The Impact of Rotavirus Vaccination on The Diarrhea Admission and Mortality Rate in Children at WMTHC, Gezira State, Sudan

**Mai Abdalla Ali[1]*, Fatima Kamal[1] , Imad Taj Eldin Mohamed[2]
and Siddig Ahmed Gibril Rahoud[1]**

[1]Center of Bioscience and Biotechnology,Gezira University, P.O.Box 20 Wad Madani, Sudan
[2]Deparment of Pharmacology, Faculty of pharmacy, Gezira University, P.O.Box 20 Wad Madani, Sudan

*Corresponding Author
 E-mail: maiadil@yahoo.com

Abstract

A prospective study was conducted at Wad Madani Teaching Hospital for Children (WMTHC), among children below the age of five years. All the children included in this study were admitted with diarrheal disease in the period between January 2011-May 2012.The main objective of this research was to study the impact of rotavirus vaccination on the rate of diarrhea admission andmortality among children. The study population was checked for rotavirus vaccination status (rotavirus vaccine), stool samples were examined for rotavirus in the hospital laboratory, and

children with other illness causing diarrhea were excluded from the study. The study was divided in to three phases each of six months period, phase one six months before the implementation of the vaccine included 249 child, phase two six months after the implementation included 304 child and phase three another six months post the vaccine implementation included 120 child, according to the total number admitted during the period of the study. The total number of vaccinated children increased significantly (P.value =0.000) from the first year of vaccine adoption (7.2% to 47.5%), and the majority of vaccinated children were below six months of age. Slight decline in diarrhea related mortality was noticed after the introduction of rotavirus vaccination (from 9.6% to 7%) , while, an increase was noticed on the rate of diarrhea hospital admission(600.4 to 643.6) ,but, no significant differences (P.value = 0.71355197) was noticed between the rate of admissions or deaths in regard to the known rotavirus seasonality in Sudan pre-and after the implementation of the vaccine .A significant difference (P.value =0.000) was observed of rotavirus detection between the first post-vaccine adoption period and the pre-vaccination period ,although, no significant was noticed among the two periods of vaccine adoption.

*Keywords***:** Rotavirus –vaccine – diarrhea – children – Sudan- WMTHC.

Introduction

Rotavirus is a double-stranded RNA virus of the family Reoviridae , posses a characteristic wheel-like appearance when viewed by electron microscopy [1]. Rotavirus is considered as the most common cause of severe diarrhea among infants and young children, beside being one of several viruses that cause infections often called stomach flu , despite having no relation with influenza [2] . There are a number of different strains of rotavirus, referred to as A, B, C, D, and E. while Rotavirus A, have accounted for around 90% of infections worldwide [3]. Rotaviruses are transmitted by the faecal-oral route. Large numbers of viral particles are shed in faecal matter and the virus is quite stable in the environment, so contamination of hands and objects (fomites) is relatively easy and virus excretion can occur in individuals without symptoms [4]. Children can be infected with rotavirus several times during their lives, once a child is infected by the virus, there is an incubation period of about two days before symptoms appearance ,and the illness spectrum can ranges from mild, watery diarrhoea of limited duration to severe dehydrating diarrhoea with vomiting and fever, which can lead to death [5].

The primary public health decided the intervention of vaccination because improved sanitation

does not decrease the prevalence of rotaviral disease, and the rate of hospitalizations remains high, thus two vaccines were developed against Rotavirus A infection [6], Rotarix by GlaxoSmithKline and RotaTeq by Merck both were taken orally and contain attenuated live virus [7]. Rotavirus vaccines are licensed in more than hundred countries, but only seventeen countries have introduced routine rotavirus vaccination [8]. The World Health Organization (WHO) recommends that rotavirus vaccine be included in all national immunization programs [9]

Sudan is the first country in Africa to introduce a rotavirus vaccine   with the support of GAVI. The decision to introduce the vaccine was based on WHO-supported gastroenteritis surveillance in Sudan, which found that, from more than 9000 stool samples, 33% tested positive for rotavirus and 42% of these positive cases were among infants aged less than eight months [10]. Clinical trials of the Rotarix rotavirus vaccine in Sudan is needed to illustrate wither the vaccine significantly reduced severe diarrhea episodes caused by rotavirus, and that the infection was preventable by vaccination. Thus the objective of this study is to measure the impact of rotavirus vaccination on the rate of diarrhea admission and mortality among children at the Gezira State - Sudan.

