Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

A review of recommendations for rotavirus vaccination in Europe: Arguments for change

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ARTICLE INFO

Article history:
Received 9 August 2017
Received in revised form 15 February 2018
Accepted 19 February 2018
Available online xxxx

Keywords:
Rotavirus
Vaccine
National immunization program

ABSTRACT

Background: More than 10 years after the authorisation of two rotavirus vaccines of demonstrated efficacy and with a strongly positive benefit-risk profile, uptake in Europe remains low. Only 13 countries in Europe provide a fully-funded rotavirus universal mass vaccination (UMV) programme, three provide a partially-funded programme, and one provides full funding for a reduced programme targeting at-risk infants. Around 40% of countries in Europe currently have no existing recommendations for rotavirus vaccine use in children from the national government.

Methods: We provide an overview of the status of rotavirus vaccine recommendations across Europe and the factors impeding uptake. We consider the evidence for the benefits and risks of vaccination, and argue that cost-effectiveness and cost-saving benefits justify greater access to rotavirus vaccines for infants living in Europe.

Results: Lack of awareness of the direct and indirect burden caused by rotavirus disease, potential cost-saving from rotavirus vaccination including considerable benefits to children, families and society, and government/insurer cost constraints all contribute to complacency at different levels of health policy in individual countries.

Conclusions: More than 10 years after their introduction, available data confirm the benefits and acceptable safety profile of infant rotavirus UMV programmes. Europe serves to gain considerably from rotavirus UMV in terms of reductions in healthcare resource utilization and related costs in both vaccinated subjects and their unvaccinated siblings through herd protection.

Contents

Abbreviations: AGE, acute gastroenteritis; GSK, GlaxoSmithKline; HRV, human rotavirus vaccine; HBRV, human-bovine reassortant rotavirus vaccine; RRV-TV, tetravalent rhesus-human rotavirus vaccine; RVGE, rotavirus gastroenteritis; UMV, universal mass vaccination; WHO, World Health Organization.

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https://doi.org/10.1016/j.vaccine.2018.02.080
0264-410X/

1. Introduction

The incidence of rotavirus infection has decreased in countries where rotavirus vaccine universal mass vaccination (UMV) programmes are in place. Nevertheless, global coverage of rotavirus vaccines is estimated to be 25% and rotavirus remains one of the most common causes of severe diarrhoeal illness in children <5 years of age world-wide [1,2]. Before vaccination, 3.6 million episodes of rotavirus diarrhoea were estimated to occur annually in <5 year olds in Europe, resulting in >87,000 hospitalisations, approximately 700,000 outpatient visits and 231 deaths [1,3]. Prospective surveillance of acute gastroenteritis (AGE) during the REVEAL study in seven European countries found evidence of rotavirus in 40.6% of children with AGE, with an annual incidence of 2.07–4.96 cases/100 children <5 years of age [4]. Children with rotavirus gastroenteritis (RVGE) were more likely to have severe clinical disease including dehydration than children with non-rotavirus AGE, and up to 36.0% of children with rotavirus were hospitalised [5]. As well as contributing to healthcare burden, rotavirus infections in children have a substantial negative impact upon families. Up to 91% of parents of children with RVGE in the REVEAL study lost 2.3–7.5 work days during their child's illness [6]. Parents report concerns extending beyond clinical symptoms of severity, to weight loss, peri-anal inflammation, and pain [6–8]. Among United Kingdom (UK) families with a child with rotavirus, another family member developed secondary gastroenteritis in 52% of cases [8].

As well as causing community-acquired gastroenteritis, rotavirus is also an important cause of nosocomial infections. A review of the literature from Europe found that among children aged <5 years, RVGE accounted for between 47% and 69% of all hospital-acquired AGE and prolonged hospital stays by 4–12 days [9]. In a Belgian study, up to 12% of all inpatient bed-days were due to RVGE prior to UMV [10].

Two orally administered rotavirus vaccines were licensed in the European Union in 2006. In 2009 the World Health Organization (WHO) recommended that rotavirus vaccine be included in all national vaccination programmes [11]. However, more than 10 years after the authorisation of rotavirus vaccines of demonstrated effectiveness and safety, uptake in Europe remains low. Here we review the current status of recommendations for rotavirus vaccination across Europe and the perceptions that underlie its incomplete implementation. We consider the evidence around the benefits and risks of vaccination, arguing for greater access to rotavirus vaccines for infants living in Europe.

A summary contextualizing the content of this review and its clinical relevance is displayed in the Focus on Patient section, for the benefit of health care professionals.

2. Rotavirus vaccines

The two rotavirus vaccines currently available in Europe are both administered orally: *Rotarix* (human rotavirus vaccine or HRV: GSK), is administered as two doses to infants beginning at 6 weeks of age with an interval of at least 4 weeks between doses, and completion preferably by age 16 weeks and no later than 24 weeks; *RotaTeq* (human-bovine reassortant rotavirus vaccine or HBRV: Merck and Co), is administered as three doses beginning at 6 weeks of age with completion preferably by age 20–22 weeks and no later than 32 weeks.

HRV and HBRV showed similar efficacy in clinical trials, preventing 70–73% of all RVGE in the first year of life, 77–80% of severe cases and 80% of cases requiring hospitalisation [12]. Both vaccines show similar safety profiles, and both have addressed specific challenges since licensure including quantifying the risk of intussusception.

3. Rotavirus vaccine recommendations in Europe

In 2008 the European Society for Paediatric Infectious Diseases and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition recommended that rotavirus vaccination be offered to all healthy infants in Europe [13]. An update in 2014 re-stated the recommendation, adding that rotavirus vaccination be offered equally for breast-fed and formula-fed infants without interruption of breast-feeding [14].

Where available, we checked rotavirus vaccination and reimbursement policies from recommending bodies or national health agencies in each country, and then verified these findings with local GSK medical directors across Europe. The results of these requests are summarised in Table 1. Currently 14 countries in Europe have no existing national government recommendation for rotavirus vaccine use in children (Fig. 1). Thirteen countries in Europe provide a fully-funded (UMV) programme, and another five countries provide a partially-funded programme which is either fully funded for certain risk-groups (Croatia) or in specific regions (Sweden), or requires a parent co-payment (Belgium, Greece and Slovakia).

4. The benefits of rotavirus vaccination in Europe

Five countries in Europe with recommendations for rotavirus UMV have data evaluating vaccine impact (Table 2). The majority of these studies compare the rate of RVGE hospitalisations and/or other outcomes such as the number of rotavirus-positive samples, or outpatient/emergency department visits, over a defined post-implementation period compared to historical data prior to implementation of the UMV recommendation.

Belgium was the first country to recommend universal vaccination of infants, introduced in 2006. Vaccine coverage of the complete series [2 doses (HRV) or 3 doses (HBRV)] stands at around 85%. In the first two years after vaccine introduction, hospitalisations for community-acquired rotavirus infection decreased in children aged ≤5 years by 78%, and nosocomial RVGE decreased by 76% [15]. Impact studies have demonstrated sustained declines in RVGE hospitalisations in excess of 70% in children <5 years of age, including those too old to be vaccinated [15–17]. Compared

Please cite this article in press as: Poelaert D et al. A review of recommendations for rotavirus vaccination in Europe: Arguments for change. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.02.080