Short Communication

Adverse events following immunization with oral poliovirus in Kinshasa, Democratic Republic of Congo: preliminary results

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Aim: We investigated the nature and frequency of adverse events following immunization (AEFI) associated with oral polio vaccines (OPV) in the general population in Kinshasa, Democratic Republic of Congo (DR Congo).

Methods: The DR Congo National Pharmacovigilance Centre organized active AEFI surveillance during mass immunization campaigns for the general population from March to June 2011. A patient individual case safety report was used as a questionnaire and addressed to pupils and students from high schools and universities who had any adverse events after OPV administration. We used the preferred term from the WHO Adverse Reaction Terminology for AEFI designation. Here is presented the results of the second step of the mass immunization campaign.

Results: A total of 767 patients reported AEFI during the second step. Sex distribution shows that 512 (66.8%) students were females, while 255 (33.2%) were males, giving a female/male ratio 2 : 1. The average age was 16.8±5.19 years (ranged: 6–35.5 years). Each person reported a mean of 1.33±0.6 AEFI. The average AEFI onset duration was 1.74±1.16 days post-vaccination, ranging from 1 to 9 days. Headache (22.4%), abdominal pain (17.2%), fever (11.7%), diarrhea (9.9%), and asthenia (7.5%) were the common symptoms. Paralysis and asthma-like reactions were rare and serious adverse events in this study. The most affected systems were gastro-intestinal (33.5%) and nervous system (29.3%). Rechallenge was positive for 173 persons (22.6%).

Conclusion: OPV-related AEFIs are not uncommon, although it is under-reported. Active AEFI surveillance during mass immunization campaigns is very important and may help to detect rare and serious adverse events. Further investigation will be important to identify risk of AEFI with OPV in adults and is warranted to elucidate the cause of this association in the Congolese environment.

Keywords: Adverse events following immunization, Oral poliovirus, Students, Kinshasa, Democratic Republic of Congo

Introduction

In 1988, the World Health Assembly resolved to eradicate poliomyelitis worldwide. The global campaign to eradicate polio achieved a more than 90% reduction in the number of polio cases worldwide during the last 11 years, since it was launched.[1] The live attenuated oral poliomyelitis vaccine (OPV) has many advantages compared to the inactivated poliomyelitis vaccine (IPV) for poliovirus eradication in mass immunization campaign. It confers intestinal immunity, making recent OPV recipients resistant to infection by wild polioviruses; it provides long-term protection against paralytic disease through durable humoral immunity; its oral use excludes problems of injection safety and programmatic errors related to injection; immunization with OPV has lower cost than with IPV and should be the choice for mass vaccination campaign in developing countries. Because of the risk of vaccine-associated paralytic poliomyelitis, OPV has been replaced by IPV in some countries.[2]

AEFI surveillance systems are important tools to monitor associations between vaccination and suspected adverse events. In European countries,

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reporting and surveillance of adverse events following immunization (AEFI) was advised to be introduced in each country as part of the monitoring system.[3] In Africa, AEFI are less documented and particularly those related to OPV.[4,5] Furthermore, OPV is most of the time administered to infants, which makes AEFI description less precise, and during routine immunization, poliomyelitis vaccine is administered with other vaccines, which makes difficult causality assessment.

In the Democratic Republic of Congo (DR Congo), OPV is given four times during routine immunization to infants, in birth, in the sixth, tenth, and fourteenth weeks. Every year there are National Immunization days, when immunization campaign is organized for the whole country. If there are new cases of paralysis related to wild poliovirus in some areas, there may be a limited immunization campaign in the related area and then Supplementary Immunization Activities can be conducted.

