ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Mexican Delphi Consensus for use Immunotherapy with MV130 Vaccine in Patients with Recurrent Respiratory Infectious Diseases (Expert Panel)

Herrera García JC[1]*, Arizpe Bravo AB[2], Hernandez Treviño V[3], Sanchez S[4], Landa Alvarado PD[5], Carrasco Castillo A[6], Rosales Magallanes GF[7], Perez Juárez LK[8], Gamboa Y Gamboa MA[9], Aranda López AR[10], Field Cortazares J[11], López Sánchez G[12], Mondragón Guarneros F[13], Pech Alonso B[14] and Ramirez Crescencio MA[15]

[1]Pulmonary Function Unit and Clinical Research Unit-Hospital Ángeles Puebla, Mexico

[2]Infectious Diseases Departament- Hospital Angeles Puebla, Mexico

[3]Hospital Metropolitano, México City

[4]HGR 1 "Carlos Mac Gregor Sánchez Navarro" CdMx, México

[5]San José Hospital, Querétaro, México

[6]Specialized Center in Pediatrics-Pulmonology and Respiratory Allergies, Oaxaca, Oax, México

[7]Medical Center for Infectious Specialties, Mexicali, Baja California, México

[8]Children's Hospital "Dr. Rodolfo Nieto Padrón – Hospital Ángeles Villahermosa, Tabasco, México

[9]Pediatric Infectious Diseases Clinic, Mérida, Yucatán, México

[10] Aranda de la Parra Hospital, León Guanajuato, México

[11]Center for Infectious Diseases in Pediatrics, Ensenada, Baja California, México

[12]Medical Specialties Unit, Dalinde Medical Center – Transnational Research Unit, Médica Sur Foundation, México

[13] Hospital Angeles Metropolitano, México City

[14]Hospital Angeles Acoxpa, México City

[15]Hospital Angeles, London Clinic Mexico City

ABSTRACT

Background and Objectives: Recurrent respiratory infections are currently a public health problem due to their high costs and resistance to treatments as well increase morbidity and mortality. An imbalance in the homeostasis of progressive cellular and humoral immunity the application of immunotherapy with trained immunity vaccines (IvIE) is currently a therapeutic option in all patients with recurrent respiratory infections by training innate and adaptive immunity by reducing episodes of respiratory exacerbations and improving the quality of life of patients.

Methods: Using Delphi method and a panel of experts, a questionnaire was developed that included questions regarding the benefit and non-benefit of the treatment of patients with persistence of recurrent respiratory infections by specific criteria, from diagnosis, identification of risk factors and comorbidities, ideal candidate by consensus to receive the therapy, follow-up, and presentation of clinical data for reduction of recurrence of the conditions. There was a consensus on determining the use of immunotherapy MV130 vaccine in patients with specific criteria as long- and short-term use.

Conclusion: Immunotherapy with trained immunity vaccines (IvIE) is currently a therapeutic option in all patients with recurrent respiratory infections and associated comorbidities in patients with chronic respiratory illnesses, autoimmune diseases, hematological malignancies for improvement clinical infections and improvement quality of life.

***Corresponding author**

José Carlos Herrera García, Pulmonary Function Unit and Clinical Research Unit-Hospital Ángeles Puebla, Mexico.

Received: September 11, 2024; **Accepted:** September 16, 2024; **Published:** December 28, 2024

Introduction

Respiratory tract infections (RTIs) are a group of prevalent and diverse diseases affecting the upper and lower respiratory tract, from mild illnesses such as the common cold to severe and life-threatening diseases such as influenza, flu, or COVID-19. Due to their high prevalence and the variety of pathogens involved, these

