Journal of Vaccines & Vaccination
ISSN: 2157-7560
Attia Ibrahim et al., J Vaccines Vaccin 2013, 4:5
DOI: 10.4172/2157-7560.1000191
Short communication
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Hand Foot and Mouth Disease, from Emergence to Vaccine Control

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Hand, foot, and mouth disease (HFMD) is a contagious illness affecting primarily children although it also can occur in adults. HFMD presents with fever, oral lesions, and vesicular rash on the hands, feet and buttocks, persisting for 7-10 days. It is spread through direct contact with the mucus, saliva, or feces of an infected person. The common incubation period is from three to seven days.

HFMD results from infection with a group of non polio enteroviruses of the picorna viridae family. Most frequently, large outbreaks are caused by coxsackie virus A16 (CAV16) and enterovirus 71 (EV71) [1].

After an incubation period of 3 to 5 days, the viral infection results in mild fever, sore throat and loss of appetite. Malaise, swollen lymph glands, and mild diarrhoea may be present. Flat pink patches on the dorsal and palmar surfaces of the hands and feet are soon followed by small elongated greyish blisters. These resolve by peeling off within a week, without leaving scars. In some cases, fingernails have been reported to be shed a few weeks after the infection has recovered. Usually there are also a few small oral vesicles and ulcers. These are sometimes painful, so the child eats little and frets. In young children a red rash may develop on the buttocks and sometimes on the arms.

Infection due to CAV16 is mild, and complications are less common. In contrast, severe neurologic complications, including aseptic meningitis, encephalitis, pulmonary complications, and significant mortality, have been associated with HFMD caused by EV71 [2].

EV71 is a non-enveloped RNA virus of the family Picornaviridae, has icosahedral symmetry with 25–30 nm in diameter, contains a single molecule of plus sense ssRNA (7.5–8.5 kb), and replicates in the cytoplasm. The icosahedral viral capsid is composed of 60 identical units that consist of four structural proteins in each unit: VP1, VP2, VP3 and VP4 [3]. These play role in adsorption and uncoating of the virus in the infected human cells. Among these, VP1 is the most pathogenic and crucial one. Thus this has been a good target antigen for preparing an effective subunit vaccine [4].

Enterovirus 71 (EV71) infections has become an emerging infectious disease and presents serious public health problems in the Southeast Asia [5]. Because of there is no effective anti-EV71 agent is available, developing an effective vaccine against EV71 infection is the best strategy to control the disease. In the 4 decades since V71 illness was first described, there have been numerous outbreaks with more than 6 million cases and 2,000 fatalities. The most common type of illness includes rashes and blisters on the palms of the hands, soles of the feet, and mouth, but severe neurologic anifestations such as aseptic meningitis and encephalitis also occur. In addition, some children experience nonspecific symptoms such as mild fevers and apparent respiratory infections, while others are asymptomatic.

The inactivated EV71 virion vaccine candidate containing sub-microgram of viral proteins formulated with alum adjuvant was found to induce strong virus neutralizing antibody responses in mice and rabbits. Therefore, these results provide valuable information for cell-based EV71 vaccine development [6].

Earlier phase I and II trials suggested that the vaccine was safe and immunogenic, so Zhu and colleagues proceeded to conduct a phase III efficacy trial that included 10245 participants (5120 to vaccine versus 5125 to placebo) aged from 6 months to 3 years to receive either the EV71 vaccine or a placebo at baseline and at day 28 [7].

The vaccine efficacy was 90% for EV71-associated HFMD and 80•4% for EV71-associated disease (including herpangina, neurological complications, and non-specific illnesses caused by EV71). Serious adverse events were reported by 62 of 5117 (1•2%) participants in the vaccine group versus 75 of 5123 (1•5%) in the placebo group (p=0•27). The vaccine had a satisfactory safety profile and the results are similar to those for inactivated poliovirus vaccine.

Despite high efficacy of the EV71 vaccine for preventing EV71-associated hand, foot and mouth disease, the EV71 vaccine might have little part in reducing the overall incidence of HFMD, Where HFMD is caused by other viruses, such as Coxsackievirus A16 and even other strains of EV71, so this vaccine could not eliminate the disease.

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Received May 23, 2013; **Accepted** June 24, 2013; **Published** June 28, 2013

Citation: Attia Ibrahim SM, Kamel MI, Elsaie ML (2013) Hand Foot and Mouth Disease, from Emergence to Vaccine Control. J Vaccines Vaccin 4: 191. doi:10.4172/2157-7560.1000191