



A Comparison of Anti-Rotavirus Vaccines Monitoring of the Vaccination Activities Over the Period 2020-2022 in the Local Health Authority of Viterbo

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Abstract

Introduction: Rotavirus is an RNA virus that belongs to the family Reoviridae and is highly infectious. In addition to being one of the leading causes of acute gastroenteritis worldwide, it contributes most to mortality and morbidity in children under 5 years of age. The virus is mainly transmitted via the fecal-oral-route but it could also be spread by contact, from person to person or through contaminated objects, surfaces or food. Airborne transmission is also possible, although it is much less effective. Several studies have indicated that natural immunity acquired from infection offers both a certain degree of protection from future symptomatic infections and that repeated exposures expand a heterotypic immune response to different viral strains. This has been the essential premise upon which live-attenuated oral vaccines against Rotavirus have been developed over the past 30 years. In all countries – whether they are industrialized or developing – where vaccines against the virus have been introduced, a real impact on public health has been consistently observed, with significant reductions in mortality and hospitalizations due to Rotavirus diarrhea in children under 5 years of age. Two anti-Rotavirus vaccines, Rotarix Human Rotavirus Vaccine (GSK) and RotaTeq Human-Bovine Reassortant Vaccine (Merck & Co.), have been approved for clinical use in Europe and showed good efficacy and a favorable security profile in preventing Rotavirus disease.

Aim of the Study: The study aims to illustrate the Rotavirus vaccinations given at the vaccination centers located in the Local Health Authority of Viterbo during the three-year period 2020-2022. A comparison was conducted between the vaccination coverage reached with Rotarix and RotaTeq vaccines in newborns in 2020 and in 2021 residing in the province of Viterbo. Furthermore, adhesions to Rotavirus vaccination were detected.

Material and Methods: The scenario was defined through extrapolation of data recorded in the company software Antares. The following data were considered:

- Births in the year 2020 in the province of Viterbo
- Births in the year 2021 in the province of Viterbo
- Rotarix vaccines given in the three-year period 2020-2022
- RotaTeq vaccines given in the three-year period 2020-2022

- Anti-Rotavirus vaccination coverage among newborns in 2020
- Anti-Rotavirus vaccination coverage among newborns in 2021
- Percentage of newborns in 2020 who did not complete the anti-Rotavirus vaccination course
- Percentage of newborns in 2021 who did not complete the anti-rotavirus vaccination course

Results: From January 1st, 2020 to November 30, 2022, 9318 anti-Rotavirus vaccinations were given in the vaccination centers located in the Local Health Authority of Viterbo. Among these, 3124 patients received Rotarix, while 6194 received RotaTeq vaccine. Over the period analyzed, the 2021 birth cohort appears to be the most vaccinated, with 455 Rotarix and 3193 RotaTeq vaccinations, with a total number of 3648 vaccinations. A person can be defined as vaccinated against Rotavirus only when he/she finishes the complete vaccination course, consisting of 2 doses in the case of the Rotarix vaccine, and 3 doses in the case of the RotaTeq vaccine. For this reason, the total vaccination coverage reached among newborns in 2020 (1764 births) was 64%, in which Rotarix vaccine contributed 45%, and RotaTeq the remaining 19%. As regards the cohort of newborns in 2021 (1820 births), the total vaccination coverage reached was 66%, of which 12% with Rotarix vaccine, and 54% with RotaTeq.

Discussion and Conclusions: From the data obtained, a positive upward trend in the vaccinations against Rotavirus dispensed year by year is immediately brought to light. This is due to the success of an effective information campaign toward vaccination in general and specifically toward anti-rotavirus prophylaxis. All this gives hope that more and more persons will be vaccinated against the virus in the future. Globally, we can say that in recent years also the vaccination coverage is increasing. Particularly, an encouraging fact is a decrease in hospitalizations from Rotavirus gastroenteritis, which was made possible also thanks to the indirect immunity fostered by an increase in the vaccinations given.