infections are a major public health problem and remain one of the leading causes of death worldwide [1]. Recurrent respiratory infections (RRIs) can be caused by a a big group of pathogens, including viruses, bacteria, and occasionally fungi, making their etiology multifaceted. The fact that certain infections (e.g., viral) can predispose individuals to others (e.g., bacterial) increases this complexity. Upper respiratory tract infections, including rhinitis, pharyngitis, tonsillitis, and otitis media, account for 88% of total respiratory infections and cause mild to moderate symptoms [1]. Respiratory infections can become recurrent in certain individuals. RRIs represent a major public health problem and work-school absenteeism. Episodes are long-lasting, occur repeatedly over time, are associated with unusual complications, or are not resolved with current treatments [2]. Children, the elderly, and people with compromised immune systems are particularly vulnerable [2]. Viruses such as respiratory syncytial virus, influenza virus, and rhinovirus, among others, are the main causative agents responsible for RRIs , although secondary bacterial infections are associated with serious clinical complications [3-6]. Bacterial infections are observed in 60% of patients who present symptoms lasting 10 days or more [7,8]. Among bacteria, the most common are S. pneumoniae, H. influenza, M. catarrhales, and S. pyogenes [9]. Antibiotics are considered the main treatment worldwide, despite the viral etiology of many of these processes. Furthermore, in most cases, they are prescribed. The use of antibiotics is often performed empirically without knowing the sensitivity of the causative pathogen [10]. This leads to treatment failures and negative collateral consequences, such as adverse reactions and/or the selection of antibiotic-resistant bacteria, a serious global threat. In the case of patients who experience recurrent infections this becomes more pronounced. Therefore, it is essential to have alternatives for the management of this type of infection, particularly for people who frequently suffer from recurrent infections [10]. Prevention strategies for respiratory infections are limited due to the large number of pathogens that cause them and the restricted availability of pathogen-specific vaccines. In recent years, however, new concepts about the training and memory capacity of the innate immune system have emerged that offer the potential to develop broad-spectrum vaccines. These vaccines, known as TIbV (trained immunity-based vaccines), can consist of bacteria, fungi or viruses. Trained immunity is characterized by the long-term functional reprogramming of innate immune cells. This training process leads to an enhanced innate immune response to secondary stimulation, increasing the ability to clear infections caused by unrelated pathogens not included in TIbV. MV130 is a sublingual vaccine composed of heat-inactivated whole-cell bacteria that has been shown to induce trained immunity and is classified as TIbV. Vaccines have the potential to induce robust mucosal protective immunity at the site of infection, making them a strong alternative to parenteral vaccines. The latter, despite inducing systemic immunity, do not regularly trigger a mucosal immune response. Furthermore, mucosal vaccines have the advantage of noninvasive, needle-free administration. In this regard, mucosal immunization with MV130 has been shown to enhance cellular and humoral responses in the airways [10].

Methodology

The RAND/UCLA methodology was used to generate consensus, which uses scientific evidence, together with the judgment and opinion of a modified Delphi panel, held in person in an asynchronous manner. The panel was made up of experts from the specialty of Pulmonology, Pediatric Pulmonology, Infectology and Pediatric Infectology, as well as Geriatrics in the treatment of patients with recurrence of respiratory diseases in the different centers of the country, taking into account clinical experience and patient management. Experts as decision makers and treating patients with these characteristics.

The statistical analysis will be carried out using measures of central tendency and dispersion: maximum and minimum. The first three indicate the central tendency of the distribution or set of responses from experts, while the maximum and minimum indicate the extreme responses to characterize the set of results obtained in each of the questions. The response median will be identified with its dispersion indicators.

Questionnaire Preparation

The authors of this study formed the scientific committee of the project due to their professional experience in this field. Together with the collaboration of an external methodological advisor, they developed the contents of the Delphi questionnaire. To do so, a bibliographic search was carried out, in which priority was given to meta-analyses/systematic reviews and other types of critical synthesis of scientific literature, through the consultation of usual bibliographic databases, as well as a manual review of the bibliographic references obtained to identify others that could be of interest based on keywords such as MV130 vaccine, recurrent respiratory infections, immunotherapy, trained immunity. Each item of the survey submitted to the panel's evaluation was written taking into account whether it was an affirmative or negative statement, as a professional criterion or clinical recommendation, that responded to aspects of interest or controversy in the clinical management of patients with risk factors. The final version of the questionnaire consisted of a block of questions as follows:

- Current management algorithm for recurrent respiratory infections.
- Opinion on the relative importance of the risk factors that are taken into account when prescribing the MV130 vaccine
- Opinion on the safety profile of the MV130 vaccine
- Recommendations for the selection of the treatment for the ideal candidate to benefit from the use of the MV130 vaccine.

All questions had to be answered, in order to obtain the opinion of all the panelists participating in both rounds on all the questions raised. However, in the second round, only those items were consulted on which consensus was not obtained in the previous round, that is, those questions that did not obtain at least 80% of grouped responses. Finally, extend the recommendation in a final consensus under the following assertions (Strong: >80% agreement and Weak <80% agreement) ending by determining the doctor's criteria according to the clinical case witnessed.

Selection of the Expert Panel

The panel experts were proposed by their clinical experience and management of the drug as leaders in the prescription of the MV130 vaccine. To be representatives of their medical specialty with decision-making on the clinical situation of the study, professional recognition for their experience and scientific criteria (leadership in the field) and special interest in the field of recurrent respiratory infections. The fieldwork of the study was carried out between April-May 2024. In Madrid, Spain and Mexico City.

