Veterinary Immunology and Immunopathology 160 (2014) 184–191

Contents lists available at ScienceDirect

Veterinary Immunology and Immunopathology

journal homepage: www.elsevier.com/locate/vetimm

Evaluation of avian paramyxovirus serotypes 2 to 10 as vaccine vectors in chickens previously immunized against Newcastle disease virus

Ryota Tsunekuni, Hirokazu Hikono, Takehiko Saito*

Influenza and Prion Disease Research Center, National Institute of Animal Health, National Agriculture and Food Research Organization, 3-1-5 Kannondai, Tsukuba, Ibaraki 305-0854, Japan

ARTICLE INFO

Article history:
Received 27 December 2013
Received in revised form 26 March 2014
Accepted 6 May 2014

Keywords:
Avian paramyxovirus
APMV
Newcastle disease virus
NDV
Vaccine vector
Antibody response

ABSTRACT

Newcastle disease virus (NDV), also known as avian paramyxovirus (APMV) serotype 1, is used as a vaccine vector to express the hemagglutinin protein of avian influenza (AI) virus. However, use of live NDV recombinant vaccines expressing AI virus hemagglutinin is not desirable in emergency vaccination programs to control severe AI outbreaks in chickens, because commercial chickens often possess pre-existing NDV immunity induced by routine vaccination. Therefore, a novel vaccine vector is required for emergency vaccination of chickens to control AI during outbreaks. We investigated whether candidate APMV strains could be used as vaccine vectors that could evade the pre-existing immunity acquired by chickens through NDV vaccination and that would replicate in the mucosal tissues where AI virus primarily replicates. To this end, we examined strains of APMV serotypes 2 to 10 for their immunogenicity and replication in chickens with pre-existing immunity to NDV. APMV serotypes 2, 6, and 10 were the least cross-reactive to antibodies to NDV in hemagglutination inhibition and/or virus neutralization tests. Virus replication in mucosal tissues, as well as antibody response after oculonasal inoculation, was observed when 7-week-old chickens were challenged with APMV of serotype 2, 6, or 10. The APMV also replicated in mucosal tissues and induced antibody responses in chickens that had been vaccinated twice with NDV before challenge. These results warrant further study to develop vaccine vectors based on APMV serotype 2, 6, or 10 for emergency vaccination of chickens against AI.

1. Introduction

Recent advances in reverse genetic techniques using viral genomes have facilitated the production of recombinant virus vector vaccines against human and animal diseases. Adenovirus, fowlpox virus, infectious laryngotracheitis virus, herpesvirus of turkeys, Marek's disease virus, Newcastle disease virus (NDV), and vesicular stomatitis virus have all been evaluated as vaccine vectors in chickens (Tsukamoto et al., 1999; Nakaya et al., 2001; Qiao et al., 2003; Bangari and Mittal, 2006; Kalhoro et al., 2009;

Abbreviations: AI, avian influenza; APMV, avian paramyxovirus; DIVA, Differentiating Infected from vaccinated animals; dpi, days post inoculation; EID, embryo infectious dose; F, fusion; HA, hemagglutinin; HI, hemagglutination inhibition; HN, hemagglutinin-neuraminidase; NDV, Newcastle disease virus; rNDV, recombinant Newcastle disease virus; VN, virus neutralization.

* Corresponding author. Tel.: +81 29 838 7757; fax: +81 29 838 7758.
E-mail address: taksaito@affrc.go.jp (T. Saito).

http://dx.doi.org/10.1016/j.vetimm.2014.05.001
0165-2427/

Pavlova et al., 2009; Li et al., 2011). When a live-attenuated recombinant vector vaccine is used, the route of administration generally depends on the natural route of infection with the wild-type virus. For example, the natural route of infection of chickens with NDV is via the respiratory and digestive tract. A live-attenuated NDV vaccine is delivered by being sprayed into the eyes or is provided in the drinking water, or both, thus saving on the labor required (Office International des Epizooties, 2013a). A recombinant NDV (rNDV) vector could be delivered in a similar way to allow mass vaccination of chickens in large commercial farm settings. The effectiveness of rNDV vector vaccines against avian diseases such as avian influenza (AI) has been evaluated (Nakaya et al., 2001; Huang et al., 2004). An rNDV vector expressing the hemagglutinin (HA) protein of AI virus induces adequate protection against highly pathogenic AI infection (Ge et al., 2007; Nayak et al., 2009). However, this vaccine cannot be used as a tool for ring vaccination to prevent AI outbreaks in particular areas, because pre-existing NDV immunity from NDV vaccination in commercial chickens reduces the vaccine's efficacy.