Keywords: Rotavirus; Vaccination Activity; Anti-Rotavirus Vaccine; Acute Gastroenteritis; Prevention

Introduction

Rotavirus is an RNA virus that belongs to the family Reoviridae and is highly infectious. In addition to being one of the leading causes of acute gastroenteritis worldwide [1], it contributes most to mortality and morbidity in children under 5 years of age [2]. With gastroenteritis, a full range of severe clinical illnesses are observed, which can lead from outpatient visits to emergency rooms [3-4], up to hospitalizations due to severe illness in 40-50% of subjects [5-8], even in industrialized countries [9-10].

In Italy, before vaccines against the virus were available, more than 250.000 cases of gastroenteritis due to Rotavirus were estimated every year and 14.500 hospitalizations per year [11-13]. Some studies estimated that one-third to one-half of the acute gastroenteritis observed in hospital was due to Rotavirus infection [14]. It is a widespread disease worldwide: in Europe and in the rest of the temperate zones of the globe the virus occurs with seasonal peaks in the incidence which – in our latitudes - corresponds to the winter period between November and March. In tropical countries, peaks in incidence may occur but the virus is present essentially throughout the year [15]. Rotaviruses are classified into serotypes, according to VP4 (serotype P,

11 variants) and VP7 (serotype G, 10 variants) outer capsid proteins. Groups range from A to G. Groups are identified according to the antigenicity of the VP6 inner capsid protein. Human pathogenic viruses belong to serogroups A, B and C. Serogroup A is primarily responsible for childhood viral gastroenteritis. Worldwide, about 95% of children are infected by the age of 5 but children under 2 years of age are the most affected. Childhood viral gastroenteritis affects about 20 million children each year, of whom 200.000 die from dehydration almost exclusively in developing and underdeveloped countries [16,17]. The virus is mainly transmitted via the fecal-oral-route but it could also be spread by contact, from person to person or through contaminated objects, surfaces or food. Airborne transmission is also possible, although it is much less effective [18].

Peak virus elimination through feces occurs 2-5 days after diarrhea onset but it can occur even in the absence of symptoms [15]. Rotaviruses are excreted in huge amounts in fecal material, with more than 10 billion virions per gram, and are found to be very stable in feces and can remain viable for days at room temperature. This makes them extremely resistant and readily transmitted in many community environments, including maternity units, hospital wards, and nursery schools. As the virus is stable in the environment,

transmission can occur through ingestion of contaminated water or food or through contact with contaminated surfaces (such as toys) [15]. Person-to-person spread through hand contamination is probably most prevalent in community environments, specifically in nursery schools. In cafeterias and in other places intended for collective catering, Rotavirus can be transmitted when an infected worker handles food that does not require cooking (such as salad, fruits, and other fresh vegetables) without thoroughly washing their hands [15]. Cases of probable aerosol transmission of the viral particles have also been reported, probably related to projectile vomiting at the onset of infection and to the explosive nature of acute watery diarrhea [2,19].

Outbreaks are particularly common in kindergartens and hospitals, given the virus resistance to detergents, drying, and a wide pH and temperature range [16]. Children are most frequently infected with group A, less commonly with group B and C [17].

Rotaviruses replicate in the enterocytes of the small intestine; thus, the virus must transit the intestine to cause symptomatic disease [2]. The disease has an incubation period of about 48 hours, following which vomiting and diarrhea occur. In more than half of the cases, jet vomiting precedes profuse watery diarrhea that lasts about 3 to 8 days [19]. Fever is often present and in one-third of cases is very high, reaching and exceeding 39° [20]. However, growing research shows that Rotavirus infection is systemic and not limited to the gastrointestinal tract [21]; the disease can present without diarrhea and trigger symptoms including neurological changes (e.g., convulsions and epilepsy), neonatal complications, and autoimmune diseases, among others (e.g., diabetes mellitus and celiac disease) [22]. These findings—which need further investigation – offer new clinical perspectives on anti-rotavirus vaccination, and new opportunities for public health [22]. In most cases, in adults, the infection causes mild diarrhea or is asymptomatic, and sufferers recover without any treatment [18]. However, acute diarrhea can lead to severe dehydration of the body, a condition that is likely to be complicated or fatal without appropriate intervention, especially in children and undernourished or dehydrated subjects [18]. Death from dehydration most often occurs in low-income countries, due in part to a lack of medical care [3-4]. Group A Rotavirus infection is normally self-limiting and without sequelae, except for lactose intolerance that can be severe and persist for weeks, and sometimes be fatal in patients at risk [16]. Group B Rotaviruses cause severe gastroenteritis that can also affect adolescents and adults and is common in China [17]. Diagnosis may be made by searching for specific antigens of the virus within fecal samples taken from the patient; the strain involved can be further characterized by enzyme immunoassays or molecular assays, but these tests

