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Recipient vaccine-associated paralytic poliomyelitis in China, 2010–2015

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ABSTRACT

Introduction: Vaccine-associated paralytic poliomyelitis (VAPP) is one of the most important adverse effects of vaccines that are in current use globally. The Chinese national adverse event following immunization information system (CNAEFIS) is a passive surveillance system which collects data on VAPP.
Aims: To describe the epidemiological characteristics of VAPP and estimate the risk of recipient VAPP in China.
Methods: We retrieved information from reported cases of recipient VAPP from CNAEFIS from 2010 to 2015, examined the demographic characteristics of the cases, and used administrative data on vaccination doses and the estimated number of births as denominators to calculate VAPP incidence.
Results: During 2010–2015, 157 cases of recipient VAPP were reported to CNAEFIS (male-to-female ratio, 8.2:1); 151 cases (96.2%) were less than six months old. All cases were associated with trivalent OPV (tOPV), and 89.8% occurred after the receipt of first dose. Of the 157 recipient VAPP cases, type II, type III, and type I poliovirus vaccine strains were isolated from 27 (17.2%) , 25 (15.9%) , and 16 (10.2%) cases, respectively. One case died and one case recovered completely; the other 155 cases had various physical disabilities, such as monolateral or bilateral limping. Using the administered doses of OPV as the denominator, the incidence of recipient VAPP during the study period was estimated at 0.4 per million doses. The estimated recipient VAPP per million births ranged from 1.0 to 2.4 during 2010–2015.
Conclusion: The epidemiological characteristics of recipient VAPP cases in China, such as age distribution, were comparable to those in previous studies from other countries. The risk of recipient VAPP, using either estimated births or vaccination doses, was comparable to that in the US and Japan. We recommend using an inactive poliovirus vaccine to decrease the number of recipient VAPP cases in China.

1. Introduction

The oral poliovirus vaccine (OPV), which contains live, attenuated poliovirus strains types I, II, and III, has served as the primary tool for eradicating polio worldwide [1,2]. Poliovirus vaccines have had a dramatic effect on the incidence of polio in developed countries since their introduction [2]. OPV was developed in 1959 and manufacturing began in 1962 in China, as it was felt that an oral vaccine would more closely imitate natural infections due to its similar route of ingestion, and would thus potentially interrupt transmission much more effectively [2].

China reported 20,000–43,000 polio cases each year in the early 1960s, making it a major affected area [3]. Chinese national immunization program began in 1978, and China started to implement the planned immunization schedule, in which OPV was recommended to children in certain age brackets [4]; according to the schedule, the recommended ages for OPV were two months, three months, four months, and four years for each dose. Subsequently, the number of polio cases declined dramatically, and in 2000, the West Pacific Regional Office (WPRO) of the World Health Organization (WHO) certified the nation to be polio-free. There have been no reported indigenous wild poliovirus cases in China since 1994 [5]. In 2011, an outbreak of imported wild-type poliovirus occurred in the Xinjiang Uygur Autonomous Region in northwest China.

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Supplementary immunization activity was launched and five rounds of OPV vaccination were conducted among children and adults; the outbreak ended 1.5 months after laboratory confirmation of the index case [6], and China was again certified by the WHO as being polio-free [5].

Despite the great advantages of OPV in preventing wild poliovirus, reversion of the attenuating mutations during OPV replication could lead to an increase in neurovirulence, thus triggering abnormal reactions and even serious cases [2].

In polio eradication environments, such as China, vaccine-associated paralytic poliomyelitis (VAPP), which is the only serious adverse event associated with OPV [1], became a public health problem. In the second half of 2005, parents from different provinces sought medical treatment in Beijing for their children, who had developed abnormal limbs [3]. The Chinese government issued several laws and policies aimed to compensate VAPP patients. As neonatal immunodeficiency is a rare but natural part of infancy, "one in a million" victims cannot be avoided when using OPV.

VAPP is one of the most important vaccine-caused adverse effects of vaccines that are in current use globally. With the near-disappearance of wild-type polio, VAPP emerged as the largest cause of paralysis from polioviruses. One of the reasons for the Global Polio Eradication Initiative's Polio Endgame Strategic Plan 2013–2018 is to reduce VAPP. The WHO polio vaccine position paper indicates that countries in which VAPP is a concern, a sequential inactive poliovirus vaccine (IPV)/OPV schedule can be adopted. In response to WHO's planned global action of switching from trivalent OPV (tOPV) to bivalent OPV (bOPV) in April 2016, which was aimed at mitigating VAPP after conducting a pilot study with IPV in 2015, the attenuated poliovirus vaccine has been switched from tOPV to bOPV and IPV was included as the first polio vaccination dose across China as of May 1, 2016. Consequently, it was expected that VAPP cases would decrease significantly and ultimately disappear in the near future. We reviewed data from national AEFI surveillance to (1) describe the epidemiological characteristics of recipient VAPP cases as adverse events following immunization in China, and (2) estimate the risk of contracting recipient VAPP during the study years.

