

Evaluation of the Vaccine Effectiveness in the Field of Rotarix® in Children Aged 0 to 2 Years in Certain District Hospitals of the Center Region-Cameroon

Jeanne Valerie Emvoutou Maboulou¹, Aicha Ngoutane², Souleymanou Bakary³, Justin Olivier Essindi⁴, Dr Ngonde Marie Chantal⁵

^{1,2,5}Institute of Medical Research and Medicinal Plants Studiess

³Local Materials Promotion Mission

⁴Faculty of sciences: department of microbiology

ABSTRACT

Summary

Rotavirus (RV) is the main cause of acute gastroenteritis (GE) in children under 5 years of age with a high incidence between the ages of 6 and 23 months. After one year of introduction in the EPV in Cameroon, it was interesting to evaluate the vaccine efficacy of Rotarix in the field. To this end, we set ourselves the objective of evaluating the field efficacy of Rotarix® in children aged 2 to 24 months in selected District Hospitals of the Centre-Cameroon Region. We conducted a case-control study in children aged 2 to 24 months ; 77 subjects were included in our study and stool samples were collected from March to August of 2015. Antigenic detection of Rotavirus was carried out by an immunochromatographic test (rapid test). We had a sex ratio of 1.3 in favour of the male sex ; the age groups most represented were those of 2 to 6 months and 18-24 months, i.e. 28.6% each ; 50 subjects had been vaccinated (exposure to the protection factor) with 1 positive case and 27 non-vaccinated with 6 positive cases, i.e. a vaccination coverage of 64.94%. Of the subjects found positive, those in the 2-12 months age group represented 42.9%, compared to 57.1%. For vaccine efficacy, statistical analysis was performed using Epi info software version 7.1.3.0 and the odds ratio was estimated to be 0.0714 with 95% CI bounds 0.0081; 0.6305. The resulting field efficacy according to the WHO proposed formula is 92.86% with 95% bounds of CI 36.95% to 99.19%. These results should be complemented by similar studies for each region of the country to determine the field efficacy of Rotarix in Cameroon.

KEYWORDS: Rotavirus, vaccine effectiveness, Rotarix®, children.

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INTRODUCTION

Rotaviruses belong to the family of Reoviridae, of the genus Rotavirus, [1]. these are non-enveloped viruses, with icosahedral symmetry, whose size is between 65 and 75 nanometers in diameter [2]. Their targets are the enterocytes which are the most numerous cells of the epithelium of the small intestine and which are responsible for the absorption phenomenon [3,2], thus becoming the leading cause of severe diarrhea (gastroenteritis) in children worldwide, the mode of transmission is mainly the faecal-oral route, direct or indirect [4]. Rotavirus diarrhea is one of the main causes of infant mortality and there are approximately 527,000 deaths per year among children under five [5,6]. The highest cases of

case fatality are often recorded in Asian and African countries which are characteristic of low-income countries [7,8]. The mode of transmission of rotavirus is mainly the faecal-oral route, direct or indirect [4].

Each year, more than 110 million episodes of acute gastroenteritis worldwide are secondary to rotavirus

Infection. Severe forms characterized by acute dehydration that can lead to the death of children are to be feared in the youngest aged 6 to 24 months. According to the surveillance network coordinated by the World Health Organization (WHO), 38% of children aged under 5 hospitalized in 2012 for severe diarrhea in Africa were infected with rotavirus [9].

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In Cameroon, the total number of deaths in 2010 of children under 5 due to diarrhea was 12,150, while 5,825 of the cases of diarrhea recorded in 2008 were due to rotavirus [10]. With the marketing of two oral vaccines against rotavirus in 2006, the Rotarix® (GlaxoSmithKline) and Rotateq® (Sanofi Pasteur) vaccines, the WHO has taken a strong position by recommending that this vaccine can be integrated into all priority vaccination schedules, especially in countries with a high mortality rate for rotavirus gastroenteritis in Africa, in Southeast Asia and South America [9]. Large-scale clinical trials carried out in Africa, in Latin America, Asia, the United States of America and Europe have demonstrated the safety and clinical efficacy of these two vaccines available today on the international market. Following this clinical efficacy, many countries have added the rotavirus vaccine to their national vaccination program and, on March 28, 2014, the Cameroonian government introduced Rotarix® into its Expanded Vaccination Program. It is therefore important, after clinical efficacy has been proven and after one year of vaccination, to determine the efficacy of this vaccine in the field.