are not commonly performed [15].

No antiviral therapy is available for Rotavirus infection; treatment is supportive. This relies on replacing fluids lost through diarrhea and regulating acid-base and electrolyte balance [16]. Affected subjects should be placed in isolation to avoid potential contagion of other patients. Prevention is achieved by maintaining good hygienic conditions, particularly in school and health facilities. Washing hands with detergents is useful to limit the spread of the virus, although it is not sufficient to kill it [17].

In general, it is essential to maintain good hygienic conditions both at home and in nursery schools and in all collective environments where people at increased risk live—such as the elderly or the immunocompromised – so as to prevent the spread of diarrheal diseases [15]. If someone contracts the disease, the greatest danger is that a severe form of diarrhea develops resulting in dehydration, especially in young children or the elderly. In this case, the body loses an excessive amount of water and essential salts and minerals, and it is unable to restore them [15]. The signs of dehydration are clear: reduced urine output, excessive thirst, dry mouth, and unusual drowsiness. Hospitalization and intravenous fluid administration may be necessary, but treatment is usually nonspecific and consists of oral rehydration to compensate for fluid loss. Difficulty in rehydrating with plenty of clean safe water is the major risk for the lives of many children in low-income countries [15].

Several studies have indicated that natural immunity acquired from infection offers both a certain degree of protection from future symptomatic infections and that repeated exposures expand a heterotypic immune response to different viral strains [23]. This has been the essential premise upon which live-attenuated oral vaccines against Rotavirus have been developed over the past 30 years [24]. In all countries – whether they are industrialized or developing—where vaccines against the virus have been introduced, a real impact on public health has been consistently observed, with significant reductions in mortality and in hospitalizations due to Rotavirus diarrhea in children under 5 years of age [25].

Two anti-Rotavirus vaccines, Rotarix Human Rotavirus Vaccine (GSK) and RotaTeq Human-Bovine Reassortant Vaccine (Merck & Co.), have been approved for clinical use in Europe and showed good efficacy and a favorable security profile in preventing Rotavirus disease [26]. As regards HRV, the vaccination course consists of two doses: the first dose is given at the age of 6 weeks and the second at an interval of at least 4 weeks between doses. The vaccination course must be completed within 24 weeks of age [27].

Regarding HBRV, the vaccination course consists of three injections: the first dose is given between 6 and 12 weeks of age, with intervals of at least 4 weeks between doses. Preferably, the three-dose vaccination course should be completed within 20-22 weeks of age. If necessary, the third final dose can be given up to the age of 32 weeks [28]. It is common experience that the total number of doses required to complete a vaccination course affects the chances of compliance within the timeframe specified by the vaccination plan (adhesion) [29,30]. Rotavirus vaccine can be given at the same time as the other proper vaccinations in the first months of life (hexavalent, pneumococcal conjugate and meningococcal B vaccines) [15].