Materials and methods

The study included children admitted with GE to Wad Medani Teaching Hospital for Children between January 2011 and May 2012 .The inclusion criteria concerned with children admitted with GE for more than 24 hours, while the exclusion criteria includes children admitted with GE due to pathogens other than rotavirus ,children whose care providers givers refuse to be enrolled in the study and children diagnose to have other illnesses presenting with diarrhea eg malaria.

The Study tools

A questionnaire was distributed to medical personnel during the study. The questionnaire

investigated the duration of the illness, vaccination status and the outcome of the illness. Ethical consideration was discussed with the hospital ethical committee and it was approved, beside a verbal consent was taken from care providers giver before enrolling children in the study. Stools samples were tested for rotavirus infection using Enzyme link immunosorbent assay (ELISA) test at the hospital laboratory.

Sample collection

A total of 673 stool samples were collected from children who fall within the period of study (January 2011-May2012) with gastroenteritis, after each patient was examined by a physician, the stool samples were collected using a sterile wide mouth universal containers and these container were covered and labeled accordingly. Between 4-5 mls of diarrheic stool samples were collected from each child.

Procedure for the ELISA test:

Both test devices and extracted samples were allowed to attain room temperature prior to the test. A disposable dropper was used to add 1 ml of sample diluents into a sample collection tube. A bout 50mg of the feces were collected from the stool sample that presented the most secretion under visual inspection using a sterile sample collection swab. The swab was inserted into a sample collection tube which contained 1 ml of sample diluent and swab was swirled for at least 10 times to make a mixture. Faecal specimen storage can be   done at 2-8°C for 72 hours. About 3-4 drops of the mixture were added into the sample well at the ELISA plate. The plate was incubated for 10-20 minutes at room temperature and result was read.

Results and discussion

The total number of children who received the vaccine was 22 in the first 6month , in the 2nd 6month post vaccine implementation the number of vaccinated children increased to 57.The vaccine coverage increased from 7.2% in year 2011 to 47.5% in year 2012 (Table .1.). The

Table 1: Vaccine coverage

Vaccine Coverage during the period of July – December 2011			Vaccine Coverage during the period of January –May2012	
Vaccination status	Frequency	Percent	Frequency	Percent
Vaccinated	22	7.2	57	47.5
Not vaccinated	282	92.8	63	52.5
Total	304	100.0	120	100.0

- **Chi-square value = 92**   **d.f = 2**   **P.value =0.000**

Table 2: Age of vaccination

	The age of vaccination in the period of 2011(July-December)			The age of vaccination in the period of 2012 (January –May)		
Age/M	vaccinated	Not vaccinated	Total	vaccinated	Not vaccinated	Total
2m-6	18	37	55	40	14	54
7m-12	3	173	176	14	26	40
13m-18	0	50	50	0	17	17
19m-24	1	16	17	1	5	6
25m-30	0	1	1	0	0	0
31m-36	0	3	3	0	1	1
37m-42	0	1	1	2	0	2
43m-49	0	1	1	0	0	0
Total	22	282	304	57	63	120

Chi-square value = 65.674,   d.f = 7, P.value =0.000   Chi-square value = 38.58, d.f = 7, P.value =0.000

majority of vaccinated children were below 6month of age in both 2011 and 2012 (Table 2).It was noticed that there is increase in the society awareness about the importance of the vaccine and this awareness was reflected on the significant increment of the vaccine coverage in the second post vaccine adoption period (P.value =0.000**) .**

Before and after the implementation of the vaccine , the age of five to nine month represent the highest age of admission 34% ,39.8% and 39.2% ,and showed a great significance (P.value =0.000) when compared to the others ages of admissions throughout the different periods of the study (Table. 3.).This was expected as most of the Sudanese mothers starts the supplementary feeding around the age of four months. The overall age of admissions according to the diarrheal diseases were less than five years of age , as stated by Salinas *et al*. [11] and Nokes *et al*. [12].

After the implementation of the vaccine, higher hospital admission rate was noticed, due to diarrhea (643.6 case) compared to the rate of admission prior to vaccination (only 600.4 case), while, a slight decline occurred on the related mortality from 9.6% to 7% , however, in other countries like Brazil after the introduction of the rotavirus vaccine for three years continuous decline was noticed in both diarrhea mortality and hospital admissions [13], so an accumulation time factor may be needed in order to get the same effect in Sudan.

