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EDITORIAL

Varicella complications and universal immunization☆,☆☆

Complicações e imunização universal contra a varicela

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Varicella is one of the most common infectious diseases, with a worldwide distribution. According to a WHO position paper, the global annual disease burden of varicella is estimated to be 140 million cases.[1] Despite the public perception of varicella infection as a harmless childhood affliction, it can be a very serious disease. As Martino Mota & Carvalho-Costa highlight in ''Varicella zoster virus related deaths and hospitalizations in Brazil before the introduction of universal vaccination with the tetraviral vaccine,'' varicella can cause death or can lead to potentially serious complications, which require hospitalization and eventually long-term sequelae.[2]

Varicella-related hospitalization rates differ widely worldwide. Varicella may potentially afflict any organ; hematological, neurological, respiratory, cutaneous, hepatic, gastrointestinal, urinary, and bone complications are the most frequently reported.[3]

The incidence of varicella complications differs among scientific reports. For example, the pooled prevalence of neurological complications resulting from a systematic review of the literature identifies the likelihood of pediatric neurological complications in the range of 13.9–20.4%.[4] Nevertheless, in some reports the rate of varicella neurological complications is lower than the incidence reported in the literature, while other complications, such as skin infections, are the most frequently detected.[5,6] In other reports, the rate of both neurological and cutaneous complications is low, while other complications are frequently detected, such as respiratory ones.[7] This finding may be related to differences in the sociodemographic structure of the population or to a broader availability of outpatient skin-infection treatments or to different hospitalization policies.

Patients with a history of underlying malignancy, steroid use or immunosuppressive therapy, HIV infection, or solid organ transplantation are susceptible to disseminated varicella due to impaired cellular immunity. Immunosuppressed hosts who develop varicella experience severe morbidity and higher mortality rates more frequently than normal hosts. For example, patients with rheumatologic or gastroenterological diseases treated with tumor necrosis factor (TNF) antagonists remain at selectively increased risk for more severe primary varicella infections compared with the general population.[8,9]

In the report by Martino Mota & Carvalho-Costa, the majority of deaths and of varicella-associated complications occurred in children aged 1–4 years. Similarly, in the literature, the highest frequency of varicella complications occurs in those younger than 5 years.[3,6,10]

Varicella may also be very serious in the elderly, as it may be fatal or lead to prolonged hospitalization.[8] Pregnant women are a particular concern. If a woman develops varicella at an early gestational age, the child may experience congenital varicella syndrome; if she gets ill at the end of

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pregnancy, the neonate may present varicella. Both conditions are very serious for the newborn.[11]

Vaccination may prevent varicella infection and its complications. A varicella vaccine, based on the attenuated live varicella zoster virus Oka strain, was developed in Japan in the mid-1970s. Since then, different formulations of varicella vaccines had been proposed. All of them contain live attenuated varicella zoster virus, and all, except the vaccine licensed in South Korea, are based on the Oka strain isolated in Japan. Currently, varicella vaccines are licensed as a monovalent or as a combination measles, mumps, rubella, varicella vaccine (MMRV). MMRV vaccines are currently used on the basis of a comparable immunogenicity and overall safety profile compared with simultaneous administration of MMR and varicella vaccines.[12] Moreover, as it requires a single injection, MMRV vaccine is expected to offer several benefits: facilitation of universal immunization against these four diseases, increased compliance with immunization, and reduced healthcare costs.

In a study focusing on post-licensure varicella vaccine effectiveness among healthy children, the authors analyzed systematic reviews and meta-analyses of the MEDLINE, Embase, Cochrane Library, and CINAHL databases for reports published during 1995–2014. They concluded that one dose of varicella vaccine was moderately effective in preventing varicella diseases (81%) and highly effective in preventing moderate and severe manifestations of varicella (98%). The authors concluded that a second dose adds increased protection against varicella (92%).[13]

Nevertheless, vaccination policies differ from country to country. In some, such as the United States and Australia, universal immunization was introduced many years ago. Such mass vaccination progressively led to a substantial decrease in disease burden.[14]

With regard to Europe, there is no consensus on varicella immunization policy. Consequently, some countries, such as Germany and Greece, have national childhood immunization programs. Others adopt heterogeneous or no official recommendations.[15] In Italy, since its commercialization, some regions have offered universal vaccination in childhood, with a consequently reduced incidence of the disease.[16]

In other regions, varicella vaccine coverage strongly depends on the acceptance of the vaccination by parents and on pediatricians' recommendations. Pediatricians may underestimate both the potential risk of the disease and the economic burden for the community. Parents may consider the potential profit for the community as less important than the individual risk to their child from potential unintentional side effects of vaccination. Vaccine-declining parents believe that the vaccine is unsafe and ineffective, as well as that the disease it is given to prevent is mild and harmless. Moreover, in some cases, parents mistrust health professionals, the government, and officially-endorsed vaccine research but trust media and non-official information sources, which discourage immunization policies. In most cases, families must pay the cost of vaccination if they wish their children to be immunized. Hence, high coverage levels may be difficult to achieve.

Decisions on vaccine funding are based on many considerations, including the likely cost-effectiveness of different immunization strategies. In European countries that have implemented vaccination on a national level, mass immunization has resulted in both decreased disease incidence and reduced hospitalization rates. Moreover, data have also revealed benefits for unvaccinated groups, such as infants younger than one year.[17] In fact, a high immunization rate contributes in preventing the spread of varicella infection, a concept known as herd immunity. Herd immunity provides protection to those who are at highest risk for severe varicella infection, including pregnant women, infants, persons with human immunodeficiency virus and other immunodeficiency disorders, those receiving chemotherapy, and patients treated with high-dose corticosteroids. This is a very important goal, as many hospital admissions occur in infants too young to be vaccinated.[3] Therefore, as rates of vaccine refusal increase, herd immunity wanes, and certain vulnerable populations will be at higher risk for severe varicella infection.

Further, an economic analysis of a universal vaccination program indicates that it would likely be cost-saving due to reduction in both medical costs and in loss of parents' work time.[18] Finally, countries should also consider vaccination of seronegative health-care workers, especially in settings where the risk of severe varicella is high (*i.e.*, immunocompromised patients, premature infants, *etc.*).

Conflicts of interest

The authors declare no conflicts of interest.

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