Analysis and Results

To analyze the group opinion regarding each question raised and give a numerical score to the agreement of the statement or question. Consensus was defined when at least 80% of the panelists had responded that they agreed or disagreed. The data were analyzed globally, establishing a consensus of statements

that resulted in:

- STRONG Recommendation: Agreement more than 80%
- WEAK Recommendation: Agreement less than 80%.

Results

The following findings were found from the experts who participated in the Delphi panel study: Specialists in Pulmonology and Infectology for Adults and Pediatrics, as well as Geriatricians with more than 10 years of experience in their field. 100% participation was received in person and electronically. Obtaining 21 recommendations for the use of the MV130 vaccine according to consensus for its indication in patients with specific characteristics (13 strong recommendations and 8 weak recommendations). The consensus is concluded with the recommendations for the use of the MV130 vaccine in patients with respiratory infections currents in Mexico.

Recommendation on the Use of Immunotherapy with Mv130 Vaccine in Patients with Recurrent Infectious Respiratory Diseases

INDICATION	
1. All patients with recurrent respiratory infections (more than 3 per year) require an immunotherapy vaccine that improves the immune system.	STRONG
2. Patients with more than 3 episodes of rhinitis, sinusitis and otitis in the year are candidates for use of the MV130 vaccine	STRONG
3. Patients with more than 2 cases of complicated bronchitis in the year should receive the MV130 vaccine.	WEAK
4. Patients with more than 2 episodes of moderate to severe pneumonia in the year require the application of MV130.	STRONG
5. Patients with more than 1-2 moderate exacerbations of COPD should receive the MV130 vaccine	STRONG
6. Patients with more than 1 severe exacerbation of COPD per year should receive the MV130 vaccine.	STRONG
7. Patients with immunosuppressant use and recurrent respiratory infections are candidates for the MV130 vaccine.	STRONG
8. Patients with rheumatologic diseases and recurrent respiratory infections are candidates for the MV130 vaccine.	STRONG
9. Patients with hematologic diseases and recurrent respiratory infections are candidates for the MV130 vaccine.	STRONG
10. All patients using the MV130 vaccine should have laboratory tests such as complete blood count, albumin, C-reactive protein, and procalcitonin taken during treatment	WEAK
11. All patients using the MV130 vaccine should have laboratory tests such as CD4/CD3 subpopulation taken to ensure systemic and immune effects.	WEAK
12. Patients with comorbidities, over 60 years of age, are candidates for the prophylactic use of the MV130 vaccine.	WEAK
13. The use of the MV130 vaccine should be for a minimum of 3 months.	STRONG
14. The MV130 vaccine is considered a preventive treatment in patients with risk factors for recurrent respiratory infections. (after the first cycle)	WEAK
15. The use of the MV130 vaccine should be included in the preventive treatment of recurrent respiratory infections in national and clinical practice guidelines.	WEAK
16. The use of MV130 is considered in the pediatric population that attends daycare centers	STRONG
17. The use of the MV130 vaccine is considered in the pediatric population with recurrent wheezing associated with infections.	STRONG
18. The use of MV130 is considered in patients with asthma and exacerbations associated with viral infections.	STRONG
19. The use of MV130 vaccine is considered in patients with post-viral status.	WEAK
20. The use of MV130 vaccine can be started in patients with prolonged steroid use.	WEAK
21. The use of MV130 is considered in the pediatric population (from 5 months) with recurrent respiratory infections.	STRONG

Discussion

There is an urgent need in our environment for new vaccines or vaccine preparations for our large population of patients susceptible to recurrent respiratory infections, which are one of the main consultations in our country, the development of these has been hampered. In this regard, MV130 is a sublingual polybacterial TIbV that has been shown to be effective in reducing recurrent respiratory infections in particularly vulnerable subjects. For example, it has been beneficial for patients with primary or secondary immunodeficiencies and especially useful for children prone to bronchiolitis [10,11]. The ability of MV130 is useful in preventing the most common recurrent respiratory infections in a wide demographic spectrum of patients and has allowed the reduction in antibiotic consumption in a real-world setting. The results in the studies with MV130 vaccine indicate that prophylaxis with MV130 effectively reduced the frequency of most respiratory infections in all age groups. Both children and adults, particularly those suffering from urinary tract infections and respiratory infections such as pharyngitis and pharyngotonsillitis, observed an approximately 80% reduction in infection rates. By inducing trained immunity, MV130 provides broad protection against different pathogens, including viruses [12,13].