MATERIALS AND METHODS

Materials

We conducted an analytical case study in the Central Cameroon region, from March to August 2015. It took place in the following hospitals: Biyem-Assi district hospital, Cité Verte district hospital and Mfou hospital. We obtained permission to collect data from the various hospitals contacted and informed consent from the children's parents. We included a total of 77 children of both sexes and aged 2

to 24 months. The inclusion criteria were as follows: any child aged between 2 and 24 months, brought to the hospital with diarrhoea as the reason for consultation. The inclusion criteria were as follows: any child aged between 2 and 24 months, brought to the hospital with diarrhoea as the reason for consultation. Excluded from the study were any children who had received a single dose of Rotarix vaccine less than two weeks prior to stool collection or children who did not have a vaccination record. A questionnaire which included the child's socio-demographic data, the mother's knowledge, attitudes and practices towards the vaccine and rotavirus gastroenteritis and the child's vaccination status on the Rotarix vaccine. Finally, once the questionnaire was completed, we collected the child's stools in sterile stool jars directly or in their nappies.

METHODOLOGY

All stools in the study were subjected to the GlaxoSmithKline rotavirus Antigen Rapid Test. It is a qualitative immunochromatographic test based on the principle of the recognition of an antigen by its antibody and the formation of an antigen-antibody complex detectable on the test control area and the control area by the appearance of a red band in case of the presence of rotavirus antigen in the child's stool. The test is negative if there is a single red band in the control area and the test is invalid if there is no red band in the control area. The numerical analysis of the data (Questionnaire) and their presentation were carried out using two software packages : Epi Info™ version 7.1.3.0 and Microsoft Excel 2013.

The odd Ratio was used to make statistical comparisons.

RESULTS

Table 1 : Sociodemographic characteristics

Variables	Frequency	Percentage %
SEXE		
Female	39	50.74
Male	38	49.30
AGE(Month)		
2-6	22	28.6
6-12	11	14.3
12-18	22	28.6
18-24	22	28.6

Of the 77 subjects in our study, a total of 39 were female (50.65%) and 38 were male (49.35%). We also observed that the age ranged from 2-24 months and the brackets were almost homogeneous with a percentage of 28.6% for each except the 6-12 months bracket which was 14.3%.

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Table 2: Knowledge about rotavirus

Variables	Frequency	Percentage %
Have you ever heard of rotavirus ?	N =77	
Yes		
No	26	33.77
Do you know the modes of transmission ?	51	66.23
Yes		
No	N=26	
Modes of transmission	14	53.85
Soiled water and soiled diapers	12	46.15
Soiled water	N=14	
	8	57
	6	43

To the question "Have you heard of rotavirus diarrhoea? Only 33.77% of mothers answered "YES", i.e. 26 out of 77. Regarding the transmission of rotavirus diarrhoea, 53.85% or 14 out of 26 mothers who had heard about rotavirus said they knew how it was transmitted. Regarding the transmission of rotavirus diarrhoea, 53.85% or 14 out of 26 mothers who had heard about rotavirus said they knew how it was transmitted. Of the 14 mothers who knew how rotavirus is transmitted, 8 said that it can be transmitted by drinking dirty water alone, while the other 6 added handling nappies and children's stools to dirty water.

Table 3 : Attitudes towards the rotavirus vaccine

Variables	Frequency	Percentage %
Have you had your child vaccinated against rotavirus ?	N=77	
Yes		
No	50	65
Have you observed any side effects?	27	35
Yes	N=50	
No		
No response	13	26
	35	70
	02	4

We recorded 50 subjects who were vaccinated, i.e. a vaccination coverage of 65%. Of the 50 children vaccinated, the mothers of the 48 children answered the question on side effects and 2 mothers gave no answer. Thirteen said that their children experienced side effects after vaccination, i.e. 26%.