In Italy, universal Rotavirus vaccination has been introduced in the National Plan for Vaccine Prevention 2017-2019 [31], with active and free offer throughout the country. In addition, the Italian Ministry of Health has reiterated that Rotavirus vaccination is highly recommended for newborns from 2017 on [32]. In 2017, the National Immunization Plan introduced the Universal Mass Vaccination (UMV) against Rotavirus, which was actively and freely offered to all newborns in Italy, with the purpose of reaching a vaccination coverage > 95% by 2020 [33]. However, previous reports have testified some difficulties in achieving optimal coverage in Italy, even years after its implementation [34]. Universal Mass Vaccination against Rotavirus was initiated in the Lazio Region in January 2018. Both anti-Rotavirus vaccinations were made available in Lazio with different age specifications [11].

Since the vaccination has been implemented, several positive and unexpected results have been reported. Hospitalizations decreased by 74% in the age group eligible for vaccination, if compared to previous pre-vaccination years [28]. In addition, a further 22% decrease in hospitalizations was noted among children who were ineligible for vaccination because of their age. It is hypothesized that the high coverage reached has led to this indirect protective effect, thus reducing the transmission and the spread of the virus from vaccinated children [35].

The benefits of vaccination have been widely demonstrated in terms of vaccine efficacy and safety, reduction of gastroenteritis morbidity, and cost savings for the National Health System and society [10]. This favorable risk-benefit profile and the positive experience in Italy to date should support an improved coverage and help achieve the 95% coverage goal [9]. Furthermore, the high coverage is expected to have generated herd immunity, and new evidence suggests that the vaccine could have a positive indirect impact against other diseases such as epilepsy, diabetes, and celiac disease [9]. A delay in the complete protection period could imply an extension in the vulnerability to the virus for

children and could exert an impact on the overall protection of the pediatric population [36]. In principle, the risk of developing Rotavirus disease increases with increasing age [36].

Aim of the Study

The study aims to illustrate the Rotavirus vaccinations given at the vaccination centers located in the Local Health Authority of Viterbo during the three-year period 2020-2022. A comparison was conducted between the vaccination coverage reached with Rotarix and RotaTeq vaccines in newborns in 2020 and in 2021 residing in the province of Viterbo. Furthermore, adhesions to Rotavirus vaccination were detected.

Material and Methods

The scenario was defined through extrapolation of data recorded in the company software Antares. There the vaccine information flow in the province of Viterbo is managed. The following data were considered:

- Births in the year 2020 in the province of Viterbo
- Births in the year 2021 in the province of Viterbo
- Rotarix vaccines given in the three-year period 2020-2022
- RotaTeq vaccines given in the three-year period 2020-2022
- Anti-Rotavirus vaccination coverage among newborns in 2020
- Anti-Rotavirus vaccination coverage among newborns in 2021
- Percentage of newborns in 2020 who did not complete the anti-Rotavirus vaccination course
- Percentage of newborns in 2021 who did not complete the anti-rotavirus vaccination course

Results

From January 1st, 2020 to November 30, 2022, 9318 anti-Rotavirus vaccinations were given in the vaccination centers located in the Local Health Authority of Viterbo. Among these, 3124 patients received Rotarix, while 6194 received RotaTeq vaccine (Tables 1 & 2). Throughout 2020, 2371 doses of Rotavirus vaccine were given: 2172 with Rotarix, of which 1075 first doses and 1097 second doses; 199 with RotaTeq, of which 135 first doses, 38 second doses, and 26 third doses (Table 1). In 2021 an increase was registered, with 3543 anti-Rotavirus vaccinations given. 531 patients received Rotarix, of which 232 were first doses and 299 second doses. 3012 patients received RotaTeq, of which 1125 were first doses, 1021 second doses and 866 third doses (Table 1).

Finally, from January 1st to November 30, 2022, 3004 doses of anti-Rotavirus vaccine were dispensed. Among these, 421 patients received Rotarix, of which 222 were first doses and 199 second doses; 2983 patients received RotaTeq, of which 1039 were first doses, 1000 second doses

and 944 third doses (Table 1). Over the period analyzed, the 2021 birth cohort appears to be the most vaccinated, with 455 Rotarix and 3193 RotaTeq vaccinations, with a total number of 3648 vaccinations (Table 2).

