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EDITORIAL

Mucosal vaccines: promising strategy, constant challenges

Vacunas mucosas: estrategia prometedora, desafíos constantes

Vacinas de mucosa: estratégia promissora, desafios constantes

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The current pandemic of the new coronavirus has exposed the enormous need for health professionals to understand, more up-to-date and in depth, the fundamental concepts and technological trends in the field of vaccination. The simple classification of vaccines for human use according to the ability to replicate the basic antigenic principle, into "live" and "non-live", is no longer sufficient. Currently, it is necessary to know the technological production platform, which is directly correlated with the mechanism of action of each vaccine. We then added, in our practice, terms such as messenger RNA vaccine, recombinant proteins, subunits, among others. It is also important to recognize whether the presentation of the antigenic principle is given parenterally or by transport through the mucosa. Most vaccines are administered parenterally (intramuscularly and subcutaneously), but orally administered vaccines are still widely used, which use the gastrointestinal mucosa to generate an immune response[1,2].

It is intuitive to imagine that vaccines against pathogens that have the digestive mucosa as a gateway can be administered by the same route, and thus generate a localized response. However, when dealing with infections whose first barrier against the pathogen is the respiratory mucosa, we still have few practical examples. The greatest expertise comes from a vaccine administered via nasal spray against influenza, composed of an attenuated virus, which was never licensed for use in Brazil, but was widely used in some European countries and in the United States. There are also some respiratory administration vaccines against COVID-19 in the final stages of development, including some already approved for use in countries such as China (CanSino Biologics®, inhaled) and India (Bharat Biotech®, nasal drops), which may represent an important advance in the fight against the disease. Although vaccines currently in use have already demonstrated undeniable effectiveness in preventing serious conditions and deaths from COVID-19, these new vaccines applied in the airways promise to play a promising role in preventing infection by SARS-CoV-2 and, consequently, of its inter-human transmission, a concept currently defined as sterilizing immunity[3,4].

It should be noted that the mucosal immune response is complex and different from what occurs internally in the circulation. It is known that the antibodies produced in each of these compartments do not reach the other easily. So far, the results of research with mucosal vaccines against COVID-19 suggest the induction of robust immunogenicity with doses smaller than those standardized for intramuscular administration, in addition to the production of more generic IgA antibodies, acting on all or almost all of the variants of the virus, which can be an advantage at this time of the epidemic. The use of the

nasal or inhalation routes still have the appeal of dispensing with the use of syringes and needles, which represents not only a matter of comfort and safety, but also of environmental responsibility[4].

The main limitation of these vaccines is precisely the need to overcome the natural defenses of the mucosa without the use of physical instruments and to attract an effective immune response. For this purpose, specific vehicles have been developed or adapted, such as viral vectors, virus-like particles (VLPs), pattern recognition receptor (PRR) agonists, cytokines, among others, which, when added to specific adjuvants, can result in an effective vaccine. That is, it is not enough to simply use the same product for intramuscular use directly in the nose. At least not at first[5].

There are still challenges arising from the historical moment itself, such as the difficulty of finding volunteers never exposed to infection or vaccination to serve as a comparison group, and knowledge gaps such as, for example, which biomarkers could be used as correlates of protection induced by immunity of mucosa. It is unclear at this time whether mucosal vaccines will do better if used as boosters or as a primary immunizer. And it is still not known what logistics would be necessary to distribute and administer these immunizers en masse, nor their real cost. The solution to all these challenges can only be obtained through comprehensive research[3].

During this recent pandemic, subjects such as scientific studies, phases of clinical trials and voluntary participation in research received great attention, not always with an understanding of their real concepts, both among health professionals and the general population. In Brazil, despite the debate in society not always being treated with due seriousness, a large part of the population showed empathy in participating in clinical trials with vaccines. This positive movement was reinforced by the demonstration, by the regulatory sector, of seriousness and rigor in complying with good practices widely used in entities with the same responsibility in influential countries on the global stage. Furthermore, it is likely that the population has persisted in trusting the National Immunization Program (PNI), which has historically been a recognized model for other countries, due to its effective maintenance of criteria of equity, universality, capillarity, quality of processes and quantity of products offered. The PNI mascot used in the media for decades is the famous “Zé Gotinha”, the figure of a drop that has as reference the oral vaccine such as poliomyelitis, a mucosal vaccine, which makes the strategy not, in a way, such an eccentric idea. We do not know, however, how the Brazilian population will be receptive to the first research results and eventual subsequent incorporation of nasal or inhaled vaccines in the program.

In this new and important stage of solving questions about the promising strategy of mucosal vaccines, it is possible that the entire discussion on research and regulation of immunizing products will regain relevance, adding to the functions of health professionals the need to obtain and replicate knowledge about the theme, transforming not always intelligible data into information accessible to all citizens.

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