2. Methods

2.1. Chinese national AEFI surveillance system (CNAEFIS) [7]

CNAEFIS is an online AEFI information reporting system. In June 2010, the Chinese Ministry of Health (MoH) and Chinese Food and Drug Administration (CFDA) jointly issued national AEFI guidelines for reporting and management [8], making the CNAEFIS the only and official vaccine safety surveillance system in mainland China.

According to national AEFI guidelines, an AEFI case for surveillance is defined as a reaction or event after vaccination that is suspected to be related to the vaccination. Healthcare facilities, vaccination units, centers for disease control and prevention (CDCs), adverse drug reaction (ADR) monitoring agencies, vaccine manufacturers, and their executive staff are the responsible reporting units for AEFI. The reporting of AEFI is implemented in line with the principle of localized management, although the public can also notify any of the reporters listed above. Case reports are compiled by local county CDCs, which can verify AEFI Case Reporting Cards and enter them into the CNAEFIS; from there, duplicate reports can be detected and deleted. Once cases are entered into the CNAEFIS, they can be viewed by all levels of CDCs and ADRs.

Any AEFI with the exception of common adverse reactions with a clear diagnosis (e.g., fever, redness and swelling at the injection site, induration) should be investigated. For an AEFI in need of investigation, county CDCs should begin by collecting relevant data and then complete the AEFI Case Investigation Form; it can then be reported to CNAEFIS.

2.2. Causality assessment in CNAEFIS

According to national AEFI guidelines [8], every level of the CDC, including county, prefectural, and provincial, should organize an AEFI Investigation and Diagnosis Expert Committee, which should include relevant experts in clinical medicine, epidemiology, laboratory practices, pharmacy, vaccinology, vaccine regulation, and related fields. This committee should be in charge of making diagnoses and determining the cause of the AEFI when needed. For deaths, severe disabilities, AEFI clusters, and an AEFI of significant public concern, prefectural or provincial CDCs should organize an AEFI Investigation and Diagnosis Expert Panel, which should include experts involved in the related committee, for diagnosis and causality assessment.

Similar to WHO vaccine safety surveillance guidelines [9,10], after the causality assessment, the AEFI should be classified into the following categories [7,8]: (1) vaccine-related reaction or vaccine product-related reaction; (2) vaccine quality reaction or vaccine quality defect-related reaction; (3) program error or immunization error-related reaction; (4) coincidental event; (5) psychogenic reaction or immunization anxiety-related reaction.

2.3. Case definition of VAPP in CNAEFIS

In 2008, the Ministry of Health of the People's Republic of China issued two regulations on the diagnosis and verification of VAPP: "Instruction advice on diagnosis and treatment of vaccine associated paralytic poliomyelitis" (Wei Ban Yi Fa [2008] No.17), and "Instruction advice on verification of VAPP and handling of remaining problems" (Wei Ban Fa [2008] No. 40).

In these regulations, there are two types of VAPP: recipient and contact. In CNAEFIS, contact VAPP is not included. Recipient VAPP, on the other hand, is defined as a case of (1) fever occurring 4–35 days after vaccination, acute flaccid paralysis (AFP) occurring 6–40 days after vaccination, and a clinical diagnosis compatible with paralytic poliomyelitis, or (2) Isolation of vaccine-related poliovirus from stool samples, which are used as supplementary conditions. Similar to other AEFI cases, recipient VAPP is also investigated by a panel of experts and receives a causality assessment based on the clinical and epidemiological characteristics of the cases.

2.4. Data analysis

For each case, we reviewed the date of occurrence, gender, age, address, OPV vaccination history, and serotype of vaccine strains.

For risk calculations, two methods were used [11]: VAPP per million administered OPV doses, and VAPP per million births. The risk of recipient VAPP per administered OPV doses was calculated by using the number of recipient VAPP cases reported during the study period divided by the total number of OPV doses administered during the same period. The OPV-administered doses were collected from a Chinese immunization information system, which collects immunization doses of all vaccines in national immunization schedules, including OPV. However, the immunization doses of OPV in supplementary immunization activities launched at the provincial level are not collected in this system. VAPP per million births was calculated by using the number of recipient VAPP cases divided by the number of estimated births during the same period.