REVIEW

Is there still space for the implementation of antisepsis and disinfection to prevent rotavirus and norovirus gastroenteritis outbreaks?

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Introduction

Gastroenteritis (GI) is one of the most common infections in children under five years as a community-acquired infection and hospital-acquired infection [1].
Community-acquired GI generates a variety of problems and costs for health care systems, due to visits, hospitalizations, laboratory activities, professional services, medications and other treatments; gastroenteritis can also cause hardship for the families of those infected, because of lost working time and reduction in labor productivity of the parents [2].
In addition, cases of nosocomially acquired infections cause prolongation of hospital stay, and outbreaks of GI may lead to ward closure and, occasionally, even closure of the whole hospital [3-5].
The majority of these diseases are viral in origin, with rotavirus (RV) and norovirus (NV) being the most common [1].
For all these reasons, defining correct and efficient infection control measures is very important in preventing RV and NV infection, especially when it is necessary to avoid the spread of the disease, and to rapidly control the outbreaks.
High incidence of RV GI encouraged research for the development of RV vaccine strategies; the first licensed RV vaccine (RotaShield, Wyeth - Ayerst) against several RV diseases have been developed, but have been withdrawn because of the slightly increased occurrence of intussusception complications in vaccinated children [6].
Intensive work lead to the availability of two new RV vaccine tested for safety and protective efficacy in both developed and developing countries [7-9].
In developed countries, these vaccines may substantially reduce the number and associated costs of child hospitalizations, and clinical visits for acute diarrhoea; in developing countries, they could reduce the death rate from diarrhoea and improve child survival through programmes for children immunisation and diarrhoeal disease control [10].
However, RV vaccines cannot be considered the only key for decreasing GI incidence. In fact, economic problems (especially in the poorest countries of the world) and a low compliance to vaccination may determine low vaccination coverage of population; besides, it is essential to consider the necessary period of time (years) for obtaining vaccination coverage in paediatric population sufficient to minimize the incidence of the disease.
In addition, technical difficulties still present in obtaining an effective vaccine against NV represent further a complication for an effective prevention of viral GI.
Finally, since multiple pathogens are involved in acute and severe diarrhea in infants and children, vaccination should be considered as a major constituent, but not the only one, of the entire prevention measures battery required against GI.
Other strategies include health care professionals training, personnel hygiene, personnel protective equipment, quality standards of health service, antisepsis and environmental disinfection; the last one playing a very interesting role.
In particular, a correct approach to antisepsis and disinfection practices must guarantee the appropriate choice of antiseptics and biocides. Selection of products, therefore, must be based on experimental evidence of their specific efficacy against RV and NV in conditions of work practice, to obtain the best possible antimicrobial effect on skin, environmental contaminated surfaces and objects.
The analysis of preventive measures generally used in many health settings, and the review of the properties of the main biocides used in hand-antisepsis and in environmental decontamination, confirm our opinion that there is space to implement antisepsis and environmental disinfection practices, in order to improve control measures for viral GI diseases [4, 11-13].

Discussion

Epidemiology of GI outbreaks

GI is one of the leading causes of mortality and morbidity. It is estimated that worldwide each child under 5 years has an average of 3.2 episodes of diarrhea per

