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ABSTRACT

The 7th African Rotavirus Symposium was held in Cape Town, South Africa, on the 8th November 2012 as a Satellite Symposium at the First International African Vaccinology Conference. Over 150 delegates participated in this symposium including scientists, clinicians, health officials, policymakers and vaccine manufacturers from across Africa. Key topics discussed included rotavirus surveillance, rotavirus vaccine introduction, post rotavirus vaccine impact analysis and intussusception data and surveillance in Africa. The symposium provided early rotavirus vaccine adopter countries in Africa (South Africa, Ghana and Botswana) an opportunity to share up-to-date information on vaccine introduction, and allowed colleagues to share experiences in establishing routine rotavirus surveillance (Tanzania, Niger and Rwanda). Overall, the symposium highlighted the high burden of rotavirus in Africa, and the need to continue to strengthen efforts in preventing rotavirus diarrhoea in Africa.

1. Introduction

The Medical Research Council/Diarrhoeal Pathogens Research Unit at University of Limpopo, in partnership with National Institute of Communicable Diseases (NICD), a division of the National Health Laboratory Services in Johannesburg and the World Health Organization (WHO) African Regional Office (AFRO), hosted the 7th African Rotavirus Symposium in Cape Town, South Africa on the 8th November 2012. This report reflects the proceedings of the symposium, which was preceded the First International African Vaccinology Conference held in Cape Town. The symposium served as a forum to disseminate up-to-date information on rotavirus disease and vaccine introduction efforts in the African region. The objectives of the symposium were: (1) to discuss and propose practical ways to strengthen rotavirus surveillance in Africa as introduction of the rotavirus vaccines is accelerating in the region, (2) to share experiences of African countries regarding establishment of rotavirus surveillance sites and vaccination programmes, (3) to exchange knowledge on how to conduct high quality surveillance in the region, (4) to discuss ways to facilitate the decision-making process for introduction of rotavirus vaccines into national immunization programmes, and (5) to discuss strategies to assess the impact of rotavirus vaccination programmes on childhood diarrhoea.

The 7th African Rotavirus Symposium was attended by approximately 150 representatives including scientists, clinicians, health officials, policymakers and vaccine manufacturers from 19 African countries, and representatives from several other countries outside the region, including international rotavirus experts who presented data. More than 55 abstracts and 45 posters were presented covering the following topics: rotavirus surveillance data and strain diversity, updates on rotavirus vaccines and clinical trials effectiveness in Africa, need for intussusception monitoring in Africa, progress towards rotavirus vaccine implementation in Africa, lessons learnt after vaccine introduction and preparation to evaluate the vaccine impact.

2. Update on rotavirus key topics and new developments

During the first session, Dr Duncan Steele from the Bill & Melinda Gates Foundation gave an overview on rotavirus in Africa. Rotavirus infection is the most common cause of severe dehydrating diarrhoea worldwide. In Africa, it is estimated that approximately 290,000 children less than 5 years of age die each year due to acute rotavirus diarrhoea, resulting in more than half of global deaths [1]. Furthermore, 14 out of 15 countries with the highest rotavirus associated mortality rates per capita are in Africa [2]. In the continent, rotavirus detection occurs in a median of ~28% of children with diarrhoeal illness and in approximately 40% of young children hospitalized with diarrhoea. Rotavirus infection occurs early in life, 36% of infants <6 months of age, 75% of children aged <12 months; 83% in children <18 months of age and peak infection occurred in children aged 6–18 months old. It was noted that eight African countries (South Africa, Sudan, Rwanda, Ghana, Malawi, Zambia; Lusaka, Botswana and Tanzania) have introduced the rotavirus vaccine into their national childhood immunization programme, or started immunization in limited introduction projects. The GAVI Alliance has approved funding for rotavirus vaccine introduction for the following additional African countries; Angola, Burundi, Cameroon, Central African Republic, Democratic Republic of Congo, Djibouti, Ethiopia, Guinea Bissau, Madagascar, Niger, Sierra Leone, Togo and Zimbabwe.

Prof George Armah, from the University of Ghana gave an overview of rotavirus vaccine efficacy trials conducted with the two commercial vaccines in Africa during the period 2002–2009. In addition to highlighting the characteristics of rotavirus that

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were important for vaccine development, Prof Armah described the observed efficacy of the two commercial vaccines [Rotarix™, GSK Biologicals, Rixensart and RotaTeq®, Merck & Co., Pennsylvania] in Africa [3,4], and the significant public health benefit of the vaccines in African populations which resulted in a WHO global recommendation for the use of these vaccines [5].

Prof Armah, also described a recent vaccine trial in Ghana with the Rhesus–human rotavirus reassortant vaccine (RRV-TV), originally licensed as RotaShield by Wyeth Vaccines, but later withdrawn from the market by Wyeth due to an observed association of increased risk of intussusception in vaccinated infants. Prof Armah explained the design, clinical efficacy (75–100% against dehydration, 70–100% against hospital admission and 69–73% against doctors' visits or illness) and occurrence of intussusception associated with RotaShield® in the USA. A comparison of the potential risk of intussusception cases associated the monovalent (Rotarix™; a registered trademark of GlaxoSmithKline) and pentavalent (RotaTeq®; a registered trademark of Merck) vaccines was also discussed [6,7], indicating that all rotavirus vaccines may carry this risk.