The comparisons of both the admissions and deaths of one year data according to the rotavirus known seasonality in Sudan, prior and after the implementation of the vaccine revealed that ,there is no significant differences (P.value = 0.71355197) between the rate of admissions or deaths pre-and after the implementation of the vaccine (Table.4.).

Before the implementation of the vaccine 47.8% (119 out of 249) of children with diarrhaeal

Table 3 : Different ages of admission

The different ages of admission in the pre – vaccination period 2011 (January –June)			The different ages of admission at the first post vaccination period 2011 (July-December)		The different ages of admission at the second post vaccination period 2012 (January-May)	
Age	frequency	Percent	frequency	percent	frequency	Percent
1m-4	51	20.4	29	9.5	37	30.8
5m-9	85	34	121	39.8	47	39.2
10m-14	62	25	94	30.9	14	11.7
15m-19	22	9	38	12.6	13	10.8
20m-24	22	9	16	5.3	6	5.0
25m-29	2	0.8	1	0.3	0	0
30m-34	2	0.8	2	0.7	0	0
35m-39	3	1	1	0.3	2	1.7
40m-44	0	0	1	0.3	0	0
45m-49	0	0	1	0.3	1	0.8
Total	249	100	304	100	120	100

Chi-square value = 50.974,   d.f = 18,   P.value =0.000

disease were rotavirus positive , while 52.2% (130 out of 249) were rotavirus negative . In the first six months of the vaccine adoption 27.3% (6 out of 22) of the total vaccinated children showed a positive rotavirus detection results , which presents only 2% from the total admission (6 out of 304) .While 72.7 % (16 out of 22) of them were negative ,that represents 98% of the total admission (16 out of 304). At the second post –vaccine period , the total detection results revealed 56 % of children rotavirus positive among the vaccinated ones (32 out of 57) which

Table 4 : Comparisons of the admissions and deaths according to rotavirus seasonality pre- and after the implementation of the vaccine.

	Pre –vaccine period (1-7-2010/30-6-2011)			Post-vaccine period (1-7-2011/30-6-2012)		
Season	Adm Average/m	Deaths Aver/m	Death% Aver/m	Adm	Deaths	Deaths%
Peak season (May-September)	303	11	3.9	300.2	7	2.4
Second mild season(October-February)	156.4	3.8	2.4	169.4	4.6	2.7
Third light season (March-April)	141	5	3.3	174	3.5	1.9

Chi-square = 0.675 d.f=2 P.value = 0.71355197

presents 27 % from the total admission (32 out of 120) .And 44 % of the vaccinated children were rotavirus negative (25 out of 57) ,and this presents 21% of the total admission(25 out of 120) (Table.5.).

An overall observation , there is a significant results obtained regarding the percentage of rotavirus detection after the first post vaccine adoption period compared to the pre vaccination period (P.value =0.000) ,although , no significant was noticed among the two periods of adoption. This could be justified by considering the fact that early infection and frequent

re-infection in a locale with high viral diversity could result in lower protection than has been reported elsewhere**.**

Table 5 : The rotavirus detection results

The Rotavirus detection results at the pre-vaccination period 2011 (January –June).			The Rotavirus detection results at the first post-vaccination period 2011 (July-December).		The Rotavirus detection results at the second post-vaccination period 2012(January-May)	
Vaccination status	Rotavirus results		Rotavirus results		Rotavirus results	
	Positive	**Negative**	**Positive**	**Negative**	**Positive**	**Negative**
Vaccinated	0	0	6	16	32	25
Not vaccinated	119	130	80	202	31	32
Total	119	130	86	218	63	57
	(1)		**(2)**		**(3)**	

1. **Chi-square value = 125.472,   d.f = 1, P.value =0.000**
2. **Chi-square value = 0.012 ,   d.f = 1, P.value =0.912 not sig**
3. **Chi-square value = 0.577,   d.f = 1, P.value =0.447 not sig**

Conclusion

The rotavirus vaccine coverage in Gezira area increased during the post vaccine period and the majority of vaccinated children were below 6 months of age. The admissions due to diarrheal diseases, was commonly for the age-range of five to nine months. Significant decline in diarrhea related mortality was noticed after the introduction of rotavirus vaccination, while , an increase was noticed on the rate of hospital admissions due to diarrhea . No significant differences between the rate of admissions or deaths in regard to the known rotavirus seasonality in Sudan pre-and after the implementation of the vaccine .A significant difference was there in rotavirus detection between the first post vaccine adoption period and the pre vaccination period ,although no significant was noticed among the two periods of vaccine adoption.

