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Editorial

Prevention strategies against respiratory syncytial virus in Costa Rica: good news for 2025

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In November 2024, the National Commission for Vaccination and Epidemiology (CNVE) and the Ministry of Health of Costa Rica approved the immunization strategy against respiratory syncytial virus (RSV) to be implemented in Costa Rica starting in 2025. This decision goes beyond administering a vaccine and turns out to be a comprehensive measure that includes:

a) Vaccination in pregnant women between 32 and 36 weeks of gestation.

b) Application of a protective monoclonal antibody to newborns whose mothers have not received the vaccine.

c) Vaccination of adults over 65 years of age.

The vaccine and a monoclonal antibody will be part of the national vaccination scheme in Costa Rica starting this year if they are acquired through the revolving fund of the Pan American Health Organization. Currently, the authorities of the Costa Rican Social Security Fund are working on the design and organization of this strategy, which aims to protect the groups most prone to this infection through resources that encourage passive and active immunity mechanisms.[1]

According to the World Health Organization, RSV is one of the leading causes of acute lower respiratory infection in children globally and represents a substantial cause of severe respiratory disease in older adults.[2]

In a systematic analysis of the global burden of disease conducted in the 1990s to 2010s, it is established that in adults over 60 years of age, RSV is a cause of severe respiratory disease comparable to seasonal influenza with an incidence of hospitalizations of 0.15-0.18%. This figure could be double given the limitations that existed for the accurate etiological diagnosis in this age group. The in-hospital mortality rate amounts to 7.1% in the elderly population and is 11.7% in adults with comorbidities.[3]

To date, RSV is the leading global cause of lower respiratory infections and the second respiratory pathogen responsible for infant mortality. It is estimated that 97% of deaths caused by RSV infections in children under 5 years of age occur in low- and middle-income countries. In high-income children, 1.8% of healthy full-term children are hospitalized for RSV infection during the first year of life. While it is true that predisposing medical conditions, prematurity, and socio-economic vulnerabilities increase the risk of hospitalization for RSV infections, three-quarters of children who are hospitalized are previously healthy. Although the incidence and hospitalization rates are concentrated in infants younger than 6 months, older infants (6-12 months) and young children (1-2 years) also have a significant burden of disease.[4]

1There is no specific treatment for RSV and hospital management is restricted to support measures of varying degrees according to the patient's criticality. In children, additionally, the possibility of recurrent hospitalizations due to bronchiolitis is high and subsequent linkage with bronchial asthma is a frequent situation.[5]

Authors' affiliation:
Departamento Clínico de Pediatría, Escuela de Medicina. Universidad de Costa Rica, San José, Costa Rica.
0000-0002-1995-0925

oargued@gmail.com

In Costa Rica, according to a retrospective study carried out at the National Children's Hospital / Hospital Nacional de Niños (HNN), in a period of 4 years (2014-2017) 8,902 children required admission to the center for severe acute respiratory infection, 2,523 of them (28.3%) required intensive therapy. Eighty percent of admissions were caused by RSV. Seventy-six children died from this cause, representing a total cohort mortality of 0.85%. The estimated average annual cost of SARI hospitalizations at the HNN was just over 15 billion colones per year. The study also showed that, except for 2016, the peak of admissions for severe acute respiratory infection always began in the second half of the year. This phenomenon had an average duration in weeks of 16.2 (range 6-22). The epidemiological week with the highest number of patients requiring intensive care was also recorded in the second half of the year in all the years studied. The peak of admissions for respiratory infections was annual and monocyclic in the observed period.[6]

Currently, fortunately in the world we can have new tools against RSV. There are two products approved by strict international regulatory agencies for use in young children: a long-acting monoclonal antibody given shortly after birth and a maternal vaccine given to late-stage pregnant women to passively transfer antibodies to the product and provide protection during the first months of life. In addition, there are three vaccines already authorized to prevent severe RSV disease in older adults and adults with predisposing medical conditions.[2] There are also a significant number of other long-acting monoclonal antibodies and RSV vaccines that are completing either their clinical studies or licensing processes.[4.7]

Strategies to ensure immunization against RSV through the approved products available are variable in different countries of the world, some use only maternal immunization, others only protect babies using long-acting monoclonal antibodies administered shortly after birth, other mixed strategies with both alternatives, with variations in the times of application according to the chronology of respiratory seasonality in each nation. Some countries offer the alternative of vaccination in a reduced way to risk groups and others do so in an open and general way for all candidates according to their time of birth (monoclonal antibody to the newborn), or height of pregnancy (maternal vaccine). It should be noted that the availability of these protection strategies is restricted to middle- or high-income countries and is not yet accessible to low-income countries.[7]