The new study with RRV-TV was conducted in neonates in Ghana, as rotavirus infection develops early in life in developing countries, and the risk of reactogenicity and intussusception should be minimized in this age group. The vaccine was given to children before 30 days of age with a second dose 30–60 days later. While the IgA sero-response rates were lower than those recorded for the pentavalent rotavirus vaccine during similar studies in Ghana, the efficacy of the rhesus vaccine against severe gastroenteritis from any serotype was 57.6% and from serotypes contained in the vaccine formulation was 60.5% [8]. These results were compared to those obtained with the monovalent and pentavalent vaccines during the first year of life against severe disease (60.5% versus 61.2% and 64.2%) and against any severity (63.1 versus 53.4% and 30.5%) [3,4,8]. Prof Armah concluded that rotavirus vaccines were safe and immunogenic in African children, had demonstrated efficacy and protection against strains not present in the vaccine formulations and that neonatal rotavirus vaccination could be considered for African children, based on the data from the RRV-TV neonatal vaccine trial.

The monovalent human rotavirus vaccine was introduced into the South African Expanded Program of Immunization (EPI-SA) in August 2009, administered at the novel schedule of 6 and 14 weeks of age. Dr Jocelyn Moyes from NICD presented data on the rotavirus surveillance initiated in April 2009 in children <5 years from four sentinel sites (Chris Hani Baragwanath Hospital in Johannesburg, Dr George Mukhari Academic Hospital in Pretoria, Edendale Hospital in Durban and Agincourt in Limpopo Province). In 2009 (May–December), 46% (404/883) of samples tested rotavirus positive, decreasing to 33% (192/580) ($p < 0.001$) in 2010 and 29% (113/396) ($p < 0.001$) in 2011 after immunization was introduced. In children aged <1 year, estimated rotavirus hospitalizations were 60% ($n = 214$) and 65% ($n = 187$) lower, in 2010 and 2011, respectively when compared to 2009 ($n = 534$). All diarrhoeal hospitalizations in children <1 year were 34% (714/1077) and 34% (712/1077) lower in 2010 and 2011, respectively. The vaccine coverage in children <1 year was 50–90%. The study demonstrated a substantial reduction in rotavirus hospitalizations in the two years following the introduction of rotavirus vaccine into the EPI. Reduction was most pronounced in children aged <1 year with a specifically design case-control study nearing completion that will quantify the vaccine effect [9].

The WHO Regional coordinator on new vaccines surveillance, immunization and vaccines development (IVD), Dr Jason Mwenda, explained that rotavirus surveillance was conducted in Africa to provide high quality data to estimate the burden of rotavirus diarrhoea in children <5 years, to document circulating rotavirus strains in the AFR region, to support awareness and regional advocacy efforts for the introduction of rotavirus vaccines, to raise awareness of diarrhoea disease, to use the current network to monitor intussusception pre- and post-rotavirus vaccine introduction and to evaluate the impact and effectiveness of the new rotavirus vaccines [10]. It was highlighted that all the African surveillance sites use standardized protocols, new vaccines surveillance data management module and report data monthly to Ministries of Health and WHO, and that performance is monitored using standard indicators. The Regional Reference Laboratories (RRL), based at University of Limpopo (Medunsa Campus), South Africa and Noguchi Memorial Institute in Ghana, support the African Rotavirus Network rotavirus strain surveillance and training.

Dr Mwenda described rotavirus surveillance data generated from 19 African countries between 2006 and 2011 [11,12]. A total of 33,068 (range 1351–10,922) children aged <5 years with diarrhoea were enrolled in the surveillance; and stool specimens were collected from 29,853 (90%; range 1206–9484) and tested for rotavirus infection with enzyme immunoassay (EIA). The rotavirus detection rate varied from 34%–45% among enrolled children with acute gastroenteritis. Strain genotyping demonstrated that the common rotavirus strains identified across the region were G1P[8], G9P[8], G2P[4], G4P[8] and notably other regionally common genotypes included G6P[6], G10P[6] and G8P[14].

3. Intussusception monitoring before and after introduction of oral rotavirus vaccines

Intussusception is a rare, but important cause of acute intestinal obstruction in young children. It occurs when one segment of the bowel invaginates into another, resulting in venous congestion and bowel wall oedema. The first licensed rotavirus vaccine (RRV-TV) was associated with an increase in the incidence of intussusception in USA in 1998 and later the vaccine was withdrawn for routine use. Since the withdrawal of RRV-TV, two rotavirus vaccines (a monovalent and pentavalent product) have been licensed in many countries. During the large clinical trials conducted in high and middle-income countries to evaluate safety of these vaccines, there was no observed significant increased risk of intussusception among infants given the two current rotavirus vaccines.

Post-licensure effectiveness and safety of rotavirus vaccines data from USA, El Salvador, Mexico, Brazil and Australia was presented by Dr Umesh Parashar from the Centers for Disease Control Prevention (CDC) in Atlanta. The data showed a marked decline in rotavirus positive samples from young children with diarrhoea, after vaccine introduction in both high and middle-income countries, and the exciting possibility of herd immunity in unvaccinated children. In addition, there was a detectable but low intussusception risk identified in post-licensure vaccine safety monitoring in Australia, Mexico and Brazil once thousands of children had been vaccinated [13].

WHO has recommended that post-licensing surveillance for intussusception, and establishing baseline data and monitoring intussusception is essential for countries introducing the currently licensed rotavirus vaccines. Dr Michelle Groome (University of the Witwatersrand, Johannesburg) summarized baseline intussusception data from South Africa. These included studies at the Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) where 97 cases (3 months to 3 years of age) were identified between January 2007 and April 2010. Further studies were done at the East London Hospital Complex at the Walter Sisulu University (identified 10 cases in 2011), Cape Town (20 cases per year) and Stellenbosch (14 cases in 2011). In some centres, more than half of the intussusception cases were referred from surrounding facilities and resection rates varied

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