From this study we concluded that although, there is marked reduction in the mortality rate after the vaccine implementation and this could not just be attributed to the vaccine as the number of vaccinated children was small and there could be other factors contributing to the overall reduction in the mortality. Additional studies including larger sample is required to improve the overall understanding of the performance of rotavirus vaccines in Sudan.

Acknowledgement

References

1. Bishop, R. F., Davidson, G. P., Holmes, I. H. and Ruck, B. J. (1973). Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. Lancet, 2, 128 1

2. Dennehy PH .(2000). "Transmission of rotavirus and other enteric pathogens in the home". Pediatr. Infect. Dis. J. 19 (10 Suppl): S103–5. doi:10.1097/00006454-200010001-00003. PMID 11052397.

3. Grimwood K, Lambert SB . (2009). "Rotavirus vaccines: opportunities and challenges". Human Vaccines 5 (2): 57–69. doi:10.4161/hv.5.2.6924. PMID 18838873. http://www.landesbioscience.com/journals/hv/abstract.php?id=6924

4. Cunliffe, N. A., and Nakagomi.O (2005). A critical time for rotavirus vaccines: a review. Expert Rev. Vaccines 4**:**521-532.

5. Dennehy PH .(2008). "Rotavirus vaccines: an overview". Clin. Microbiol. Rev. 21 (1): 198–208. doi:10.1128/CMR.00029-07. PMC 2223838. PMID 18202442. http://cmr.asm.org/cgi/content/full/21/1/198?view=long&pmid=18202442.

6. Kuzuya M, Fujii R, Hamano M, Nishijima M, Ogura H (.2007). Detection and molecular characterization of human group C Rotaviruses in Okayama Prefecture, Japan, between 1986 and 2005. J Med Virol 79: 1219-1228.

7. O'Ryan M .(2007). "Rotarix (RIX4414): an oral human rotavirus vaccine". Expert review of vaccines 6 (1): 11–9. doi:10.1586/14760584.6.1.11. PMID 17280473.

8. Matson DO .(2006). "The pentavalent rotavirus vaccine, RotaTeq". Seminars in paediatric infectious diseases 17 (4): 195–9. doi:10.1053/j.spid.2006.08.005. PMID 17055370.

9. Ward RL, Clark HF, Offit PA . (2010). "Influence of potential protective mechanisms on the development of live rotavirus vaccines". The Journal of Infectious Diseases 202 (Suppl): S72–9. doi:10.1086/653549. PMID 20684721.http://www.jid.oxfordjournals.org/cgi/pmidlookup?view=long&pmid=20684721.

10. World Health Organization-Report.(2011) The introduction of life-saving rotavirus vaccine in Sudan. 18 July .

11. Salinas B, González G, González R, Escalona M, Materán M, Schael IP. (2004) Epidemiologic and clinical characteristics of rotavirus disease during five years of surveillance in Venezuela. Pediatr Infect Dis J. Oct;23(10 Suppl):S161-7.

12. Nokes DJ, Abwao J, Pamba A, Peenze I, Dewar J, Maghenda JK, Gatakaa H, Bauni E,Scott JA, Maitland K, Williams TN.(2008) Incidence and clinical characteristics of group A rotavirus infections among children admitted to hospital in Kilifi, Kenya. *PLoS Med* ; 5:e153.

13. do Carmo GM, Yen C, Cortes J, Siqueira AA, de Oliveira WK, Cortez-Escalante JJ, Giaquinto C, Dominiak-Felden G, Van Damme P, Myint TT, Maldonado YA, Spoulou Gladstone BP et al. (2011) Protective effect of natural rotavirus infection in an Indian birth cohort. New England Journal of Medicine, ;365:337-346.

Authors Column

Mai Abdalla Ali Abdalla is presently attached to the University of Gezira, Wad Medani, Sudan as Associate professor of microbiology and biotechnology. Center of Bioscience and Biotechnology, Faculty of Engineering and Technology. She did Ph.D. in Molecular Biology in 2009. She has special training in molecular biology, RNA structure & function, molecular docking and it's application in bioactive molecule design and in bioinformatics. She has published 5 research papers in refereed journal and presented 17 papers in National & International conferences.