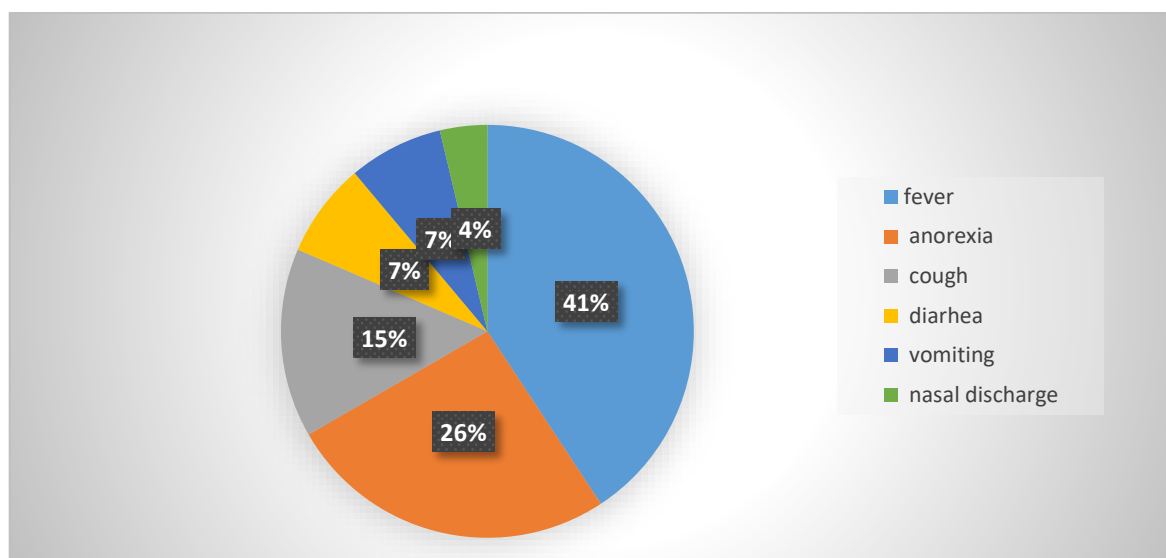


Figure 1: Distribution of adverse events in children vaccinated against rotavirus

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Table 4 : Rotavirus rapid test result

Vaccination	Positive	Negative	Total	Frequency of positives
Vaccinated	1	49	50	2%
Unvaccinated	6	21	27	22,22%
TOTAL	7	70	77	9,09%

Our sample consisted of 77 children with 7 cases (positive for rotavirus) and 70 controls (negative for rotavirus). Among the 77 subjects, 50 were vaccinated with 1 positive case or 2% and 27 non-vaccinated with 6 positive cases or 22.22%.

- Calculation of Vaccine Effectiveness (VE)

Determination of Odds Ratio (OR)

Table 4 : Cross-tabulation between rotavirus test result (Disease) and vaccination.

Disease			
Vaccination (Exposure)	Positive (Case)	Negative (control)	Total
Yes (Exposed)	1	49	50
No (Non-Exposed)	6	21	27
TOTAL	7	70	77

Table 5 : Determination of the Odds Ratio

	Valeur	Confidence interval to 95%	
	Estimation	Lower	Upper
PARAMETERS :			
Odds Ratio (cross-over product)	0,0714	0,0081	0,6305 (T)

T=Taylor series

The Odds Ratio for this cross is estimated to be 0.0714 with 95% confidence interval bounds [0.0081; 0.6305].

Vaccine Effectiveness (VE) formula :

$$VE = (1 - OR) \times 100$$

$$VE = ?$$

$$OR = 0,0714 \quad 0,0081 ; 0,6305 (T)$$

Numerical application : $VE = (1 - 0,0714) \times 100$

$$VE = 92,86\%$$

$$EV=92,86\% \text{ (95\% IC } 36,95\% \text{ à } 99,19\%)$$

The field efficacy of Rotarix found in this study is 92.86% with a 95% confidence interval (36.95% to 99.19%).

DISCUSSION

After one year of introduction in the extended vaccination program (in Cameroon), the health authorities and the population need to know the real vaccine effectiveness in the field after those obtained during the studies carried out before the marketing authorization. market, like those carried out on African children [11]. and studies to determine safety and

extent of side effects [12]. This case-control study responds to this expectation by highlighting the real effectiveness in the field of vaccination against rotavirus (Rotarix-GSK) undertaken in Cameroon since March 2014 in children under 5 years of age in the Center region. -Cameroon. Indeed, after two doses of Rotarix vaccine, each child in the Center region of Cameroon has a 92.86% (95% CI 36.95% to 99.19%) chance of being protected from rotavirus diarrhea.

1- Socio-demographic characteristics

The sex ratio of this study was 1.3 in favour of boys, which corroborates the results of Etoa's study carried out in Yaoundé in 2008/2009, which obtained a sex ratio of 1.19, i.e. 53.8% for boys against 46.2% for girls [13] and also with Fadoua's study in 2010, which obtained a predominance of boys of up to 60% [14]. The distribution of positive cases by age group in this study showed a slight bias towards the 13-24 month age group ; however, other studies have shown that the disease was more prevalent in children younger than 12 months, with 70.12% in the 2-11 month age group compared to 25% in the 12-23 month age group in Etoa [13] the age

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group 2 to 11 months represented 45.8%, against 41.3% for the age group 1-2 years in Akoua Koffi [15]; and up to 80% for the section < 12 months at Fadoua [14].