year, and the associated mortality rate is 4,9 deaths per 1,000 children in this age group [14].
While in industrialized countries infectious diarrhea is mainly a problem of morbidity and economic cost, in developing countries it is a major cause of mortality, accounting for about 2.5 million deaths in children younger than five years annually (20% of all mortality in this group) [15].
Despite the lack of surveillance system has historically limited the ability to study the aetiology and the epidemiology of viral GI, many recent studies have demonstrated that NV and RV are a major cause of pediatric GI as community acquired and hospital acquired GI.
In a recent review, relevant papers published as early as 2004 are discussed in the context of viral GI outbreaks [16]. All community-based studies confirmed that NVs are the most common cause of viral GI, especially in young children; furthermore, RVs were ranked among the most important cause when hospitalized children were studied, with NVs coming in second place [16].
In addition, NVs have been identified as the cause of approximately half of all GI outbreaks worldwide and although infecting all age groups, they cause particularly severe diseases in young children [17].
Parashar et al. estimated that each year RV causes approximately 111 million episodes of GI that require home care only, 25 million clinics visits, and 2 million hospitalizations in children < 5 years of age worldwide [18].
The Pediatric Rotavirus European Committee (PROTECT) review's on pediatric burned of RV disease in Europe showed that 40% of the hospitalizations for acute GI in children aged < 5 years old were attributable to RV disease with an average cost of € 1,417 per case [19].
In an epidemiological study of health care-associated GI outbreaks in England and Wales, the systematic assessment of GI outbreaks, carried out by active monitoring of GI, demonstrated that NV was the predominant etiologic agent and that RV was the second cause of GI [20].
Italy, unlike other countries, has no specific and constant surveillance system for viral GI, and laboratory diagnosis is rarely performed; thus, in our country, only a small number of studies have investigated the prevalence and aetiology of viral GI in children, as a community-acquired infection and hospital-acquired infection.
Colomba et al. described the epidemiologic characteristics of acute viral GI in hospitalised children in Sicily, an Italian Region, for a period of one year, from January to December 2003; the results of this study confirmed viruses as the most common cause of severe enteric illness in childhood, with RV and NV playing the main role. The researchers, therefore, underline the need of a specific surveillance system for viral GI outbreak and the socioeconomic impact of GI prevention [21].
Moreover, even if NV is considered the leading cause of gastroenteritis outbreaks in other countries, in Italy only a few NV outbreaks have been described [22-24], suggesting the magnitude of the introduction of routine testing for NV to evaluate the real prevalence of viral GI by different agents.
Another survey conducted in Italy, analyzing the hospital discharge forms of all children admitted to the Paediatric Department of an hospital from 2001 through 2005, confirmed that RV infections represents an important cause of hospitalization in children, and is responsible for significant costs for the Public Health Care System [25].
The high prevalence and incidence of NV and RV infections is mainly attributed to some characteristics of both viruses: low infectious dose, high infectivity, short incubation period, persistence of viruses in the environment and multiple routes of transmission (person to person, by fecal-oral and aerosol spread, through the vomit as well as through ingestion of contaminated food, water and environmental surfaces) [16, 26].
Since in institutions housing infants and young children, "hand to hand" and "hand to objects" contact is frequent, the role of hands, respiratory system and vomit in RV and in NV transmission may be complementary and synergic.
In the study of Isakbaeva et al., the Authors described an outbreak of NV diarrhea in a community playground; they observed a rapid spread of viruses and a high attack rate despite good hygienic practices, in absence of obvious soiling or vomit, consistent with the low dose of the virus and the easy mode of transmission [27].
The 5th Edition (2000) of the Block textbook pointed out the long environmental survival of RV [28] and this was confirmed by studies of other authors [29-32].
In some studies performed in Canada about 30 years ago, the persistence of RV for several hours on the hands of the examined volunteers supported the viral transfer occurring between animate and non-porous inanimate surfaces, as vehicles for virus transmission [30].
The high number of hospitalizations of children, the high prevalence of NV and RV as cause of GI, combined with the characteristics of the viruses determine a large number of GI as community-acquired infections in nursing homes, residential homes, day care centres, dormitories, cruise ships, and schools [4, 33-36], and also as explosive outbreaks in hospitals, especially in neonatal and pediatric wards.
All reported epidemiologic data emphasize that prevention of viral GI should be a fundamental practice in Public Health worldwide.

Antisepsis and environmental disinfection for the prevention of GI outbreaks

Antisepsis and environmental disinfection procedures are important contributions to the prevention of viral GI, both at home and in sanitary and enclosed settings [4, 11, 37].
Many enteric viruses can remain viable on inanimate surfaces for days and, in particular, infectious RV particles have been detected on hands and a variety of surfaces and objects. Casual contact can lead to the transfer of these viruses from contaminated to clean surfaces and, consequently, animate and inanimate surfaces usually play a complementary role in the spread of these viruses.
Hence, prevention of viral GI outbreaks must take into account protocols related to antisepsis and disinfection. In