Conclusion

The presence of recurrent respiratory infections is a reality in our country as a public health problem. It is one of the principal causes of respiratory medicine consultation and the development of persistent symptoms that lead to a deterioration in the quality of life of patients. The existence of the MV130 vaccine under the development of medicine based on trained immunity allows us another alternative in the treatment of recurrent diseases.

This consensus is a result of a group of specialist doctors and experts who make recommendations for use and application in clinical practice [14,15].

References

1. Dagenais A, Villalba-Guerrero C, Olivier M (2023) Trained immunity: A "new" weapon in the fight against infectious diseases. Front. Immunol 14: 1147476.
2. Brandi P, Conejero L, Cueto FJ, Martínez-Cano S, Dunphy G, et al. (2022) Trained immunity induction by the inactivated mucosal vaccine MV130 protects against experimental viral respiratory infections. Cell Rep 38: 110184.
3. Subiza JL, Palomares O, Quinti I, Sanchez-Ramon S (2021) Editorial: Trained Immunity-Based Vaccines. Front Immunol 12: 716296.
4. Netea MG, Domínguez-Andrés J, Barreiro LB, Chavakis T, Divangahi M, et al. (2020) Defining trained immunity and its role in health and disease. Nat Rev Immunol 20: 375-388.
5. Giamarellos-Bourboulis EJ, Tsilika M, Moorlag S, Antonakos N, Kotsaki A, et al. (2020) Activate: Randomized Clinical Trial of BCG Vaccination against Infection in the Elderly. Cell 183: 315-323.
6. Ochoa-Grullón J, Benavente Cuesta C, Fernández González A, Cordero Torres G, Pérez López C, et al. (2021) Trained Immunity-Based Vaccine in B Cell Hematological Malignancies with Recurrent Infections: A New Therapeutic Approach. Front Immunol 11: 611566.
7. Sánchez-Ramón S, Conejero L, Netea MG, Sancho D, Palomares Ó, et al. (2018) Trained Immunity-Based Vaccines: A New Paradigm for the Development of Broad-Spectrum Anti-Infectious Formulations. Front Immunol 9: 2936.
8. Cirauqui C, Benito-Villalvilla C, Sánchez-Ramón S, Sirvent S, Diez-Rivero CM, et al. (2018) Human dendritic cells activated with MV130 induce Th1, Th17 and IL-10 responses via RIPK2 and MyD88 signalling pathways. Eur J Immunol 48: 180-193.
9. Alecsandru D, Valor L, Sánchez-Ramón S, Gil J, Carbone J, et al. (2011) Sublingual therapeutic immunization with a polyvalent bacterial preparation in patients with recurrent respiratory infections: immunomodulatory effect on antigen-specific memory CD4+ T cells and impact on clinical outcome. Clin Exp Immunol 164: 100-107.
10. Hutubessy R, Lauer JA, Giersing B, Sim SY, Jit M, et al. (2023) The Full Value of Vaccine Assessments (FVVA): A framework for assessing and communicating the value of vaccines for investment and introduction decision-making. BMC Med 21: 229.
11. Guevara-Hoyer K, Saz-Leal P, Diez-Rivero CM, Ochoa-Grullon J, Fernandez-Arquero M, et al. (2020) Trained Immunity Based-Vaccines as a Prophylactic Strategy in Common Variable Immunodeficiency. A Proof of Concept Study. Biomedicines 8: 203.
12. Del Fresno C, Garcia-Arriaza J, Martinez-Cano S, Heras-Murillo I, Jarit-Cabanillas A, et al. (2021) The Bacterial Mucosal Immunotherapy MV130 Protects Against SARS-CoV-2 Infection and Improves COVID-19 Vaccines Immunogenicity. Front Immunol 12: 748103.
13. Brandi, P, Conejero L, Cueto FJ, Martinez-Cano S, Dunphy G, et al. (2022) Trained immunity induction by the inactivated mucosal vaccine MV130 protects against experimental viral respiratory infections. Cell Rep 38: 110184.
14. Ochando, J, Mulder WJM, Madsen JC, Netea MG, Duivenvoorden R (2023) Trained immunity — basic concepts and contributions to immunopathology. Nat Rev Nephrol 19: 23-37.
15. Pérez-Sancristóbal I, de la Fuente E, Álvarez-Hernández MP, Guevara-Hoyer K, Morado C, et al. (2023) Long-Term Benefit of Perlingual Polybacterial Vaccines in Patients with Systemic Autoimmune Diseases and Active Immunosuppression. Biomedicines 11: 1168.