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Rotavirus immunization: Global coverage and local barriers for implementation

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ABSTRACT

Background: Rotavirus (RV) is a major agent of gastroenteritis and an important cause of child death worldwide. Immunization (RVI) has been available since 2006, and the Federation of International Societies of Gastroenterology Hepatology and Nutrition (FISPGHAN) identified RVI as a top priority for the control of diarrheal illness. A FISPGHAN working group on acute diarrhea aimed at estimating the current RVI coverage worldwide and identifying barriers to implementation at local level.

Methods: A survey was distributed to national experts in infectious diseases and health-care authorities (March 2015–April 2016), collecting information on local recommendations, costs and perception of barriers for implementation.

Results: Forty-nine of the 79 contacted countries (62% response rate) provided a complete analyzable data. RVI was recommended in 27/49 countries (55%). Although five countries have recommended RVI since 2006, a large number (16, 33%) included RVI in a National Immunization Schedule between 2012 and 2014. The costs of vaccination are covered by the government (39%), by the GAVI Alliance (10%) or public and private insurance (8%) in some countries. However, in most cases, immunization is paid by families (43%).

Elevated cost of vaccine (49%) is the main barrier for implementation of RVI. High costs of vaccination ($rs = -0.39$, $p = 0.02$) and coverage of expenses by families ($rs = 0.5$, $p = 0.002$) significantly correlate with a lower immunization rate. Limited perception of RV illness severity by the families (47%), public-health authorities (37%) or physicians (24%) and the timing of administration (16%) are further major barriers to large- scale RVI programs.

Conclusions: After 10 years since its introduction, the implementation of RVI is still unacceptably low and should remain a major target for global public health. Barriers to implementation vary according to setting. Nevertheless, public health authorities should promote education for caregivers and health-care providers and interact with local health authorities in order to implement RVI.

1. Introduction

Rotavirus (RV) is the most common agent of acute gastroenteritis (AGE) in children under five years of age, and the

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most severe independent of age [1,2]. Despite a progressive decrease in diarrhea-related deaths, RV is still a major cause of mortality mainly in developing countries [3]. RV disease can be prevented by vaccination, and 95% of RV-induced deaths occurred in 72 countries, which were all eligible to receive GAVI Alliance support. As of January 1, 2016, 80 of the 193 countries worldwide have introduced RV vaccines in their National Immunization Programs (NIP) [4]. Although there are public health barriers to the implementation of RV immunization (RVI), WHO and other authorities recommend universal immunization and considered it a priority in countries with high rotavirus gastroenteritis-associated fatality rates, such as in south and south-eastern Asia and sub-Saharan [5]. Two oral vaccines with high efficacy and good safety profiles are currently available: Rotarix™ administered in a 2-dose schedule, and RotaTeq® administered in a 3-dose schedule. Both vaccines aim to prime broad immune responses followed by progressively broader protection developing through successive natural rotavirus infections [6–9].

Thus far, RV vaccines have been introduced in United States, some European countries, and Australia and are being implemented in selected countries in Asia.

Limited time frame (six to eight weeks following birth) for administration was considered a potential barrier to large-scale immunization. Therefore, even if early immunization is still favored, WHO loosened its recommendation and allowed infants to receive RV vaccine (either RotaTeq® or Rotarix™) together with DTP [5].

The likelihood of intussusception following RVI is low based on the results of both large clinical trials and post-marketing surveillance data. Furthermore, the benefit in lives saved by broadening age restrictions for immunization may well exceed the risk of potential deaths related to intussusception [10].

In 2012, the Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN) identified the spread of RV vaccination as a top priority for the control of diarrheal illness in childhood [11].

In order to estimate current RVI coverage and identify the major barriers to local implementation, the FISPGHAN Working Group (WG) on AGE conducted a global survey aimed at collecting information on RVI worldwide.

2. Methods

2.1. Working group and survey

The WG on AGE was created during the FISPGHAN World Congress held in Taiwan in 2012 and encompasses two experts of each continental Society of Pediatric Gastroenterology, Hepatology and Nutrition: European (ESPGHAN), Asian Pan Pacific (APPSGHAN), Commonwealth Association (CAPGHAN), Latin American (LASPGHAN) and North American (NASPGHAN) Societies.

In order to identify and promote practical interventions that will help to reduce the burden of AGE in children worldwide, the WG on AGE collaborated with experts in the field of RVI actively involved in the dissemination of RVI around the world.

The WG coordinators developed a survey including information on the availability of RV vaccines, inclusion in the NIP, immunization coverage according to local available data, costs and financial support, main perceived barriers to implementation, possible interventions to achieve >90% global coverage (see Supplemental material).

2.2. Study design

National experts in infectious diseases and vaccination from several countries in the world were contacted between October 2015 and May 2016. Experts were identified among the members of national institutes for health, panels for local immunization programs, scientific societies working and/or reporting data on RVI (see Supplemental material).

All of them were asked to fill-in a survey to give information on inclusion of RV vaccination in their country's NIP, implementation programs, costs and their perception of local barriers to implementation. All participants were encouraged to provide original local evidence supporting their data and to report the source of information (see Supplemental material).

2.3. Data analysis

The WG planned to reach at least one referral expert for each world country. When more than one expert from the same country participated to the survey, the data were discussed and combined and analyzed as a single source.

Since data and opinions about local barriers may vary slightly according to the setting, rough data were analyzed and reported according to the Human Development Index (HDI) list of countries with advanced economy (http://hdr.undp.org/en/content/human-development-index-hdi) and countries were differentiated into high HDI countries, medium HDI countries and low HDI countries.

Data were summarized as means ± SD for continuous variables and as percentage and frequencies for categorical variables. Comparison of groups was performed using one-way analysis of variance (ANOVA) for multiple group comparisons. Chi-square test with Fisher's correction was used to address any differences for categorical variables, as needed. A p value of 0.05 or less was considered as significant. Results were updated in December 2015.

3. Results

Ninety-one experts in the field were contacted by e-mail or met personally at medical meetings, symposia and workshops worldwide. Among the 79 countries contacted, 49 provided a survey eligible for analysis (response rate 62%) (Fig. 1). Forty-two of the 49 responders provided data for all required fields, but for other seven countries the data on RVI coverage were not available (Ireland, Lithuania, Portugal, Romania, Singapore, Slovenia, Switzerland) although the survey was completed in all other fields.

Responders were equally distributed between low- (23, 47%) and medium/high-income countries (26, 53%).

3.1. Rotavirus immunization coverage and costs

RVI was recommended in 27 out of the 49 countries (55%) participating in the global survey (eTable 3). Although some countries have recommended RVI since 2006, most countries (16/49, 33.3%) first included RVI in the NIP between 2012 and 2014 (eTable 3). RVI rates showed a scattered pattern from 0 to over 90% according to different countries. Overall RVI coverage is reported in Fig. 2.

Rotarix™ and Rotateq® are both distributed worldwide, with 40 (81.6%) and 38 (77.5%) countries respectively, but Rotarix® resulted to be prevalent in African countries (Table 1).

The costs of vaccines are substantially different, being higher in European and American and lower in Asian and African countries (Table 2). Costs reported for a complete vaccination cycle with Rotateq® were slightly higher than those of Rotarix™ in average (176.8 vs 103.8USD, $p = 0.14$). In most countries these costs were charged directly to families (42.8%) (Table 2). In other nations the costs are covered by the government (38.7%), by international organization such as the GAVI Alliance (10.2%) or public and private insurance (8.1%). However, in the countries in which financial support by public authorities is limited or related to by family

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