these protocols, selection of appropriate biocides should be based on scientific documentation of their efficacy against specific virus and on information about their correct use.
Unfortunately, available literature often shows conflicting results, due to a lack of internationally shared regulatory frameworks, indicating experimental standard conditions for tests on biocidal efficacy on viruses.
In some European countries, disinfection practioners still rely on tests performed on "reference viruses", as poliovirus type 1, adenovirus type 5, vaccinia virus strain Elstree, papovavirus strain 777, and a few others [38, 39].
Consequently, many biocidal products report label claims of a general virucidal activity based on data obtained by tests performed on few classes of viruses.
In United States, disinfectants are regulated by U.S. Environmental Protection Agency (EPA) and U.S. Food and Drug Administration (FDA). In health-care settings, EPA regulates disinfectants that are used on environmental surfaces and FDA regulates liquid chemical sterilants/high-level disinfectants used on critical and semicritical patient-care devices. CDC provides guidance to practitioners regarding appropriate application of EPA and FDA-registered liquid chemical disinfectants and sterilants in health-care settings.
To be labeled as an EPA hospital disinfectant, the product must pass Association of Official Analytical Chemists (AOAC) effectiveness tests against three target organisms (*Salmonella Choleraesuis*, *Staphylococcus Aureus*, and *Pseudomonas Aeruginosa*). Substantiated label claims of effectiveness of a disinfectant against specific microorganisms other than the test microorganisms are permitted, but not required, on condition that the test microorganisms are likely to be present in or on the recommended use areas and surfaces [40].
Thus, biocidal specific efficacy is evaluated on the basis of "specific" tests performed on each virus [41]; when the studied virus cannot be cultivated in vivo or in vitro, or its handling is unsafe, surrogate virus testing results may be accepted [42], as recommended by the Centres of Disease Control and Prevention (CDC) [43].
The selection of safe and efficient virucidal biocides may be easier if Regulatory Frameworks, internationally shared, indicates:

- methods for the assessment of virucidal efficacy of antiseptics and disinfectants against specific viruses (as suggested by the CDC [43]);
- necessity of reliable label claims, based on specific virucidal tests performed as indicated in the previous paragraph.

Antisepsis

Hand washing is considered as the single most important procedure for preventing the transmission of infections [44]. However, the impact of hand washing depends on the type of hand-washing agent selected and on the regularity and care of the procedures used by health care workers [30].
Traditional hand washing with water and liquid soap has often proven insufficient.
The Advanced Draft Guidelines on Hand Hygiene in Health Care of the World Health Organization (WHO) reviewed a great number of studies about efficacy of plain soap, antimicrobial soaps and alcohol-based handrubs; the results showed that antiseptic soaps and detergents are more efficacious than plain soap and that alcohol-based rubs are more efficacious than antiseptic detergents.
WHO recommends an alcohol-based formulation for hand antisepsis not only for the excellent microbiocidal characteristics, fast acting and broad-spectrum activity, but also to overcome the lack accessibility to sinks or other facilities to perform hand cleansing action that require the use of water, to improve compliance with hand hygiene by reducing the time required to perform it and to reduce costs [45].
Furthermore, in many hospitals, compliance of health care workers to hand-washing is approximately 40%, and changing hand washing habits in physicians has proven difficult.
Hand antisepsis could be improved by increasing the number of sinks equipped with liquid antiseptic soap distributors, and by introducing bed-side dispensers of alcoholic antiseptic products containing emollients [46, 47].
Most health care workers are still not familiar with the evidence that incorporation of glicerol or other emollients into alcohol rinses or gels reduces skin dryness. For this reason, some caregivers do not accept new alcoholic products, even if they show rapid antimicrobial activity and asking minimal time commitment [48-52].
The rapid activity of these products may be particularly useful when health care workers with "apparently" clean hands, pass from one patient to the next.
Considering that alcoholic products lose their biocidal activity on heavily soiled hands, a preliminary proper washing with liquid soap and water is mandatory before antiseptic treatment.

Disinfection

The use of chlorine compounds for environmental disinfection has been applied and studied for about two centuries: only a few years after the discovery of calcium hypochlorite biocidal activity, use of sodium hypochlorite solution (Labarraque water – year 1789) was suggested for disinfection of surfaces and equipments.
Sodium hypochlorite is the cheapest and the best available biocide for many applications in clinical settings and at home. It may kill vegetative viruses, bacteria, mycobacteria, spores, enveloped and naked fungi and protozoa [53].
Dychdala reported that chlorine, in absence of organic contaminations, may kill vegetative bacteria, spores, fungi and viruses in diluted solutions (100 ppm or less); if organic contaminants are present, the loss of chlorine biocidal activity is complete when minute amounts of chlorine are used [54].
The Public Health Laboratory Service Viral Gastro-enteritis Working Group listed, as a first control measure for NV and RV GI control, aggressive cleaning of surfaces in wards, bathrooms, toilets, and also on bed