This observed difference could be explained by the sample size of the cases which is very small $n=7$ for this study compared to that of Etoa's study which was 164 [13] or the other studies which also had a larger sample.

2- Mothers' knowledge and attitudes towards rotavirus diarrhoea

As for the mothers' knowledge of rotavirus diarrhoea, 26 mothers out of 77 said they had heard of this disease, i.e. 33.77% ; of the other 26, only 14 knew how this disease is transmitted; 8 of them thought that transmission was only waterborne, and the other 6 said that, in addition to contaminated water, transmission could take place through the handling of children's nappies or stools. There was no statistically significant relationship between knowledge of rotavirus diarrhoea and the occurrence of the disease in children: we obtained an Odds Ratio of 1.5326, (95% CI 0.3164; 7.4250). However, in the absence of other data for comparison, it could be assumed that a larger sample size would have produced different results and may explain the low vaccination coverage found. Concerning the vaccination against rotavirus, the vaccination records allowed us to determine the vaccination coverage of our study population which was 65%, i.e. 50 vaccinated and 27 unvaccinated; contrary to Detol who had found in his study a vaccination coverage of 61.47% in Yaounde [16], in Panama V. Bayard et al had found in their studies vaccine coverage of 30%, 62% and 71% respectively for the years 2006, 2007 and 2008 [17]. The vaccination coverage determined in our study is much lower than that observed in Belgium in 2011, which was 90% [18]. These differences can be explained by the fact that in Cameroon this vaccine has just been set up (1 year in the field) whereas in Belgium, for example, this vaccine has already been in the field for about 5 years and the populations have already been well sensitised to adhere to the vaccination. This study allowed us to detect some side effects related to the vaccination with Rotarix from GlaxoSmithKline Vaccines; out of the 50 children vaccinated, 13 presented some after vaccination; we counted 11 cases of fever, 7 cases of lack of appetite, 4 cases of coughing and other signs of lesser recurrence such as diarrhoea, vomiting and runny nose; this corroborates with the results of Buyse who found similar side effects [12]. However, these side effects could well have been those of other vaccines given to children on the same day; however, no conclusions can be drawn without further, well-founded studies on the subject.

3- Determination of vaccine efficacy

To calculate vaccine efficacy in the field, we determined an Odds Ratio of 0.0714 at 95% CI [0.0081; 0.6305] statistically significant and being well below 1, this indicates that exposure to the factor studied, which is vaccination with

Rotarix®, provides good protection against the disease. The vaccine efficacy obtained was 92.86% (95% confidence interval 36.95% to 99.19%), this value was much higher than that found in the available randomized clinical studies conducted before the authorization of marketed like the study by Shabir et al in Africa which had obtained an efficacy of 61.2% (95% confidence interval, 44.0% to 73.2%) [19]. This vaccine efficacy was also higher than Bernstein's data [20] compared to the two doses provided by the Rotarix® vaccine: 53.9 to 81.5% and 81.2 to 93.0%. It was slightly higher than that found in the case-control study carried out between 2008 and 2010 in Belgium where the vaccine efficacy was 90% (95% confidence interval 81% to 95%) [18].

The vaccine efficacy closest to that found in our study was 91% (95% confidence interval 80 to 95%) this was the study carried out by Cortese et al in the United States from 2010-2011 [21].

Compared to our study, the lowest vaccine efficacy in the field was found in Latin America in Nicaragua with 46% according to the report by Desai et al [22]. Another field vaccine efficacy of two doses of Rotarix was 76% for the study by Palma et al between 2007 and 2009 in El Salvador [23] which is also low compared to that of we obtained by our study;

The field vaccine efficacy of Rotarix could also be compared to that of Rotateq which was determined in the United States by Boom et al where they obtained 89% (95% confidence interval: 70% to 96%) [24].

Several studies had been conducted to determine the vaccine efficacy of the rotavirus vaccine, despite the different socio-demographic situations, different epidemiology, different disease severity and different lifestyles, the majority of studies that had been carried out in the field (in various countries) had shown that the vaccine efficacy observed was greater than that expected.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

CI : Interval confidence
EPV : Expanded Program of Vaccination
GE : Gastro enteritis
GSK : GlaxoSmithKline
OR : Odds Ratio
RV : Rotavirus

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VE : Vaccine effectiveness

WHO : World Health Organisation

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