In most countries, vaccination of poultry against AI is discouraged, because stamping-out programs are the primarily means of eradication (Office International des Epizooties, 2013b). However, emergency mass vaccination of susceptible poultry is required as an alternative method of control when stamping-out is difficult—for example, when AI has spread to commercial poultry populations, and the population density in the outbreak area is too high for a stamping-out program to be used (Capua and Marangon, 2003). Because the currently available inactivated AI whole-virion vaccines can suppress signs of disease but cannot always inhibit viral replication in vaccinated animals, mass vaccination with an inactivated AI vaccine may lead to undetected virus circulation in vaccinated populations. To prevent this situation, mass vaccinations need to be accompanied by a Differentiating Infected from Vaccinated Animals (DIVA) strategy, which consists of serological surveillance to differentiate animals with antibodies raised against a vaccine from those with antibodies induced by infection. The use of recombinant vector vaccines has an advantage in the DIVA strategy: because recombinant vaccines expressing AI virus HA protein do not induce antibodies against other viral proteins, the distinction between vaccinated, uninfected animals and vaccinated animals infected with enzootic AI virus is easily made.

Avian paramyxoviruses (APMVs) of the genus *Avulavirus* in the family Paramyxoviridae are classified into 10 serotypes (APMV-1 to -10) on the basis of the antigenicity of their hemagglutinin-neuraminidase (HN) proteins, and NDV is designated APMV-1 (Alexander, 2000; Lamb and Parks, 2007; Miller et al., 2010). Recently, the complete genome sequences of novel APMVs proposed to be an 11th and 12th APMV serotype were reported (Briand et al., 2012; Terregino et al., 2013). NDV has been isolated from chickens, ducks, and pigeons, and velogenic NDV causes severe respiratory disease with high mortality rates in chickens (Alexander, 2003). In contrast, the viruses belonging to other serotypes rarely cause serious disease in chickens. APMV-2, APMV-3, APMV-6, and APMV-7 cause mild disease in poultry. APMV-2 causes mild respiratory disease in chickens and turkeys (Bankowski et al., 1981; Alexander, 2003). APMV-3 has been isolated from turkeys with mild respiratory disease and causes impaired growth in chicks (Tumova et al., 1979; Alexander and Collins, 1982). APMV-5 causes an acute fatal enteritis in budgerigars that has a high mortality rate, but it is avirulent in chickens (Mustaffa-Babjee et al., 1974). APMV-6 is often isolated from ducks and causes mild respiratory disease and a drop in egg production in turkeys (Alexander, 2003). APMV-7 was isolated from an outbreak of respiratory disease in turkeys and causes a mild respiratory disease in experimental infections (Saif et al., 1997).

Thus most APMVs, except APMV-5, infect the respiratory tract of chickens and rarely cause severe disease in poultry. They are therefore ideal vaccine vector candidates with potential for use in mass vaccination against respiratory diseases of chickens (Samuel et al., 2010; Kim et al., 2012). A recombinant APMV-3 expressing NDV fusion(F) and hemagglutinin-neuraminidase (HN) proteins induces protective immunity against oculonasal challenge with NDV (Kumar et al., 2011). However, APMV-3 vector can be used only to construct a prophylactic vaccine, not an emergency vaccine as with rNDV vector, because of serological cross-reactivity with NDV (Alexander, 2003). Because other serotypes also cross-react with NDV to various degrees (Lipkind and Shihmanter, 1986), the efficacy of APMV vaccine vectors in chickens could be affected by immunity to NDV. Here, we selected the most suitable serotypes for use as vaccine vectors in chickens previously immunized against NDV by evaluating cross-reactivity with NDV, replication ability, and the induction of specific antibodies in the presence of immunity to NDV.

2. Materials and methods

2.1. Viruses

The prototype strains of the APMV serotypes used were APMV-1 strains B1, Ishii, and Mukteswar; APMV-2 strain chicken/Yucaipa/1956; APMV-3 strain turkey/Wisconsin/1968; APMV-4 strain duck/Mississippi/320/1975; APMV-6 strain duck/Hong Kong/199/1977; APMV-7 strain dove/Tennessee/4/1975; APMV-8 strain goose/Delaware/1053/1976; APMV-9 strain duck/New York/1978; and APMV-10 strain penguin/Falkland Islands/324/2007. APMV-2, APMV-3, APMV-4, APMV-6, and APMV-7 were kindly provided by Dr. H. Kida of the Department of Disease Control, Graduate School of Veterinary Medicine, Hokkaido University, Japan. APMV-8, APMV-9, and APMV-10 were kindly provided by Dr. David E. Swayne of the Southeast Poultry Research Laboratory, USDA-Agricultural Research Service, Athens, Georgia, USA. APMV-5 was excluded because it cannot replicate in the allantoic cavity of chicken eggs (Alexander, 2003). All APMVs were grown in the allantoic cavities of 10-day-old embryonated chicken eggs. The titers of each APMV were determined in embryonated chicken eggs and measured as median embryo infectious dose (EID_{50}) by using the Reed and Muench method (Reed and Muench, 1938).