Vaccines Administered in 2020				
	I	II	III	Tot
Rotarix	1075	1097	0	2172
RotaTeq	135	38	26	199
Vaccines Administered in 2021				
	I	II	III	Tot
Rotarix	232	299	0	531
RotaTeq	1125	1021	866	3012
Vaccines Administered in 2022				
	I	II	III	Tot
Rotarix	222	199	0	421
RotaTeq	1039	1000	944	2983
Rotarix Tot 3124		RotaTeq Tot 6194		

Table 1: Distribution of vaccinations dispensed by year of administration.

Births in 2019				
	I	II	III	Tot
Rotarix	272	462	0	734
RotaTeq	10	11	21	42
Births in 2020				
	I	II	III	Tot
Rotarix	859	801	0	1660
RotaTeq	397	365	334	1096
Births in 2021				
	I	II	III	Tot
Rotarix	237	218	0	455
RotaTeq	1127	1075	991	3193
Births in 2022				
	I	II	III	Tot
Rotarix	161	114	0	275
RotaTeq	765	608	490	1863
Rotarix Tot 3124		RotaTeq Tot 6194		

Table 2: Distribution of vaccinations administered by year of birth.

A person can be defined as vaccinated against Rotavirus only when he/she finishes the complete vaccination course, consisting of 2 doses in the case of the Rotarix vaccine, and 3 doses in the case of the RotaTeq vaccine. For this reason, the total vaccination coverage reached among newborns in 2020

(1764 births) was 64%, in which Rotarix vaccine contributed 45%, and RotaTeq the remaining 19% (Table 3). As regards the cohort of newborns in 2021 (1820 births), the total vaccination coverage reached was 66%, of which 12% with Rotarix vaccine, and 54% with RotaTeq (Table 3).

Births in 2020					1764
	I	II	III	Tot	Vaccination Coverage
Rotarix	859	801	0	1660	45%
RotaTeq	397	365	334	1096	19%
					Total Vaccination Coverage 64%
Births in 2021					1820
	I	II	III	Tot	Vaccination Coverage
Rotarix	237	218	0	455	12%
RotaTeq	1127	1075	991	3193	54%
					Total Vaccination Coverage 66%

Table 3: Vaccination coverage in the 2020-2021 cohort.

Births in 2020				
	I dose	Course Completed	Course Not Completed	Course Not Completed (%)
Rotarix	859	801	58	7%
RotaTeq	397	334	63	16%
Births in 2021				
	I dose	Course Completed	Course Not Completed	Course Not Completed (%)
Rotarix	237	218	19	8%
RotaTeq	1127	991	136	12%

Table 4: Focus on unfinished vaccination course in the 2020-2021 cohort.

Discussion and Conclusion

From the data obtained, a positive upward trend in the vaccinations against Rotavirus dispensed year by year is immediately brought to light. This is due to the success of an effective information campaign toward vaccination in general and specifically toward anti-rotavirus prophylaxis. All this gives hope that more and more persons will be vaccinated against the virus in the future. Globally, we can say that in recent years also the vaccination coverage is increasing. Particularly, an encouraging fact is a decrease in hospitalizations from Rotavirus gastroenteritis [25], which was made possible also thanks to the indirect immunity fostered by an increase in the vaccinations given [35].

In this last three-year period [11], compliance for the Rotarix vaccine is confirmed to be higher than for RotaTeq, as in previous years. This is most likely due to the fact that its vaccination course consists of only 2 doses, compared to RotaTeq which includes 2 booster shots in addition to the first dose. However, it should be noted that in the last two years, RotaTeq vaccine has been the one most dispensed, in comparison to previous years where it was always second to Rotarix. While it is true that on one hand RotaTeq vaccination course consists of 3 doses compared to only 2 of Rotarix, on

the other it has also proven to be much more elastic and adaptable, since the first dose can be given by 12 weeks. This provides a longer time frame for parents in vaccinating their child, considering the fact that the child must undergo many other vaccine cycles within his/her first year of life.

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