sheets, carpets and soft furnishing contaminated by vomit, faeces, excretions and secretion of human origin. After cleaning with detergents, hot water and disposable clothes, a freshly prepared solution containing 1,000 ppm of available chlorine (AvCl) in water has be used for "standard" disinfection procedures [33].
Some years ago, an experimental study reported that 5,000 ppm of AvCl are able to inactivate human RV suspended in liquid faeces and dried on inanimate surfaces [55]. More recently, Doultree et al. [56] have emphasized the relative resistance of NV to a variety of disinfection protocols and have recommended freshly reconstituted hypochlorite solution, at a concentration of 1,000 ppm, or, if hypochlorite based product is already in solution, a concentration of 5,000 ppm.
Sattar et al. found a significant reduction in RV contamination on environmental surfaces by using chlorine solutions of either 2,000 ppm or 6,000 ppm [57].
Consequently, in many wards, it is an invariable standard procedure to routinely disinfect surfaces and instruments with no less than 5,000 ppm AvCl to guarantee the antiviral activity of chlorine compounds against RV and NV.
In some cases, it will be advantageous to substitute sodium hypochlorite with sodium dichloroisocyanurate (NaDCC), a chlorine compound that maintains the same biocidal properties of sodium hypochlorite, while presenting lower corrosivity and susceptibility to proteic inactivation [13, 58-61].
When the corrosive, discolouring, or irritating effects of chlorine compounds are harmful, a valuable alternative in environmental disinfection is represented by phenolic biocidal products associated with detergents, which add cleaning effect to biocidal properties in "one step" treatment.
The ability of phenolic compounds to inactivate "enveloped" (lipophilic) viruses was evidenced by Klein and Deforest about 40 years ago (1963). The Authors found that 5% phenol solution was active against "naked" and "enveloped" viruses, and that ortho-phenil-phenol (OPP) was highly effective against lipophilic viruses [62].
Sattar et al. have shown the antiviral properties of various phenolic derivates on adenovirus type-5, AD-5, with intermediate sensibility to disinfectants, and against cocksakievirus B3, CB-3, selected to represent enteroviruses [63].
The same Authors compared also the capacity of different biocidal products to interrupt RV spread; their results showed that domestic bleach (6% sodium hypochlorite diluted to give 800 ppm free chlorine) and the phenolics reduced the virus titer by 97.9% +/- 0.4% and 95% +/- 5.36%, respectively [64].
In addition to constant efficacy of phenolic derivates on RV, proved by various Authors, the experiments by Gulati et al. using a feline calicivirus, as NVs "surrogate virus" [65] drew attention to the phenolics activity against small naked viruses previously reported by pertinent literature; the results of this study suggested that NV is very resistant to commercial disinfectants, but phenolic compounds at two to four times their recommended concentrations appear to be effective at decontaminating environmental surfaces.
To confirm the efficacy of phenolic compounds, as demonstrated by the reported experimental studies, Centers of Diseases Control and Prevention (CDC) suggested phenolics to prevent spreading of NVs infections on cruise ships, in the wake of 21 outbreaks of acute GI occurred during July-December 2002, on 17 cruise ships [43].
Finally, Widmer and Frei, considering numerous experimental data, confirm that phenolic compounds associated with detergents result in products with excellent cleaning properties, dissolving proteins and disinfecting in one step [66].
Therefore, in alternative to chlorine disinfectants, phenolic-detergents products should represent the gold standard disinfectants used in prevention of viral GI.

Conclusions

Chlorine compounds and formulations containing phenolic compounds associated to detergents play an important role as environmental disinfectants. Phenolic-detergents should be considered as possible active environmental disinfectants in a wide spectrum of viral infections including lipophilic viruses, intermediate viruses and some naked idrophilic viruses. The use of such compounds is strongly recommended by recent studies.
Surface decontamination performed by accurate cleaning and followed by treatment with chlorine compounds, or, as an alternative, done by the use of phenolic compounds associated with detergents (which may clean and disinfect in one step) may improve the antimicrobial effects in presence of viral GI, interrupting the risks of persistence of infective properties due to faeces, vomit and involuntary physical contact.
A better cleaning, antisepsis and disinfection program, based on laboratory tests and clinical experiences, will result in further improvement in the prevention of viral GI outbreaks, and will provide the best protection to patients and health care workers.

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