broad-spectrum antibiotics such as Ampicillin, 22mg/kg or amikacin 10mg/kg, can be given (Pollock and Coyne 1993; Decaro and Buonavoglia 2012).

Canine Parvovirus Disease Vaccines in Nigeria

The DHLPP vaccine is a multivalent vaccine routinely used for the immunization of dogs against CPD (Tizard, 2021). The vaccine is regarded as a core and vital to the health of dogs, based on exposure risk, the severity of disease, and its transmissibility to other dogs. The vaccine contains levels of attenuated or killed aetiologic agents of the five diseases which are potentially fatal: canine distemper, hepatitis, leptospirosis, parvoviral disease and parainfluenza (Tizard, 2021).Yearly booster doses are also needed of the DHLPP vaccine to ensure optimal immunity.

Different DHLPP vaccine brands are available in Nigeria, such as the PRO-VAC® DHLPP vaccine, Vanguard Plus 5® manufactured by Zoetis and Nobivac Canine DAPPv® manufactured by Merck Animal Health. However, there are no monovalent vaccines specifically for CPD. Most of the commercially available vaccines are known to be produced from the wild-type CPV which is no longer in circulation (Nandi *et al*., 2013). Though vaccination is believed to be effective, vaccinated dogs still come down with the disease especially in Nigeria (Nandi *et al*., 2013). This has raised doubts about the efficacy of the CPV vaccines available in the country and the effectiveness of the vaccination procedure and schedule.

Vaccination Protocol

Vaccination of companion animals have helped substantially in reducing the incidence of potentially fatal infectious diseases of animals and humans over the past 40 – 50 years and have contributed both to the health of animals and to public health (Appel, 1999). Vaccines reduce the risk of infection by working with the body's natural defenses to develop immunity to disease. It has been posited that vaccination programs need to be scheduled as an individualized medical procedure, based on an analysis of risks and benefits for each vaccine in an individual animal in accordance with the manufacturers' instructions, government regulations, scientific standards, professional organizational guidelines, and veterinary recommendations (Roth and Spickler, 2010). There is thus the need for clients to be educated on the regimen for vaccinations.

In the late 1970s when canine parvoviral enteritis was first reported, it caused severe morbidity and mortality in both puppies and adult dogs (Pollock and Carmichael, 1979). Bitches which were vaccinated prior to whelping will transfer maternal immunity to the puppies; and such puppies have been reported to be protected for a period of 6 weeks before the maternal immunity wanes (Odueko, 2020). Puppies are generally vaccinated in a series of doses, extending from the earliest time that the immunity derived from the mother wanes (Oh *et al*., 2006; Schultz, 2006). The vaccination protocol for CPD with the recombinant vaccine DHLPP is the schedule endorsed by the World Small Animal Veterinary Association, which involves the initial administration of the vaccine at 6 – 8 weeks of age, followed by a booster at 10 – 12 weeks of age and a second booster shot given at 14 – 16 weeks of age. The vaccination is further repeated at 6 and 12 months of age later, and then yearly afterwards (Odueko, 2020).

Vaccination and Vaccine Failure

A vaccine failure is said to have occurred when an animal develops a disease in spite of being properly vaccinated against it. Vaccines can fail when several series are given and fail to produce a protective immune response. Vaccine failure occurs in two form – primary and secondary forms. Primary vaccine failure arises due to the body's inability to produce protective antibodies at detectable levels or a situation where the body produces inadequate antibodies that are not capable of protecting the animal from the particular disease being vaccinated against. Secondary vaccine failure occurs when the body is able to produce adequate antibodies in response to vaccination, but the antibody level wanes and declines at a rate faster than normally expected (Tizard, 2021).

The two common reasons for vaccine failure are: failure of the vaccine delivery system to provide potent vaccines and failure of the immune response of the animal or human that is vaccinated, whether due to inadequacies of the vaccine or factors inherent in the host. The first category is by far the most important worldwide (Hinman *et al*., 1992). The major factor contributing to failure of the delivery system is inadequacy of vaccine supply chain. Other important factors include improper use of vaccines, vaccine ineffectiveness at the time of use, and factors relating to client attitudes and knowledge (Hinman *et al*., 1992). Failure of the immune response may be either primary or secondary loss of protection after initial effectiveness (Tizard, 2021). Some specific factors responsible for vaccine failure in Nigeria include: the use of foreign vaccines which may not be effective against the circulating strains of the virus in Nigeria, inadequate/incomplete vaccination due to negligence on the part of the animal owner/handler, breakdown in cold chain, improper handling and administration of the vaccines (Francis *et. al.,* 2019; Ukwueze *et. al., 2022*).

For the development of an effective immune response after a course of vaccination, two or more weeks may be required. If the animal had been exposed to an infectious agent prior to vaccination or shortly after, there is very high likelihood of the vaccinated animal coming down with the disease, as the vaccine antigen may not

have stimulated the immune response of the host before the exposure to infection (Decaro *et al*., 2020). The same situation may be applicable for an animal already incubating the disease at the time it was vaccinated. In fact, the modified live vaccines can cause immunosuppression (Tizard, 2021), hence vaccination of an animal that is already sick may precipitate mortality. Care should therefore be taken as canine parvovirus, canine distemper and the use of polyvalent vaccines that contain these attenuated viruses have been implicated in inducing immune dysfunction (Tizard, 2021). Other factors that can cause immunosuppression are stresses including pregnancy, malnutrition, concurrent infections, not allowing enough time between scheduled vaccinations and the use of immunosuppressive drugs such as prednisone. Another possible cause of vaccine failure is incorrect administration, including splitting a vial between animals (Decaro *et al*., 2020).

However, the most common reason for DHLPP vaccine failure is thought to be the presence of maternal antibodies; that is, passive immunity gained from the dam's colostrum during the first 72 hours of parturition (Decaro *et al*., 2020). Maternal antibodies interferers more with viral vaccines than bacterial vaccines and with the parvovirus vaccines more than any other type of viral vaccine (Decaro *et al*., 2020). Unfortunately, the amount of antigen that causes disease is less than that needed to overcome maternal antibodies, so there is a period of vulnerability when the protection afforded by maternal antibodies is not sufficient to prevent disease and the puppy's immune system is not yet fully functional (Decaro *et al*., 2020).

Conclusion and Recommendations

Canine parvoviral disease is a very important and economically significant viral disease of dogs, associated with high morbidity and mortality in both puppies and adults, and it is endemic in Nigeria. Dogs are protected from CPD by vaccination with the multivalent five-way Distemper-Hepatitis-Leptospirosis-Parvovirus-Parainfluenza (DHLPP) vaccine. However, cases of CPD are still recorded in vaccinated dogs due to either vaccine failure or inadequate management practices by dog owners/handlers. Strict adherence to the vaccination protocol is still the foremost effective preventive measure against CPE in susceptible pet populations. Vaccine failure could be curbed by sensitization and public awareness about CPE and the need for completion of the scheduled vaccination against CPE. Further research needs to be carried out to ascertain the efficacy of the vaccines used here in Nigeria and greater attention should also be directed towards the specific CPV-2 variants and strains circulating within specific geographical locations. This will forestall using vaccines made for exotic strains of the virus, which may not be protective of Nigerian dogs, for the disease. Researchers can also explore the new generation technologies for the production of a more effective monovalent vaccine for CPD which has more likelihood to confer protective immunity in dogs.

Conflicts of interest

The authors declare that no conflict of interest was associated with this work

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