The long-acting monoclonal antibody that was first registered and is in wider use today is Nirsenimab. The efficacy and safety studies that preceded its initial approval by the European Medicines Agency in 2022 showed very strong positive results. Nirsenimab works by binding to the RSV antigenic site Ø prefusion (pre-F), blocking the fusion of the virus with the cells of the respiratory tree and thus preventing hospitalizations for respiratory infections of the lower respiratory tract due to that virus. It is administered intramuscularly to infants younger than 6 months of age, shortly before the RSV season begins. Compared to palivizumab, the first monoclonal against RSV recorded more than a decade ago, nirsenimab has the advantage of its 50-100 times greater neutralizing capacity, and a longer half-life, so that a single dose can protect during the RSV season (7,8). Long-acting monoclonal antibodies against RSV can also be administered in children aged 8 to 19 months who have risk factors for severe RSV disease (preterm, chronic lung disease, immunocompromised and cystic fibrosis). These monoclonal antibodies against RSV provide protection for at least 5 months.[2]

The HARMONIE (Hospitalized RSV Monoclonal Antibody Prevention) study is a phase IIIb clinical trial carried out in almost 250 centers in France, Germany and the United Kingdom, during the VRS 2022-2023 season, under conditions like those that would be used in real practice, which included 8,050 children under 12 months of age. Four thousand thirty-seven received nirsenimab compared to 4,021 in standard care. The primary objective was to determine the efficacy and safety of nirsenimab compared with standard care in children who were in term or preterm ⩾29 weeks' gestation and not eligible to receive palivizumab, and as for secondary objectives is the prevention of hospitalization of severe cases, defined by oxygen saturation <90% and need for supplemental oxygen, and hospitalizations for lower respiratory tract infections due to any cause. 180 days after admission, the efficacy of Nirsenimab in RSV lower respiratory tract infections was 83.21% (95% CI = 67.77-92.04 p<0.001), the efficacy in preventing hospitalization for severe cases was 75.71% (95% CI = 32.75 - 92.91 p<0.001), and the efficacy in preventing lower respiratory tract infections by any etiology was 58.04% (95% CI = 36.69-71.19 p<0.001). The safety profile has been favorable and consistent with the data already presented in previous studies.[8]

In August 2023, the bivalent recombinant protein subunit vaccine (RSVPreF) was approved by the US Food and Drug Administration (FDA) for administration at 32-36 weeks of gestation. The vaccine achieves the transfer of antibodies against RSV to the unborn baby through the placenta, in addition to allowing protection for 6 months after birth. This is a passive immunization (transfer of maternal antibodies to the fetus) from the infant through active immunization (vaccine) to the pregnant woman. The approval was based on the results of the MATISSE phase III study. This study included 7,358 healthy pregnant women between 18 and 49 years of age. Three thousand six hundred and eighty-two received RSVPreF and 3,676 placebo. Data on efficacy in

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infants against lower respiratory tract infection due to RSV showed efficacy for severe disease up to day 90 of life of 81.8% (99.5 CI = 40.6-96.3) and up to day 180 of life, 69.4% (97.58 CI = 44.3-84.1). There were no safety alerts in pregnant women or their children after follow-up for 24 months of age. The incidence of adverse events reported one month after injection or one month after birth was similar in the vaccinated group (13.8% of women and 37.1% of infants) and in the placebo group (13.1% and 34.5%, respectively).[9]

Public health authorities should decide which strategy to choose, considering RSV seasonality patterns in each country and the elements that influence coverage, as well as the sustainability of vaccination programs.

With the introduction of new prevention strategies against RSV, there is already a high impact on reducing the burden of disease, hospitalizations and complications attributable to lower respiratory infections due to RSV, especially in the most vulnerable groups: children under 5 years of age, older adults and people with comorbidities at any age. This will not only decongest pediatric hospitals and pediatric areas in general hospitals but will allow a more adequate functioning of emergency services and critical care areas, both pediatric and geriatric. The careful reporting of adverse events, as well as their follow-up and the lessons that each country contributes to the implementation of the strategy against RSV should be shared generously and transparently in the international scientific community.

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Olga Arguedas-Arguedas
Clinical Department of Pediatrics,
School of Medicine.
University of Costa Rica
0000-0002-1995-0925
oargued@gmail.com