In 2010 and 2011, after outbreak of poliomyelitis mutant virus in Central African Region, some cases were reported even among adults.[6] Ministry of health of the DR Congo launched mass immunization campaign for the general population. Most people, including adults, received OPV four times in 4 months. During the first and the second steps, monovalent OPV type 1, was administered. Bivalent OPV types 1 and 3 were administered during the third step. The 'Centre National de Pharmacovigilance (CNPV)' of DR Congo, which is located in the University of Kinshasa, developed active AEFI surveillance during these mass immunization campaigns to gain further information about OPV-associated AEFI.

Our ultimate goals are to develop the basis for designing and implementation of effective preventive interventions. Our research was designed to inform clinical practice, education, counseling guidelines, and all the stakeholders involved in the immunization system. The aim of this work is to assess the nature and frequency of AEFI associated with OPV in the general population in Kinshasa.

Patients and Methods

This is a cross-sectional study conducted among pupils and students attending universities between March 2011 and June 2011 in Kinshasa, DR Congo. In 23–27 March, monovalent OPV type 1 (mOPV1) was administered to 9 863 458 patients. From 28 April to 2 May, 10 091 567 persons received mOPV1. In 26–30 May, bivalent OPV types 1 and 3 (biOPV) were administered to 9 724 982 patients and 10 206 785 received mOPV1 in 25–29 June.

A questionnaire created by the CNPV was addressed mainly to those who experienced any AEFI after immunization with OPV. The questionnaire was provided as a patient individual case safety report (patient ICSR) and included necessary information for AEFI reporting in successive mass campaigns. Mandatory information included in the questionnaire were: patient initial, age, sex, drug therapy history during the last week before immunization, and information about the adverse event including patient description, onset date, end date, and history of a reaction on previous immunization. Before completing the questionnaire, vaccination benefit was explained as well as the possibility of occurrence of adverse events. All questionnaires were gathered and processed by CNPV.

This study is the result of active surveillance of AEFI by the National Pharmacovigilance Center of the University of Kinshasa, as recommended by the World Health Organization for a mass immunization campaign as well as for routine immunization.

Each month, data collection started on the fourth day of immunization, which normally was the end date, and had 10 days duration after the end of the immunization campaign. Data collection was completed only on the first three steps of this four-step mass immunization campaign. Over 1500 persons reported occurrence of AEFI during the first three steps. In this preliminary study, we focused only on the results of the second step, which allow us to assess the frequency of re-challenge related to AEFI-associated with monovalent type 1 OPV.

A written consent was obtained from institutional authorities before addressing the students. Students' reporting of AEFIs was free.

For analysis, we used the preferred term from the WHO Adverse Reaction Terminology. Data are represented as means$\pm$SD when the distribution was normal and median with range when the distribution was not normal. Frequency of various symptoms and sign findings are expressed as proportions (%).

Results

The CNPV received and analyzed AEFI reports from 767 persons during the second step. All the patients who completed the questionnaire were healthy during immunization. Sex distribution shows that 512 (66.8%) were females, while 255 (33.2%) were males, giving a female: male ratio of 2 : 1. The average age was 16.8$\pm$5.19 years.

Each person reported a mean of 1.33$\pm$0.6 AEFI. We recorded a total of 1020 AEFI. Headache, abdominal pain, fever, diarrhea, and asthenia were the common symptoms at presentation with a frequency of 22.4%, 17.2%, 11.7%, 9.9%, and 7.5% respectively (Table 1). There were five cases of muscle weakness and two cases of paralysis after immunization. One of them recovered before 1 month, the

second was still paralyzed after 1 month. One case of asthma-like reaction with a positive re-challenge was reported. The average AEFI onset duration was 1.74±1.16 days post-vaccination, ranged from 1 to 9 days. Re-challenge was positive for 173 persons (22.6%). The most affected systems were gastro-intestinal system (33.5%), central and peripheral nervous system (29.3%), and body as a whole (21.8%). In this series, 4.2% of persons reported musculoskeletal disorders and 3.2% skin and appendages disorders, including urticaria, rash, and pruritus.

Discussion

To our knowledge, the present study is the first attempt to describe AEFI in our population. It is the first to assess clinical events after an OPV immunization campaign in the region of Central Africa. This study is the result of an active AEFI surveillance during a mass immunization campaign including different ages of the population and indicated for an outbreak of poliomyelitis occurring even in adults. However, this studied sample was a subset of the population of Kinshasa

Headache, abdominal pain, fever, diarrhea, and asthenia were the common symptoms at presentation with a frequency of 22.4%, 17.2%, 11.7%, 9.9%, and 7.5%, respectively. There were five cases of muscle weakness and two suspected vaccine-associated poliomyelitis. Two cases of paralysis were reported after immunization. One case of asthma-like reaction with a positive re-challenge was reported.

We recorded headache as the most frequent symptom (22.4%). Similar observations have been described with other vaccines.[7–10] The other signs and symptoms reported in this study were found to be similar to those described elsewhere with other vaccines.[8–10]

Table 1 AEFI following OPV in our study population

AEFI	Number of cases	Frequency (%)
Headache	228	22.4
Abdominal pain	175	17.2
Fever	119	11.7
Diarrhoea	101	9.9
Asthenia and/or malaise	79	7.7
Dizziness	65	6.4
Nausea and or vomiting	47	4.6
Musculoskeletal pain	23	2.3
Coughing	21	2.1
Rhinitis	21	2.1
Conjuctivitis	18	1.8
Pharyngitis	17	1.7
Rash	17	1.7
Arthralgia	15	1.5
Back pain	9	0.9
Pruritus	7	0.7
Urticaria	7	0.7
Muscle weakness	5	0.5
Dyspnoea	2	0.2
Paralysis	2	0.2
Other	42	4.1
Total	1020	100

No case of AEFI associated with OPV in adult population and in the pediatric population could be found with the use of available computer-assisted medical literature search programs. However, according to a WHO document entitled 'supplementary information on vaccine safety, background rates of adverse events following immunization',[11] common minor vaccine reaction associated with OPV are fever, irritability, malaise, and non-specific symptoms, such as diarrhea, headache, and/or muscle pain. This result is similar to ours. According to this document, these common reactions occur within one or two days of immunization. This is close to our study where the average AEFI onset duration was 1.74±1.16 days. The same document reports vaccine-associated paralytic poliomyelitis as the main rare and serious vaccine reaction associated with OPV with an estimated risk of 1 per 1.4–3.4 million for the first dose. The two cases of paralysis we reported occurred after administration of the first dose and close to 10 million of persons received this dose; unfortunately, no further investigation was performed to confirm whether or not it was a vaccine-associated paralytic poliomyelitis.

Conclusion

OPV-related AEFIs are not uncommon among Congolese adults, although it is under-reported. Active surveillance after a mass immunization campaign allowed detecting some rare OPV-related AEFI, such as a possible vaccine-associated poliomyelitis.

Bearing in mind the significance of immunization for personal and collective immunity, good collaboration of all stakeholders involved in each single case of adverse event is required. Further investigation will be important to identify the risk of AEFI associated with OPV in adults and is warranted to elucidate the cause of this association in the Congolese environment. This is the first step in individualized management of this clinical entity.

Limits of the Study

We declared the patients of our study healthy before immunization, based on their declaration of lack of drug therapy history. No further investigation was performed to confirm whether or not they were really healthy before immunization. In this cross-sectional study, no control groups (e.g. adults who do not receive OPV) were included because of the massive nature of the vaccination campaign among all the general population in Kinshasa during the study period; therefore, it is difficult to interpret this information. Better data to estimate the frequency of AEFI due to OPV and to compare with a control group are needed in a prospective study. The future

prospective studies should answer the following questions:

1. Whether the AEFI seen in adults with OPV was different than in children?
2. Any difference between AEFI following mOPV and biOPV?
3. Can OPV be dubbed as a safe vaccine among adult also based on the findings of current and future prospective studies?

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